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Abstract Book

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Invited Symposia Abstracts

Thursday September 7, 2023

Science of Learning Symposia

The Typical and Atypical Reading Brain: How a Neurobiological Framework of Early Language and Reading Development Can Inform Educational Practice and Policy

Nadine Gaab, *Harvard University*

Learning trajectories are shaped by the dynamic interplay between nature and nurture, starting in utero. Learning differences are often not identified until childhood, but diverging trajectories of brain development may be present as early as prenatally. Furthermore, children's experiences and their interactions with their environment have long-lasting influences on brain development. This talk will primarily focus on learning differences in language and reading acquisition and will present results from our longitudinal behavioral and neuroimaging studies that characterize differences in learning to read as a complex outcome of cumulative risk and protective factors interacting within and across genetic, neurobiological, cognitive, and environmental levels. Results are discussed within an early multifactorial framework of learning differences, emphasizing preventive strategies. Implications of these findings for contemporary challenges in educational and clinical practice and policy are discussed.

Leveraging Educational Neuroscience to Optimize Active Gameplay Contexts that Promote Executive Function Skills and Brain Plasticity

Cassondra Eng, *Stanford School of Medicine*

With the exponential growth of technology and digital learning required in K-12 core curriculum standards and in higher education, digital game play and its impact on development has become of much interest. As video game use and virtual reality (VR) applications grow at an exponential rate and sedentary behavior and reports of cognitive impairments increase, evidence-based practices of game play grounded in learning sciences and developmental psychology theories that promote both cognitive and physical activity are needed. This study employs a multimethodological approach and examines how we can incorporate immersive technology into exercise activities to be the most impactful on physical and cognitive health, and whether effects generalize to exercise enjoyment and EF skills particularly for students who may struggle with the sustained attention, organization, distraction resistance, and daily functioning crucial for students' well-being.

The domain-specificity of domain-generality: Attention, executive function, and mathematical skills

Eric Wilkey, *Vanderbilt University*

Attention and executive functions (EFs) are crucial for academic skill development. However, we lack clear understanding of the neurobiological mechanisms that integrate the higher-order cognitive processes of EF with lower-level cognition. While the role of attention and EF in learning is recognized, the focus on their domain-generality may hinder exploration of their domain-specific roots. Using the example of number processing, I detail a series of neuroimaging studies exploring how domain-specific mechanisms interact with domain-general processing. They emphasize the need to understand the hierarchical nature of higher-order control and lower-level processing for a comprehensive explanation of the relationship between attention, EF, and, academic skills.

The Role of Environmental Chemicals and Social Stressors in the Etiology of Learning Difficulties
Amy Margolis, *Columbia University*

Children living in economic disadvantage experience disproportionately high rates of reading problems and exposure to chemical and social neurotoxicants. We hypothesize that these environmental factors contribute to reading problems, widening the achievement gap for disadvantaged youth. We have shown that air pollution and stress exposure are associated with reduced hippocampal volume and lowered word reading in disadvantaged youth. Now, we show hippocampal volume positively associates with reading (p=.04;N=201), and this association is partially mediated by working memory (p=.04). Findings suggest that environmental exposures alter domain general circuits, rather than left-lateralized cortical reading circuits, leading to reading problems in disadvantaged youth.

Friday September 8, 2023

Local Symposium: Vulnerability and resilience in brain development

Trial-level dynamics of event-related potentials reveal unique patterns of risk for externalizing and substance misuse
Keanan Joyner, *University of California, Berkeley*

Stress phenotypes and risk for psychopathology
Camelia Hostinar, *University of California, Davis*

Childhood adversity is a leading transdiagnostic risk factor for psychopathology. However, major unresolved theoretical challenges stem from the nonspecific and probabilistic nature of the links between childhood adversity and psychopathology. Focusing on stress phenotypes -biobehavioral patterns activated in response to stressors that can disrupt future functioning when persistent- would help delineate pathways from childhood adversity to psychopathology with greater specificity and certainty. Supporting this notion, accumulating evidence suggests that psychopathology appears to be more strongly predicted by behavior and biology during states of stress. Studying stress phenotypes would advance our conceptualization of mediating pathways from childhood adversity to psychopathology.

Risk, resilience, and adaptation among children in poverty in the ABCD sample: The role of brain network associations
Monica Ellwood-Lowe, *University of California, Berkeley*

On average, children living in poverty perform worse than their peers in school, but this misses massive variability: some perform quite well. Have these children mastered ways of thinking similar to children above poverty? We review evidence to the contrary. In the ABCD study, higher connectivity between lateral frontoparietal network (LFPN) and default mode network (DMN) is maladaptive for children above poverty, but adaptive for children below poverty. This is true for both lab-based and real-world measures (e.g., grades in school) and holds longitudinally through early adolescence. We discuss implications for long-term mental health risk and supporting children in poverty.

Neurocognitive risk and chronic disease: The case of childhood asthma
Nicholas Christopher-Hayes, *University of California, Davis*

Asthma is a common pediatric disease characterized by systemic inflammation and respiratory symptoms. Non-human animal models of asthma have provided evidence of neuronal injury and cognitive impairments, but little research has assessed neurocognitive functioning in childhood, the period in which the disease typically onsets. By leveraging data from the Adolescent Brain and Cognitive Development (ABCD) Study, we report cross-sectional and longitudinal findings revealing that children with asthma exhibit reduced performance on measures of memory abilities, attention, and processing speed as compared to a matched comparison group of healthy children. This study provides initial evidence that asthma in childhood may result in altered trajectories of neurocognitive development.

Oral Session 5: Thinking outside the box: Alternative methods in developmental cognitive neuroscience

What Can Precision Functional Mapping Tell Us About the Developing Brain?
Damion Demeter, *University of California San Diego*

Developmental cognitive neuroscience studies typically rely on group average data to study brain development. While group averaging is necessary for statistical reliability with shorter scan times, individual reliability suffers. Precision Functional Mapping (PFM) takes the approach of densely sampling individuals - hours of fMRI data over repeated scans - to measure individual functional network connectivity with high reliability. With PFM, we accurately identify individual children's functional network organization, quantify network integration, and highlight individual variations in network connectivity. PFM is a promising method for understanding an individual's neural and cognitive developmental trajectories, which are often obscured or underrepresented in group average data.

Imaging the developing brain with functional Near Infrared Spectroscopy (fNIRS)
Anna Blasi Ribera, *University College London*

Over the last three decades functional Near Infrared Spectroscopy (fNIRS) has helped shape neurocognitive developmental research by facilitating the expansion of our understanding of the neural underpinnings of sensory perception, language acquisition and socio-cognitive skills, and by providing avenues of exploration for markers of compromised brain development and risk metrics. Recent instrumentation advances have enabled its expansion into the global health field to investigate the effects of socio-economic and environmental adversities on brain development. I will briefly discuss the technology and present some of the work from the collaborative effort of physicists from UCL and neuroscientists at Birkbeck, KCL and Cambridge.

Ultra high field MR Spectroscopy and EEG evidence of frontal neuroplasticity in adolescence
Finnegan Calabro, *University of Pittsburgh*

Animal models and human post-mortem studies show refinements of excitatory and inhibitory (E/I) neurotransmitter systems in PFC through adolescence indicative of critical period plasticity, but in vivo evidence is limited. We will present results from ultra high field (7 Tesla) spectroscopic imaging, providing direct quantification of excitatory (Glutamatergic) and inhibitory (GABAergic) neurotransmitter pools, demonstrating increased prefrontal E/I balance through adolescence. We identify functional consequences of this change reflected in periodic and aperiodic sources of neural activation derived

from EEG recordings. Together, these support a model of adolescent critical period plasticity which reshapes prefrontal neural processing to support cognitive maturation.

Charting neurodevelopment along the sensorimotor-association cortical axis with mechanistically-informed human neuroimaging
Valerie Sydnor, *University of Pennsylvania*

How do changes in neurodevelopmental plasticity progress across the cortex during childhood and adolescence? This talk will illustrate how we can translate mechanistic insights from animal studies of cortical plasticity to non-invasive neuroimaging in order to study developmental plasticity in the human brain. The research presented provides evidence that age-dependent changes in functional (intrinsic activity amplitude) and structural (myelin) indexes of plasticity are patterned across a sensorimotor-association cortical axis from ages 8 to 18. The talk will conclude by considering how the unfolding of plasticity mechanisms along this cortical axis influences the effects of youths' environments on the maturing brain.

Oral Session 7: Novel insights from lifespan development

A general approach for defining longitudinal models to test meaningful developmental hypotheses
Ethan McCormick, *Leiden University*

Standard polynomials (e.g., quadratic, cubic) are ubiquitous as models of change; however, substantive developmental questions, like "where is the peak?" or "what is the timing and tempo of change?" are not directly captured by parameters of these models. We can instead define equivalent nonlinear models which do include interesting developmental features as parameters, but these nonlinear models are plagued by estimation challenges. Here I outline a general approach to defining novel models of interest while bypassing many of these estimation issues and demonstrate how they apply in developmental models ranging from cross-sectional polynomials to complex random effect growth models.

Mechanisms of plasticity over development
Laurel Gabard-Durham, *Northeastern University*

Inferences with cross-sectional and longitudinal data
Yee Lee Shing, *Goethe University Frankfurt*

Developmental trends inferred from cross-sectional comparisons are not always supported – and rather are often contradicted – by data from longitudinal studies. In our work using the same dataset consisting of participants aged 6–10 years, we found that cross-sectional age associations and longitudinal developmental trends in hippocampal subfield volumes as well as brain-cognition cognitions were discrepant (Keresztes et al., 2022). In this talk, I will present several empirical examples, both from child development and aging, that showed different results from cross-sectional and longitudinal analyses conducted on the same neuroimaging dataset, ruling out obvious methodological differences. This poses questions about the validity of cross-sectional estimates of change. Potential reasons for discrepancy in results will be discussed, including nonlinearity in change, sampling time window, and difference in sources of within- and between-person variance. Limitations of cross-sectional estimates of change as well as considerations on longitudinal study design for studying multivariate brain-behavioral relationships will be discussed.

Lifespan Views on Change
Ulman Lindenberger, *Max Planck Institute for Human Development*

In this talk, I will formally and empirically demonstrate some of the limitations and potential uses of cross-sectional research designs for understanding multivariate developmental change. I will start with a formal critique of statistical mediation analysis performed on cross-sectional data. I will then empirically compare cross-sectional and longitudinal age trends in cortical thickness assessed in the ABCD data set. Across brain regions, the rank order of cross-sectional mean age differences is only weakly related to the rank order of longitudinal mean age changes; hence, cross-sectional age trends cannot serve as a surrogate for longitudinal changes. On the positive side, I will demonstrate that local structural equation modeling can be applied to multivariate age-continuous cross-sectional data to indirectly infer the covariance structure of longitudinal changes. I will end with a few examples illustrating the gains in knowledge that can be achieved by linking individual differences early in life to those later in life.

Saturday September 9, 2023

Peder Sather Foundation Symposium: Early adolescence as a window of opportunity for behavioral and emotional health

Influence of puberty on affective salience network function and risk of affective disorders in girls
Cecile Ladouceur, *University of Pittsburgh*

Sleep, memory, and anxiety in early adolescence: Opportunities to improve trajectories of mental health
Dana McMakin, *Florida International University*

Growing evidence suggests that early adolescence is a sensitive period for the impact of sleep disruption on anxiety and depression. This talk presents a clinical developmental neuroscience framework for how sleep affects emotional health in early-mid-adolescence. Data from several studies focused on youth at the cusp of puberty (ages 10-13) with a range of anxious and depressive symptoms will be presented in order to 1) characterize sleep behavior and neurophysiology using a multi-modal approach, 2) examine the effects of sleep on emotion and memory (at neural and behavioral levels), and 3) identify opportunities to translate these findings into developmentally-informed interventions.

Social learning in social (media) networks
Wouter van den Bos, *University of Amsterdam*

Adolescence is a time of social re-orientation in which peers become important sources of information and support. Social information is very useful to navigate the uncertain and novel environments faced by adolescents. Yet not all information is equally valuable, so it is an important skill to weigh information according. Here I will present a computational framework and several empirical studies on how adolescents learn how to adaptively use and select social information stemming from different sources in their social networks. Our data reinforces the importance of friends, but also reveals that adolescents also adaptively select other sources.

Pubertal maturation, brain development, and risk for depression in early adolescence
Niamh MacSweeney, *University of Edinburgh*

Puberty is widely recognised as the catalyst for the substantial biological, psychological, and social change that characterise adolescence, the peak time for the emergence of depressive disorders across the lifespan. Using longitudinal data from the Adolescent Brain Cognitive Development (ABCD) Study, we present our recent work investigating how pubertal maturation relates to features of brain morphometry and depression risk in early adolescence. We then discuss the role of sex-differences in understanding the adolescent-specific vulnerability to depression in the context of pubertal maturation and brain development, before highlighting directions for future research as we enter an era of “Big Longitudinal Data”.

Symposium Proposal

Title of session.

Applications and challenges in using computational models to predict brain development and psychopathology in youth

Organizer(s).

Name	Affiliation	Email
Sarah Whittle (Chair)	Professor, The University of Melbourne	swhittle@unimelb.edu.au
Niousha Dehestani	PhD candidature, Deakin University	ndehestanikolag@deakin.edu.au

Symposia Description.

Understanding risk factors for youth psychopathology is challenging and has been the focus of extensive research in the fields of developmental psychology and psychiatry. While some progress has been made, there is still much we do not know about the multiple factors contributing to the development of mental disorders. One reason progress has been slow is that research often does not account for the fact that psychopathology is influenced by many different factors, including genetics, environment, and individual differences in psychological factors. Additionally, the complexity of human behavior and the diversity of human experiences make it difficult to pinpoint specific risk factors that apply to everyone. Emerging research, however, has made important strides in identifying some of the factors that contribute to psychopathology. Continued research and collaboration across different disciplines will be key to making further progress in this area.

In recent years, researchers have used various algorithmic and mathematical approaches to model and predict current or future risk of psychopathology, and treatment efficacy at the level of individuals. Although predictive modeling is a promising avenue in the context of psychopathology, there are various challenges in model design that can affect robustness, reliability, and

generalizability of the predictive model. These challenges require careful attention. Design of reliable, generalizable, and robust computational models to predict psychopathology at an individual level is of tremendous value.

One aim of the symposium is to investigate different environmental and biological risk factors for psychopathology and gather experts to present an overview of various challenges and discuss best practice for predictive models of psychopathology. The specific aims are to, first, present different novel predictive models in terms of their algorithmic basis, input features, as well as their application in predicting aspects of mental health problems. Second, we aim to present the challenges with creating robust computational models that produce reliable predictive markers for psychopathology. This symposium targets the interdisciplinary fields of 1) computer science/machine learning, 2) neuroimaging, and 3) developmental psychiatry and clinical psychology. Therefore, this symposium will be of interest to a wide audience. Our presenters are diverse in terms of career stage (i.e., graduate students, postdoctoral scholars, faculty), geography (United States, Europe, Iran, and Australia), and gender.

Speakers Section.

This symposium will be moderated by Sarah Whittle as a chair of the symposium.This symposium proposes novel risk markers to predict mental health problems using computational models such as machine learning. Our first speaker will discuss environmental risk factors including early life stress (ELS) and parental control that predict internalizing problems and white matter development across adolescence. Our second speaker will examine multi-level factors including child demographic, environmental, and structural and resting-state fMRI variables, parental depression history and demographic characteristics to predict depressive symptoms in youth. The third speaker will propose a puberty age model as a biomarker for pubertal timing to predict brain age and mental health problems. The last speaker will discuss the genetic basis of brain age (based on a novel, generalizable and reliable method that utilizes raw brain images) and will discuss links with psychopathology. In summary, this symposium covers multiple risk markers that are related to different aspects of development and mental health in youth, which may be used in clinical platforms in the future.

Speaker 1.

Name: Jessica Buthmann
Email: buthmann@stanford.edu
Affiliation: Postdoctoral, Stanford University, Department of Psychology

Longitudinal clustering of brain structure and clinical symptomatology in adolescence is predicted by sex, stress exposure, and parenting environment

Early life stress (ELS) can influence trajectories of emotional and neural development in young people in ways that increase their risk for developing internalizing symptoms. Unfortunately, however, few longitudinal studies have elucidated how ELS affects trajectories of internalizing symptoms and concurrent white matter development across adolescence. Moreover, it is likely that factors such as supportive caregiving buffer the adverse effects of ELS on the development of internalizing symptoms. We conducted interviews with youth (ages 9.11-13.81 years; 56% female) at baseline (T1) assessing their exposure to early life stressors and measured perceived parental psychological control. At T1 and at two additional assessments (T2, T3) conducted approximately two years apart, participants also completed measures of anxiety and depression symptoms and diffusion MRI scans, from which we obtained white matter metrics of uncinate fasciculus microstructure. 116 participants had complete data from at least two timepoints. Symptoms of anxiety and depression and uncinate fasciculus fractional anisotropy (FA) were submitted to a k-means longitudinal clustering analysis, a data-driven approach used to identify clusters of participants with distinct longitudinal trajectories. This analysis yielded two clusters of participants: one characterized by higher symptoms and lower uncinate FA, and the other characterized by lower symptoms and higher uncinate FA. We then used logistic regression to predict cluster membership from sex, severity of exposure to ELS characterized by threatening experiences, and parental control. Being female (OR=9.55), having greater ELS exposure (OR=6.75), and experiencing higher parental control (OR=1.29) significantly predicted membership in the high-symptom, low-FA cluster. There was also a significant interaction of ELS and parental control, such that higher levels of ELS exposure were associated with increased likelihood of belonging to the high-symptom cluster at low, but not at higher levels of parental control. Although parental psychological control may be maladaptive in the absence of stressful experiences, in the context of an

unpredictable or threatening environment it may provide structure/support that reduces adolescents' risk for psychopathology.

Speaker 2.

Name: Tiffany C. Ho,
Email: tiffany.ho@psych.ucla.edu
Affiliation: Assistant Professor, Department of Psychology, University of California, Los Angeles, Los Angeles, CA

Demographic, Clinical, Environmental, and Neural Predictors of Depression Symptoms in the ABCD Study

Identifying risk factors for adolescent depression is critical for early prevention and intervention; however, most studies in this area have sought to understand the role of isolated factors. In the present study, we sought to examine multi-level factors that maximize the prediction of depression symptoms in U.S. children participating in the Adolescent Brain and Cognitive Development (ABCD) study. 7,995 participants from ABCD (version 3.0 release) provided complete data at baseline and one-year follow-up data. Depression symptoms were measured with the Child Behavior Checklist. Predictive features included child demographic, environmental, and structural and resting-state fMRI variables, parental depression history and demographic characteristics. We used linear (elastic net regression, EN) and non-linear (gradient boosted trees, GBT) predictive models to identify which set of features maximized prediction of depression symptoms at baseline and, separately, at one-year follow-up. We found that both linear and non-linear models achieved comparable results for predicting baseline (EN: MAE=3.757; R^2=0.156; GBT: MAE=3.761; R^2=0.147) and one-year follow-up (EN: MAE=4.255; R^2=0.103; GBT: MAE=4.262; R^2=0.089) depression. Parental history of depression, greater family conflict, and shorter child sleep duration were among the top predictors of concurrent and future child depression symptoms across both models. Although resting-state fMRI features were relatively weaker predictors, functional connectivity of the caudate was the strongest neural feature associated with depression symptoms at both timepoints. Consistent with prior research, parental mental health, family environment, and child sleep quality are important risk factors for youth depression. Functional connectivity of the caudate is a relatively weaker predictor of depression symptoms but may represent a biomarker for depression risk.

Speaker 3.

Name: Niousha Dehestani
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Affiliation: PhD Candidature, Deakin University

Developmental brain changes during puberty and associations with mental health problems; Puberty age and Brain age

‘Brain age’ has gained recent attention as a method to examine individual differences in global brain maturity in youth. Additionally, puberty is a predominant mechanism during adolescence that coincides with behavioral changes, onset of mental health problems, and numerous biological changes. Puberty is linked to mental health problems during adolescence, and in particular, the timing of puberty is thought to be an important risk factor. Both pubertal timing and Brain AGE are considered markers of biological aging and may represent similar pathways to adolescent-onset mental health problems. Therefore, investigating the association between pubertal timing and Brain AGE may help us better understand the biological underpinnings of mental health problems. This study developed a new measure of pubertal timing using multiple pubertal features to model their nonlinear associations with age and investigate its association with mental health problems. Using the Adolescent Brain Cognitive Development (ABCD) cohort, we implemented three models of pubertal timing by predicting chronological age from i) observed physical development, ii) hormones and iii) a combination of the two, using a supervised machine learning method. We built models of “Brain AGE” and “Puberty AGE” as indices of brain and pubertal development. These predictive measures were used to index individual differences in brain development and pubertal timing with respect to population norms. We next investigated i) associations between pubertal timing and regional and global brain development, and ii) association between Puberty AGE and mental health problems. Mediation models were additionally used to investigate the indirect effect of pubertal timing on mental health problems via brain development. Puberty AGE performed better in capturing age variance compared to previously-used methods, and the physical measure accounted for more variance in mental health, such that earlier pubertal timing was associated with higher symptoms. Earlier puberty age gap that reflect pubertal timing was associated with accelerated

brain development, particularly of subcortical and frontal regions in females and subcortical regions in males. While earlier pubertal timing was associated with elevated mental health problems in both sexes, brain age did not predict mental health problems, and nor did it mediate associations between pubertal timing and mental health problems.

Speaker 4.

Name: Esten Høyland Leonardsen
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Over the last decade, apparent brain age estimated from neuroimaging data has emerged as an intuitive and reliable marker of general brain health. The brain age gap (BAG), encapsulating the difference between brain age and chronological age, has been linked to a multitude of neurological and mental disorders and mortality. We compiled raw structural magnetic resonance imaging data from multiple openly accessible sources into a large and diverse dataset (n=53542, across the lifespan) and trained convolutional neural networks to predict brain age, achieving state-of-the-art performance (MAE=3.9 in unseen data from unknown scanners). Using this model we corroborate earlier findings related to disorders and find that an increased BAG is associated with lifestyle factors such as smoking and alcohol intake. Next, we performed a genome-wide association study to investigate the genetic basis of brain age, finding eight independent genomic loci reaching genome-wide significance, of which seven are novel. These genetic variants implicate neurological, metabolic and immunological pathways, emphasizing the polygenic architecture of BAG and solidifying it as a complex biomarker encompassing a multitude of biological systems. Last, we performed Mendelian Randomization to investigate the causal relationship between BAG and disorders and found indications of a causal influence of Alzheimer's Disease and Bipolar Disorder on BAG. In total, our results further promote BAG as a clinical biomarker, both by improving its stability and precision, and furthering our understanding of its complex etiology.

Conflict of interst:

There is no conflict of interst.

Practical Lessons for MRI in Infants and Young Children

Symposium Chair

Rhodri Cusack, Trinity College Dublin

Any conflicts of interest: No

Symposium Speakers

Acquiring Connectome Data Longitudinally in Non-Sedated Sleeping Infants and Toddlers

Brittany Howell, Virginia Tech

The ability to delve into how the structural and functional connectomes unfold beginning early in life has only recently become a reality through the efforts of many research and clinical groups. I have collected hundreds of MRI sessions during non-sedated natural sleep in infants as young as 2 weeks old, and as old as 30 months old. Acquiring these data presents unique challenges, challenges that require integrating both hard (i.e., technical) and soft skills (i.e., human). In this presentation I will share practical knowledge that I and the others working towards understanding the developing connectome employ to acquire cutting edge MRI data, with the ultimate goal being to encourage others to join these efforts.

Any conflicts of interest: No

100 Babies: Insights from awake fMRI at 2-months

Áine Dineen, Trinity College Dublin

fMRI of awake infants has rich potential as a window into the early development of brain function. I will report on the experience of scanning the first one hundred 2-month-old babies in the longitudinal foundations of cognition (FOUNDCOG) project. Typically, 20 minutes of fMRI was obtained in each infant. 80% of infants then fall asleep, allowing the acquisition of structural and resting-state fMRI. I will describe how we kept infants engaged during the scan, summarise metrics of data quality, such as the type of motion and its amplitude distribution, and show results from this initial cohort.

Any conflicts of interest: No

How to read a baby's mind: A protocol for fMRI with awake, behaving infants

Cameron Ellis, Stanford University

Infant cognition is invisible to us, but fMRI with awake infants offers a unique opportunity to look inside their mind, eschewing the limitations of their developing behavioural repertoire. In this talk, I describe a protocol we have used to collect fMRI data from over 200 participants, ranging from 3 months to 3 years of age. On average, we acquire ~7 minutes of usable functional and anatomical data per session. I will additionally present findings validating the protocol and analysis procedure.

Any conflicts of interest: No

Clinical MRI without anaesthesia in children aged 4-10

Melanie Ganz-Benjaminsen, University of Copenhagen and Rigshospitalet

It is standard procedure in most Danish hospitals to employ general anaesthesia when small children are in need of medical imaging procedures that demand anaesthesia. Anaesthesia is used to prevent the child from leaving the scanner, to reduce motion artefacts and for dealing with children that are too anxious to enter the scanning environment. Movement during the image acquisition can cause serious distortions of the imaging data, which can invalidate its quality and potentially lead to an erroneous conclusion. Even though complications directly related to general anaesthesia are rare, there is an increasing concern about the potential neurotoxic effects of general anaesthesia. Additionally, there are logistic and financial challenges associated with the use of general anaesthesia.

The aim of our project is to utilise recent developments in medical imaging hardware technology in order to show that most young children can undergo medical imaging procedures without anaesthesia and that it is still possible to obtain a high-quality diagnostic scan. We want to test the clinical efficacy of a marker-less motion tracking device that can register the child’s movements while scanning which allows for motion correction of the acquired images. Our goal is to demonstrate the clinical utility of a novel approach of imaging including training, preparation and the use of the tracking device in children with cerebral palsy that undergo MRI scans for diagnostic purposes.

Any conflicts of interest: Funded by the Elsass foundation, Danish Childhood Cancer Foundation and the Novo Nordisk and Novozymes Talent Program. Carried out in cooperation with TracInnovation who provided motion tracking data for the paediatric population; and has ongoing collaboration in a prospective clinical study on the effectiveness of preparation and motion correction in paediatric patients (Danish national ethics protocol H-20055983). Melanie Ganz's husband is an employee at TracInnovations, Ballerup, Denmark.

Leaving the baby in the bathwater: understanding real-world attention development using naturalistic dual EEG recordings of caregiver-child interactions.

Sam Wass[1], Emily Phillips[1], Ira Marriott Haresign[1], Megan Whitehorn[1], Louise Goupil[2]

[1]University of East London, London, UK
[2]CNRS, University of Grenoble, France

'Natural behaviour is the language of the brain' (Miller et al., 2022). But almost all attempts to uncover the brain mechanisms that underpin neurodevelopment do not measure natural behaviour at all. Instead, we measure brain activity while children watch identically repeated sequences of events on a screen in darkened rooms or sleep in a scanner. The core motivation for this approach is to reduce measurement noise and enable experimental control of extraneous variables: in order to directly compare individuals we need to be able to measure differences in how they respond to identical stimuli, presented in identical settings. But when we remove the influence of children's everyday environment in order to measure their brain function within controlled settings, are we 'throwing the baby out with the bathwater'?

Here, we observed N=92 young children and adults playing together while recording dual EEG and behavioural microdynamics. Our aim was to understand the neural mechanisms that underpin why children who spend more time in joint child-adult attention during early development are better at paying attention on their own later on. Our results suggested that adult-led attention episodes are in fact rather ineffective at engaging child attention, as measured from neural and behavioural responsiveness. Rather, we see a lot of child-led attention, in which children shift attention between different objects seemingly unpredictably, and with using social cues to signal to their adult partner when they are about to shift. However, even young children seem highly sensitive to whether the adult responds to their child-initiated shift. The greatest behavioural and neural responsiveness is observed for attention episodes which the child has initiated and to which the adult has responded. Implications for education, and for understanding early pathways in conditions such as ADHD, are discussed.

Talk is mainly based on:

Phillips, E., Goupil, L., Haresign, I. M., Bruce-Gardyne, E., Csolsim, F. A., Whitehorn, M., ... & Wass, S. (in press). Proactive or reactive? Neural oscillatory insight into the leader-follower dynamics of early infant-caregiver interaction. *Proceedings of the National Academy of the Sciences*

Investigating social preference of toddlers by using wearable fNIRS in an immersive virtual reality set-up

Chiara Bulgarelli[1,2], Paola Pinti[1,2], Nadine Aburumman[3], Emily J. H. Jones[1]

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[3]Department of Computer Science, Brunel University, London, UK

There is an extensive literature on young infants' preference to interact with women, regardless the infant's sex[1,2]. This might not be valid for toddlers, as by 3 year, they know which gender-group they belong to[3], use gender-terms[4], and segregate into gender-groups during social activities[5]. Moreover, while infants mainly interact with adults, toddlers often attend day-care, where they are among peers. While this seems to suggest that toddlers prefer to interact with same-sex toddlers, to date no empirical investigation assessed partner preference in toddlerhood.

To explore this, we carried out the first study on social development on 3-to-5-year-olds (N=35) in the world's first Birkbeck ToddlerLab Cave Automatic Virtual Environment (CAVE) facility. The CAVE is a virtual-reality set-up where toddlers can freely move whilst wearing a wearable functional near-infrared spectroscopy (fNIRS) to measure their brain activations from the medial prefrontal cortex (mPFC) and the temporoparietal junction (TPJ), known as crucial regions for social categorization and social preferences in adults[6–9]. In the CAVE, toddlers were asked to play "popping bubbles" with a preferred avatar among four of different sex and age, and with one randomly assigned (Fig1).

Behavioural results showed that toddlers preferred to interact with same-sex and same-age avatar, and that they popped more bubbles when playing with the preferred avatar compared to the assigned one. Connectivity analyses are undergoing and we hypothesize that toddlers had stronger mPFC-TPJ connectivity while interacting with the preferred compared to the assigned avatar.

In this talk, I will discuss the use of wearable neuroimaging and virtual-reality for the study of social development in toddlerhood. This study is highly interdisciplinary, as it advances not only our understanding of toddlers' social world, but provides a reference for future studies exploring toddlers' development with naturalistic methods, overcoming most of the challenges of testing toddlers in standard lab-settings.

References

1. Rubenstein, A. J., Kalakanis, L. & Langlois, J. H. Infant preferences for attractive faces: a cognitive explanation. *Dev. Psychol.* **35**, 848 (1999).
2. Quinn, P. C., Yahr, J., Kuhn, A., Slater, A. M. & Pascalis, O. Representation of the gender of human faces by infants: A preference for female. *Perception* **31**, 1109–1121 (2002).
3. Levy, G. D. Gender-typed and non-gender-typed category awareness in toddlers. *Sex Roles* **41**, 851–873 (1999).
4. Leinbach, M. D. & Fagot, B. I. Acquisition of gender labels: A test for toddlers. *Sex Roles* **15**, 655–666 (1986).
5. Maccoby, E. E. & Jacklin, C. N. Gender segregation in childhood. in *Advances in child development and behavior* vol. 20 239–287 (Elsevier, 1987).
6. Molenberghs, P. The neuroscience of in-group bias. *Neuroscience and Biobehavioral Reviews* (2013) doi:10.1016/j.neubiorev.2013.06.002.

7. Morrison, S., Decety, J. & Molenberghs, P. The neuroscience of group membership. *Neuropsychologia* (2012) doi:10.1016/j.neuropsychologia.2012.05.014.
8. Rilling, J. K., Dagenais, J. E., Goldsmith, D. R., Glenn, A. L. & Pagnoni, G. Social cognitive neural networks during in-group and out-group interactions. *Neuroimage* (2008) doi:10.1016/j.neuroimage.2008.03.044.
9. Chen, A. C., Welsh, R. C., Liberzon, I. & Taylor, S. F. 'Do I like this person?'A network analysis of midline cortex during a social preference task. *Neuroimage* **51**, 930–939 (2010).

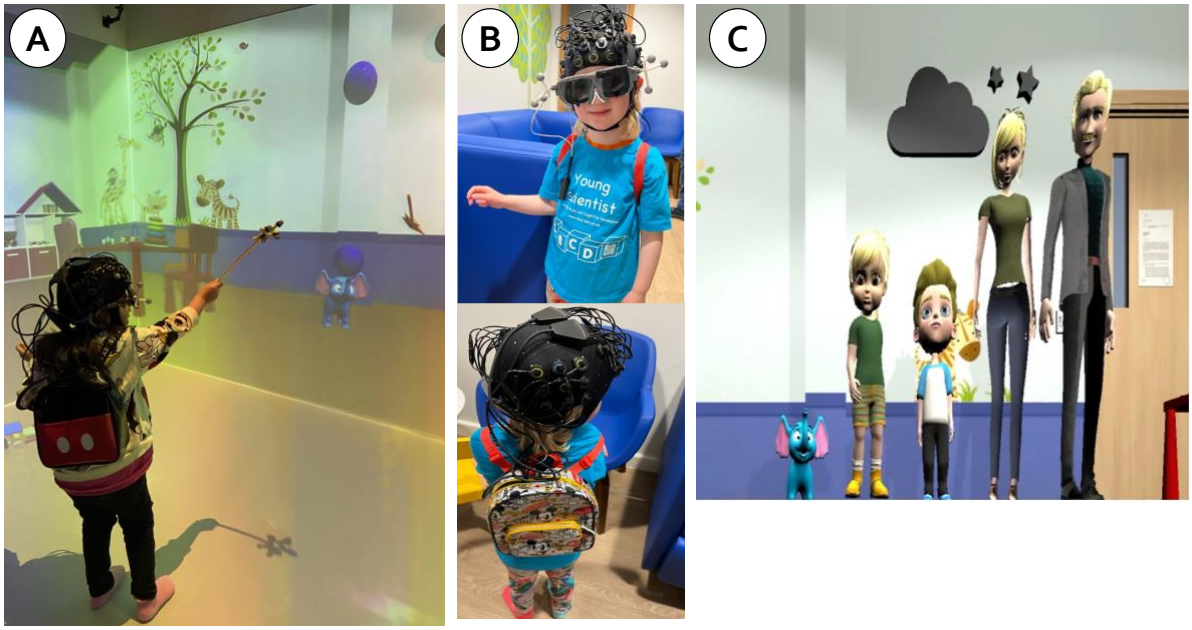

Fig1. A) A participant in the CAVE playing popping bubbles. B) wearable fNIRS system and shuttered glasses to see 3D images in the CAVE stored in a backpack to allow toddlers to freely move around. C) The four human-like avatars among which participants can choose one to play popping bubbles with.

Illuminating brain function underlying gross motor imitation with high-density diffuse optical tomography (HD-DOT)

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Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by persistent social communication deficits and restricted and repetitive behaviors[1]. Impaired imitation has been observed in children and infants with ASD[2-5] and may be an early precursor to profound social communication and language deficits later in childhood[6,7]. Imitation is associated with the development of behaviours crucial to social interaction and communication, including joint attention[8-10], play initiation[11], and prosocial behaviors[12,13]. Therefore, ASD-associated difficulties with imitation may disrupt the acquisition of a range of skilled actions. Behavioural interventions targeting imitation could help improve how and when children with ASD develop these crucial skills.

Efforts to establish imitation behaviour and the underlying brain function and connectivity as a biomarker of ASD have been limited by neuroimaging techniques such as fMRI that constrain movement. High-density diffuse optical tomography (HD-DOT) provides an open scanning environment that facilitates assessment of brain function underlying naturalistic overt motion[14]. Herein, we established the feasibility of a gross motor imitation paradigm in a population of neurotypical adults (n = 54; 18-59 years) with HD-DOT neuroimaging and simultaneous recordings of motor imitation with a Kinect 3D camera for computer vision-based imitation assessment during motor observation and imitation tasks. Statistical maps of brain responses to observation and imitation of gross motor movements reveal localized responses in sensorimotor and socially relevant areas such as the superior temporal sulcus. The contrast between imitation and observation shows increased activation in motor cortex during imitation and increased activation in bilateral temporal-parietal regions during observation.

We show herein that HD-DOT is feasible for neuroimaging during gross motor imitation. Ongoing funded studies are applying this multimodal paradigm to interrogate brain function and connectivity underlying motor imitation and their relation to quantitative metrics of dimensional ASD traits throughout childhood development in school-age (8-12 years), and pre-school age children (3-6 years).

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.) (2013).
2. Dowell LR, Mahone EM, Mostofsky SH. Associations of postural knowledge and basic motor skill with dyspraxia in autism: implication for abnormalities in distributed connectivity and motor learning. *Neuropsychology*. 2009;23(5):563-70.

3. Dziuk MA, Gidley Larson JC, Apostu A, Mahone EM, Denckla MB, Mostofsky SH. Dyspraxia in autism: association with motor, social, and communicative deficits. *Dev Med Child Neurol*. 2007;49(10):734-9.
4. Carpenter M, Tomasello M, Striano T. Role reversal imitation and language in typically developing infants and children with autism. *Infancy.* 2005;8(3):253-78.
5. Bhat AN, Srinivasan SM, Woxholdt C, Shield A. Differences in praxis performance and receptive language during fingerspelling between deaf children with and without autism spectrum disorder. *Autism*. 2018;22(3):271-82. doi: 10.1177/1362361316672179. PubMed PMID: 29671643.
6. McAuliffe D, Zhao Y, Pillai AS, Ament K, Adamek J, Caffo BS, Mostofsky SH, Ewen JB. Learning of skilled movements via imitation in ASD. *Autism Res*. 2020;13(5):777-84.
7. Tunçgenç B, Pacheco, C., Rochowiak, R., Nicholas, R., Rengarajan, S., Zou, E., Messenger, B., Vidal, R., Mostofsky, S. H. . Computerised Assessment of Motor Imitation (CAMI) as a scable method for distinguishing children with autism. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. 2021
8. Tomasello M, Carpenter M, Call J, Behne T, Moll H. Understanding and sharing intentions: the origins of cultural cognition. *Behav Brain Sci*. 2005;28(5):675-91; discussion 91-735.
9. Field T, Field T, Sanders C, Nadel J. Children with autism display more social behaviors after repeated imitation sessions. *Autism.* 2001;5(3):317-23.
10. Carpenter M, Tomasello M, Savagerumbaugh S. Joint Attention and Imitative Learning in Children, Chimpanzees, and Enculturated Chimpanzees. *Soc Dev*. 1995;4(3):217-37.
11. Fawcett C, Liszkowski U. Mimicry and play initiation in 18-month-old infants. *Infant Behav Dev*. 2012;35(4):689-96.
12. Carpenter M, Uebel J, Tomasello M. Being Mimicked Increases Prosocial Behavior in 18-Month-Old Infants. *Child Dev.* 2013;84(5):1511-8.
13. Chartrand TL, Lakin JL. The antecedents and consequences of human behavioral mimicry. *Annu Rev Psychol.* 2013;64:285-308
14. Eggebrecht AT, et al. Mapping distributed brain function and networks with diffuse optical tomography. *Nat Photonics*. 2014; 8(6):448-54.

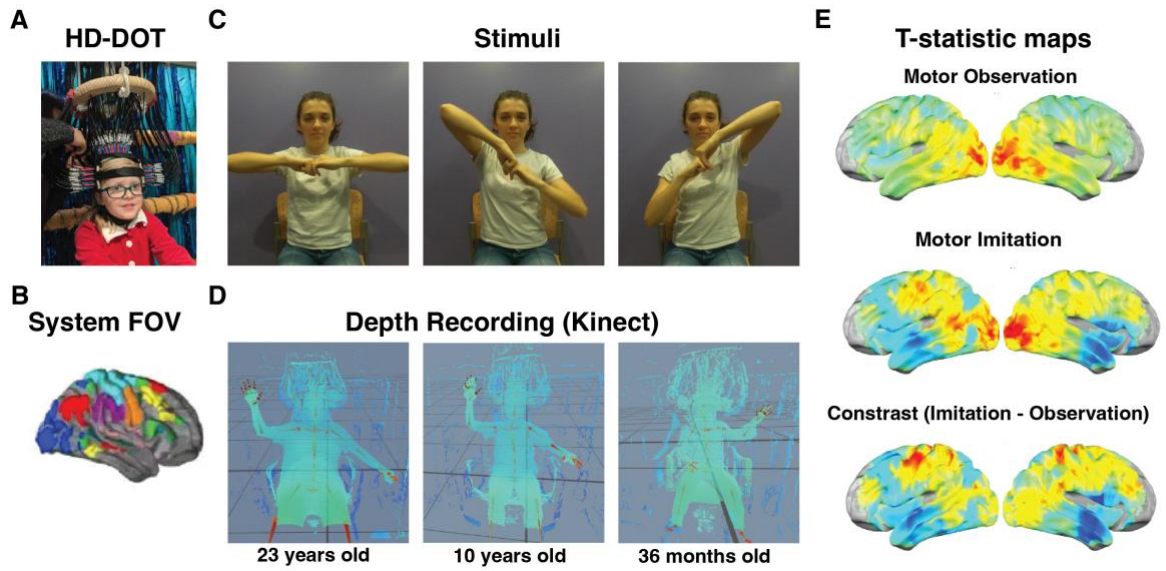

Figure 1 | **A)** Child participant wearing our HD-DOT system which consists of 128 sources (685nm and 830nm) and 125 detectors, that together provide over 3500 measurements. **B)** The field-of-view of our HD-DOT system covers cortical sensorimotor systems and higher-order association networks. **C)** Three images from the motor imitation stimulus video, showing examples of the upper extremity movements the participants performed. **D)** Depth recordings collected with the Kinect 3D camera during the motor imitation task from an adult, school-aged, and toddler-aged participant. **E)** T-maps of motor observation showing activations over visual and temporal cortex. T-maps of motor imitation show activations over visual, motor, and temporal cortex. T-statistic maps of the contrast imitation > observation show increased activity in premotor and motor cortex during imitation and increased activity in temporal cortex during motor observation.

Gradients go to the movies:
Macroscale cortical organization during naturalistic viewing in children and adolescents

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Movie-fMRI has been especially impactful in paediatric studies of functional connectivity (FC)[1-3]. Here, we present a brief overview of the use of movies to study FC. We then present findings from a new approach that uses naturalistic viewing conditions to study large-scale FC organization. We recently used diffusion embedding on movie-watching FC matrices to characterize large-scale principles of cortical organization during complex, dynamic processing in adults for the first time[4-6]. We found that the top movie components, or gradients, were all hierarchical, and each gradient subserved a specific perceptual modality (sensorimotor, visual, language/auditory)[6]. Movie gradients are thus different from resting state gradients and provide a unique level of granularity with which to interrogate brain organization and brain-behaviour relationships in different populations.

Here we present new data using this movie gradient approach in a developmental population for the first time. We examine age- and sex-based differences in movie gradients in a large sample (N=1244) of children and youth ages 6-18 years from the Healthy Brain Network Biobank[7]. We show that the principal movie gradients are identifiable throughout development, but that age-based differences exist in both the amount of variance explained by the gradients, and in some key aspects of their topography. The auditory/language gradient shows the most dramatic age-based differences, with significantly more complexity and the inclusion of heteromodal language regions in older age groups. We also relate gradient scores to social cognitive behavioural measures, and show that movie gradient scores are more closely related to social functioning scores relative to standard FC measures.

These findings provide an ecologically valid representation of the principles underlying cortical organization while the developing brain is actively engaged in multimodal, dynamic perceptual and cognitive processing. They also present a novel framework to assess developmental trajectories of functional connectivity.

References

1. Vanderwal, T., Eilbott, J. & Castellanos, F. X. Movies in the magnet: Naturalistic paradigms in developmental functional neuroimaging. *Developmental cognitive neuroscience* **36**, 100600, doi:10.1016/j.dcn.2018.10.004 (2019).
2. Vanderwal, T. *et al.* Stability and similarity of the pediatric connectome as developmental measures. *NeuroImage* **226**, 117537, doi:10.1016/j.neuroimage.2020.117537 (2021).
3. Cantlon, J. F. & Li, R. Neural activity during natural viewing of Sesame Street statistically predicts test scores in early childhood. *PLoS biology* **11**, e1001462, doi:10.1371/journal.pbio.1001462 (2013).

4. Margulies, D. S. *et al.* Situating the default-mode network along a principal gradient of macroscale cortical organization. *Proceedings of the National Academy of Sciences of the United States of America* **113**, 12574-12579, doi:10.1073/pnas.1608282113 (2016).
5. Bernhardt, B. C., Smallwood, J., Keilholz, S. & Margulies, D. S. Gradients in brain organization. *NeuroImage* **251**, 118987, doi:10.1016/j.neuroimage.2022.118987 (2022).
6. Samara, A., Eilbott, J., Margulies, D. S., Xu, T. & Vanderwal, T. J. b. Cortical gradients during naturalistic processing are hierarchical and modality-specific. *bioRxiv*, 2022.2010. 2015.512379 (2022).
7. Alexander, L. M. *et al.* An open resource for transdiagnostic research in pediatric mental health and learning disorders. *Scientific data* **4**, 170181, doi:10.1038/sdata.2017.181 (2017).

Conflict of interest

All the speakers declared they have no conflict of interest.

Symposium title: The Role of Puberty in Brain Development: A Translational Approach
Chair: Cecile D. Ladouceur, Ph.D.
Moderator: Kristen Delevich, Ph.D.

Talk #1

Title:
The role of puberty in the relations between family environment and the development of amygdala-mPFC circuitry

Authors:
Sandra Thijssen, Paul F. Collins, Michael I Demidenko, Dominic P Kelly, Felicia A Hardi, Ka I Ip, Sujin Lee, Hannah Becker, Sunghyun Hong, Monica Luciana, Daniel P Keating

Abstract: (word count 245)
Psychosocial acceleration theory suggests that early stress accelerates pubertal development. Relatedly, recent research suggests that development of the amygdala-medial prefrontal cortex (mPFC) circuit may be accelerated in response to early stressful family circumstances. As pubertal development drives neurodevelopment, in this talk, I will present our work examining whether accelerated pubertal development may be a mechanism linking stress to accelerated neurodevelopment. Using data from the Adolescent Brain and Cognitive Development Study, we assessed to what extent pubertal development mediates the association between family-related stress, measured by a latent construct capturing SES, and parent and child-reported family relationships, and function and structure of the amygdala-mPFC circuit (amygdala volume, anterior cingulate cortex thickness, area and fractional anisotropy, and amygdala-cingulo-opercular network functional connectivity). We used a split-half approach and examined these associations both cross-sectionally and longitudinally and explored sex differences. Moreover, using multiverse analyses, we further tested whether results are specific to the constructs we originally studied, or whether they hold more broadly. In all studies, both direct and indirect effects of the family environment on the amygdala-mPFC circuit were found. Pubertal development, therefore, may be one of the mechanisms driving accelerated neurodevelopment in response to normative variation in familial stress. This mechanism may be especially relevant for functional connectivity (and possibly cortical thickness development) for girls, whereas for other modalities and for boys, direct effects were reported, indicating other mechanisms may be at play. The multiverse analysis suggests the family effects found may be mostly driven by SES.

No conflicts to report.

Talk #2

Title:
Pubertal hormones modulate neural oscillatory activity: Emergent sex differences and developmental fine-tuning

Authors:
Giogia Picci, NM Petro, AD Killanin, J Son, L Weyrich, SH Penhale, LR Ott, P Wang, VD Calhoun, JM Stephen, TW Wilson

Abstract: (word count 196)
Adrenarche represents the first hormonal event during pubertal development, which is closely linked to the earliest physical indicators of puberty (e.g., skin changes, pubic hair). Dehydroepiandrosterone (DHEA) production is closely associated with adrenarche, but is poorly understood in humans. Few studies have documented the modulatory effects of DHEA on functional brain development, with even fewer examining effects of DHEA on spontaneous cortical activity using magnetoencephalography (MEG). Here, in a set of MEG studies with adolescent participants (6 – 16 years), we document modulatory effects of DHEA on resting-state oscillatory power, as well as task-based measures examining higher-order cognition. Effects of DHEA were observed primarily in brain regions involved in complex, integrative cognition (e.g., temporo-parietal

junction, precuneus), which continue developing during adolescence. Although not typically associated with sex differences, we also report subtle, emergent sexual-dimorphism linked with DHEA levels, primarily in frontal and temporal cortices that are spectrally specific. For example, at rest, compared to boys, girls with greater DHEA levels exhibit reduced delta activity in frontal and temporal cortices. Taken together, these data suggest that spontaneous and task-based cortical activity relate to endogenous DHEA levels during adolescence, particularly in regions that are known to undergo protracted development.

No conflicts to report.

Talk #3

Title:
Immature amygdala excitatory neurons migrate and mature during puberty in humans and mice

Authors:
Shawn F. Sorrells, Pia J. Alderman, Dave Saxon, Lucia Torrijos-Saiz, Malaz Sharief, Chloe Page, Sean Biagiotti, Stefano Vicini, Jose-Manuel Garcia-Verdugo, Vicente Herranz-Pérez, Joshua Corbin.

Abstract: (word count 280)
The amygdala is a brain region important for human emotional and social functions that mature throughout childhood and into puberty and adolescence. Across this timeframe, the human amygdala increases in the total number of mature neurons. Interestingly, this growth is due to a delayed maturation trajectory displayed by a pool of immature excitatory neurons comprising ~20% of all human amygdala neurons. These immature neurons display large-scale neurodevelopmental processes throughout puberty including soma and dendritic expansions and, remarkably, axon growth and neuronal migration. Despite this enormous investment in this form of cellular plasticity by the human amygdala, little is known about these neurons, including fundamental questions about their development and function, or if a tractable animal model like the laboratory mouse possesses similar neurons. We recently identified a homologous population of neurons in mice that share molecular, developmental, and anatomical features with those in humans. In both mice and humans these immature amygdala neurons remain dormant for weeks to months after their embryonic birth before maturing or migrating into neighboring brain regions during adolescence. They then grow into excitatory neurons in a form of neurogenesis-like plasticity that is distinct from olfactory bulb or hippocampus neurogenesis. The identification of this previously undescribed region in mice points to its significance as a conserved cellular mechanism of neuron recruitment and migration during puberty across species. Sex hormones changing during this timeframe can promote developmental processes such as neuron migration, dendritic outgrowth, and synaptic plasticity, and may therefore be involved in sculpting the unique developmental trajectory of these neurons. The timing and location of this unique form of whole-cell structural plasticity suggest extended critical periods for the maturation of amygdala-dependent functions and related neuropsychiatric conditions.

No conflicts to report.

Talk #4

Title: The role of puberty on brain development: A longitudinal study in male rhesus macaques

Authors:
MM Sanchez, ZA Kovacs-Balint, J Raper, R Richardson, A Gopakumar, KP Kettimuthu, M Higgins, E Feczko, E Earl, KF Ethun, L Li, M Styner, D Fair, J Bachevalier.

Abstract: (word count 198)
This study examined the role of male pubertal maturation on physical growth and development of neurocircuits that regulate stress, emotional and cognitive control using a translational nonhuman primate model. We collected longitudinal data from male macaques between pre- and peri-puberty, including measures of physical growth, pubertal maturation (testicular volume, blood testosterone -T- concentrations) and brain structural and

resting-state functional MRI scans to examine developmental changes in amygdala (AMY), hippocampus (HIPPO), prefrontal cortex (PFC), as well as functional connectivity (FC) between those regions. Physical growth and pubertal measures increased from pre- to peri-puberty. The indexes of pubertal maturation -testicular size and T- were correlated at peri-puberty, but not at pre-puberty (23 months). Our findings also showed ICV, AMY, HIPPO and total PFC volumetric growth, but with region-specific changes in PFC. Surprisingly, FC in these neural circuits only showed developmental changes from pre- to peri-puberty for HIPPO-orbitofrontal FC. Finally, testicular size was a better predictor of brain structural maturation than T levels -suggesting gonadal hormones-independent mechanisms-, whereas T was a strong predictor of functional connectivity development. We expect that these neural circuits will show more drastic pubertal-dependent maturation, including stronger associations with pubertal measures later, during and after male puberty.

No conflicts to report.

Title: Top-down regulation of somatosensory processing in the premature neonate brain as an early marker of neurodevelopmental susceptibility

Authors: Victoria Dumont[1], Anne-Lise Marais[1], Marie Anquetil[1,2], Anne-Sophie Trentesaux[3], Nadege Roche-Labarbe[1]

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[3]Caen University Hospital, Neonatal Intensive Care Unit, F-14000 Caen, France

Abstract:

Premature neonates are born before 37 weeks of gestational age (GA). 11% of births are premature in the world and this proportion increases because of many factors such as advances in neonatal intensive care and assisted reproduction technology. Children born prematurely have a high risk of pervasive cerebral and behavioral impairments because they are confronted with multiple risk factors: brain insults, physiological instability, abnormal and noxious stimuli, and parental separation. They have a 3- to 4-fold increased susceptibility to neurodevelopmental disorders (ND), and even those who are not diagnosed with ND often suffer from attention and executive deficits, motor deficits, and atypical sensory processing, which have long-lasting effects on school achievement and quality of life. Recent integrative and cross-syndromic approaches to atypical neurodevelopment propose that early sensory atypicality, both in terms of input and processing abilities, may constitute the foundation of atypical neurodevelopmental trajectories. In particular, sensory prediction deficits would alter the development of attention and auto-regulation, both relying on the anticipation of changes in the environment. In the proposed talk, I will present unpublished data on a large sample (current N=50) of premature neonates born at all gestation ages, therefore exposed to various adversity levels after birth. At 35 weeks of corrected GA, we present them with a hybrid oddball and omission tactile stimulation paradigm. Using 128-channel EEG and fNIRS, we measure evoked potentials and neurovascular responses to repeated familiar stimuli, rare deviants, and unexpected omissions. Preliminary results provide evidence of prediction in the somatosensory cortex and top-down regulation of sensory cortex activity from frontal areas. Findings suggest that a higher degree of prematurity is associated with impairment in this regulation and may result in atypical processing of somesthetic stimuli. This difficulty could be a very early marker of atypical neurodevelopment and an important target for neonatal care.

Title: Neonatal Sensory Responses and Early-Life Sensory Sensitivity in Relation to Prenatal Maternal Stress

Authors: Rebecca F. Schwarzlose[1], Michael J. Myers[1], Jennifer Harper[1], Tara A. Smyser[1], Cynthia E. Rogers[1], Barbara B. Warner[2], Deanna M. Barch[1,3], Joan L. Luby[1], Christopher D. Smyser[4], Chad M. Sylvester[1]

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3. Department of Psychological and Brain Sciences, Washington University School of Medicine in St. Louis
4. Department of Neurology, Washington University School of Medicine in St. Louis

Abstract:

Maternal psychological stress during pregnancy can affect fetal programming through its impact on the prenatal environment. It is associated with elevated postnatal sensory reactivity and sensory sensitivity in early childhood, which in turn are risk factors for later anxiety and behavioral challenges (Davis et al, 2011; Carpenter et al, 2019). Although these associations are established, the specific relationship between prenatal stress and neural mechanisms of postnatal sensory processing remains unknown. Here we report results from a diverse, longitudinal sample of mothers and infants enriched for early life adversity (ELA) and socioeconomic disadvantage. Mothers in the study completed self-reports on the Perceived Stress Scale during pregnancy. After delivery, 43 full-term neonates participated in functional MRI scanning during an adapted auditory oddball paradigm and parent reports of sensory sensitivity on the Infant-Toddler Social and Emotional Assessment (ITSEA) were obtained in 35 of these children at two years of age. Supporting prior results, we found that prenatal maternal perceived stress was positively associated with child sensory sensitivity scores collected 2 years later. To identify candidate neural differences in neonatal sensory processing associated with prenatal stress, we performed an exploratory whole-brain analysis of neonatal responses to infrequent auditory oddball stimuli with a corrected cluster-wise error rate of $p<.01$. The analysis identified 25 brain regions in which blood oxygenation level dependent (BOLD) oddball responses were associated with prenatal maternal stress, with approximately half of these regions located in cortical networks linked to error detection, externally driven attention, and auditory processing (*i.e.*, cingulo-opercular, ventral attention, and auditory networks). BOLD responses to oddball auditory stimuli were elevated in the right auditory cortex of neonates exposed to higher prenatal maternal stress, suggesting that differences in cortical sensory processing associated with prenatal stress exposure and ELA may be present at birth.

Title: Neural Mechanisms Underlying Sensory Over-responsivity in Youth Adopted from Foster Care

Authors: Shulamite A. Green[1], Megan Banchik[1], Laura Alba[2], Adriana Méndez-Leal[3], Audra Langley[1], Jill Waterman[3], Jennifer A. Silvers[3], Mirella Dapretto[1], Susan Bookheimer[1]

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Abstract:

Exposure to early caregiving adversity (ECA) such as abuse, neglect, separation from parents, or institutional care is well known to impact early brain development and increase risk for mental health challenges. However, emerging research also suggests that ECA confers risk for more basic sensory processing challenges such as sensory over-responsivity (SOR), an aversive response to stimuli such as loud noises or being touched which is associated with significant daily life impairment. Both SOR and ECA have been independently related to altered amygdala function which could place youth with ECA at risk for SOR, but there is currently little understanding of the biological mechanisms underlying SOR in ECA. Here, we build on recent findings from our group that adopted children with diverse ECA experiences show significantly higher levels of SOR compared to their non-adopted peers (Méndez-Leal & Alba et al., 2022). Here, we examined brain responses to aversive sensory stimulation in youth exposed to ECA who were adopted from foster care. Twenty-six ECA and 26 non-adopted control (NAC) youth aged 8-18 years participated in fMRI scans in which they experienced six blocks each of aversive tactile (a scratchy sponge), auditory (white noise), and joint (tactile+auditory) stimulation. Similar to prior results in children with autism, the AFC youth showed neural hyper-responsivity to sensory stimulation, however in this group the hyper-responsivity was more localized to somatosensory cortex. Unlike in children with ASD, *lower levels* of SOR was related to *greater* brain activation, including in regions that have previously been shown to play a role in sensory regulation such as the thalamus and cingulate gyrus. Thus, while ECA does confer early risk for SOR, it may be that later-developing neural regulatory mechanisms help to compensate and provide resiliency such that SOR is not associated with the widespread brain hyperactivation seen in neurodevelopmental disorders.

Title: Alteration of maternal perinatal interoception after early childhood trauma exposure is linked to perinatal depression

Authors: [1]Callaghan, B. L., & [1]Savoca, P.

[1]Department of Psychology, University of California, Los Angeles.

Abstract:

Perinatal depression affects up to 20% of pregnant women and mothers, and is more common in those who experienced childhood adversity. Beyond the impact of perinatal depression on maternal health and wellness, this condition is also an adverse caregiving environment for the developing fetus/child. Thus, assessing the mechanisms by which childhood trauma can impact peripartum depression will help to address intergenerational cycles of adversity. One potentially important mechanism to examine in this respect is changes in interoception during the peripartum. Interoception refers to the perception of the internal physiological state of the body (e.g., heart rate, hunger, taste, muscle tension etc.). Interoceptive ability is required for physiological regulation, and is thus a critical component of homeostatic functioning. Interestingly, dysregulation of interoception is recognized to play an important role in mental health. While the peripartum period is characterized by vulnerability to mental illness, and tremendous physiological change, we still know very little about how interoception changes during this important stage of adult development. In the proposed talk I will highlight unpublished data from the first wave of our ongoing longitudinal study (Sensations of Motherhood), comparing interoception in never pregnant women and first-time mothers in the second trimester (current N = 100). We report striking differences in interoception in pregnant women, characterized by higher interoceptive accuracy, greater interoceptive attention, and more worrying about interoceptive cues relative to the never pregnant group. We also see that within the pregnant group, there is a negative association between childhood trauma exposure and interoception, and across all individuals there is a negative relationship between interoception and depression. These data suggest that childhood trauma impairs a normative boost in interoceptive accuracy in pregnancy that may place mothers at risk for depression.

Developmental Cognitive Neuroscience in Real-World Educational Contexts: Opportunities and Challenges for crossing the "Bridge Too Far"

Keywords: education, naturalistic neuroscience, community engaged methods

Overall Abstract

In a famous commentary, Bruer (1997) argued that the gap between neuroscience research and educational practice is too wide for meaningful implications, and that—at the time—linking the brain and education was a "bridge too far." In this symposium, we ask whether the field has finally built this bridge, allowing for basic developmental cognitive neuroscience (DCN) research to have true translational impact on educational practice, and how this can in turn critically inform basic DCN research. While most educationally relevant DCN research takes place in decontextualized lab settings under precise experimental control, the field is experiencing an emergence of more ecologically valid work during real-time learning and in real-world school settings, including classrooms and online learning environments. However, a question remains about the implications of this work for meaningfully transforming educational practice, especially for struggling and/or at-risk learners. Here we present novel findings from three studies examining the neural mechanisms underlying children's learning in real-world school contexts, and examine the potential of research-practice partnerships for transforming the relevance of basic science findings. First, Jennie Grammer (UCLA) will present neurobehavioral indicators of science learning during online and in-person instruction in elementary school children with and without ADHD. Next, Elizabeth Toomarian (Synapse School) will describe an innovative research-practice partnership that has embedded educational neuroscientists and an electroencephalography lab into a K-8 school, and discuss opportunities and challenges for advancing developmental neuroscience research. Then, Fang Wang (Stanford University) will present findings from a classroom-based reading intervention study, co-designed by teachers, that demonstrates how the neural bases of lexical access develop during formal training in beginning readers. Finally, co-chairs Bruce McCandliss and Rachel Romeo will lead a moderated discussion on the benefits, limitations, and present/future potential of implementing cognitive neuroscience research in educational settings, and whether we have built the "bridge too far." We aim to spark a critical dialogue for how our field can help address the fundamental challenges facing education, and how education can transform the scope of our central investigations.

Talk 1: Examining Children's Attention During Online Learning

Jennie Grammer[1], Zoe Mao[1], & Agatha Lenartowicz[2]

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Children's attentional skills are important for their ability to engage in learning activities; however we know relatively little about how to best support the development of these skills during instruction. The transition to online learning introduced new demands on student's attentional, particularly for those with greater difficulty paying attention and inhibiting distraction, including students with Attention Deficit Hyperactivity Disorder (ADHD). One main challenge in the study of attention in learning environments is that it is difficult to measure reliably from behavior alone. In this presentation, we will report findings from an experiment in which children (aged 6-10) with and without a diagnosis of ADHD participated in science lessons while their behavior and electrophysiological correlates (EEG and ERP) of attention were measured. All children participated in four learning activities including in-person instruction, online synchronous instruction, online asynchronous instruction, and independent work. Activities were

counterbalanced and varied in terms of who was directing learning (teacher vs. student) and the modality of instruction (online vs. offline). Results revealed differences in both behavioral and EEG/ERP indicators of attention as a function of instructional condition, suggesting that who directs the learning activity and the modality of the activity impact student attention. In addition, preliminary results indicate that the nature of the learning activity impacts student attentional behaviors above and beyond ADHD diagnosis, suggesting that specific types of instruction may be particularly beneficial for supporting attention in students with ADHD. Implications for educator practice, and the planning on online instruction, will be addressed.

Talk 2: Lessons Learned from a Research-Practice Partnership Approach to Educational Neuroscience

Elizabeth Y. Toomarian[1,2], Radhika S. Gosavi[1,2], Fang Wang[1], Lindsey Hasak[1], Madison Bunderson[1], Bruce D. McCandliss[1]

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The field of educational neuroscience offers significant promise for better understanding the developing mind, but advances have been limited by a fundamental separation between university neuroscience laboratories and school communities. This historical structure has constrained our ability to co-create and conduct research studies germane to authentic school environments. Moving the field forward requires innovative models to effectively bring neuroscience researchers and educational practitioners together in the rich, shared context of schools. In this session, we will discuss successes and challenges of one such model– the Brainwave Learning Center, a research-practice partnership that has embedded educational neuroscientists and an electroencephalography lab into a K-8 school. This model integrates the affordances of school-based neuroscience research with teacher research involvement and high student engagement. We will specifically discuss this partnership through the lens of a recent collaborative EEG training study, which involved teachers as co-creators of aspects such as training materials, framing, and implementation. Teachers recorded insights and provided feedback before, during and after the study, allowing the research team to effectively iterate on procedures (e.g., length and framing of assessments). Specific successes of this approach have included: relationship-building with students and teachers, co-creation of novel research paradigms, more inclusive recruitment practices, higher data collection throughput, and local teaching practices newly informed by the science of learning. Challenges include balancing classroom-based constraints with demands of rigorous research, terminology alignment, establishing a defined niche within two existing organizational structures, and other such considerations. This unique model highlights the value of researchers and teachers co-conceptualizing and implementing research studies, and also represents a significant step forward in breaking the structural constraints that have historically limited educational neuroscience progress.

Talk 3: Lexical processes underpinning word recognition in early readers: insights into naturalistic education by bringing SSVEP and EEG into schools

Fang Wang[1], Elizabeth Y. Toomarian[1,2], Radhika S. Gosavi[1,2], Suanna Moron[1], Lindsey R. Hasak[1], Bruce D. McCandliss[1]

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Segregating the lexical processes underpinning word recognition, especially in early readers, has been challenging in previous literature employing Steady-State Visual Evoked Potential (SSVEP) paradigms. Recently, we found lexical responses in early readers (kindergarteners to second graders) by slowing down SSVEP presentation rates, and using high frequency words. Study 1 extends this approach to the word frequency effect, which has been incorporated into the basic architecture of many models of word recognition, due to its crucial role in lexical access. Five-letter high frequency words (HFW, > 500/million), medium frequency words (MFW, 100~500/million), and well-matched pseudowords (PW) were prepared. EEG data were recorded while the participants (first and second graders, 6-8 years, n=28) were presented with contrasts of HFW vs. PW and MFW vs. PW, at 1/3 Hz frequencies (e.g., one HFW followed by two PW per second). We found that both HFW and MFW elicited stronger response amplitude than PW with stronger neural responses to HFW than to MFW, indicating lexical processing in early readers. Because word frequency is known to be highly correlated with word familiarity, a follow-up classroom-based training study casually manipulated word familiarity. Three lists of five-letter low frequency (<1 per million) words were prepared, with 20 items for each list. These lists were semi-randomly assigned across three classes (the same participants in Study 1). After training on the assigned word list, EEG data were recorded while participants were presented with contrast of trained (from their own class) and untrained (from other classes) LFW, at 1/3 Hz frequencies. Trained LFW evoked neural responses similar to those evoked by HFW. These findings suggest that lexical processes underpinning word recognition can be detected in early readers and that word lexical access develops rapidly after a short term of formal training in school.

Flash Talk Abstracts

Friday, September 8, 2023

2-D-14 - Microstructural differences in the brains of young children with attention-deficit/hyperactivity disorder compared to typically developing children: Evidence from restriction spectrum imaging.

Anthony Dick [1], **Mohammadreza Bayat** [1], **Melissa Hernandez** [1], **Madeline Curzon** [1], **Nathalia Garcia** [1], **Wilfredo Renderos** [1], **Donald Hagler** [2], **Anders Dale** [2], **Paulo Graziano** [1]

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Details

Attention-Deficit/Hyperactivity Disorder (ADHD) is the most common reason for early childhood mental health referral affecting between 10 to 25% of preschoolers. A prominent theory of ADHD is that the disorder is associated with dysfunction of dopaminergic (DA) circuits. For example, Nigg and Casey (2005) reviewed the potential association of basal ganglia (i.e., fronto-striatal) and cerebellar thalamocortical loop dysfunction with ADHD symptomology, noting the importance of DA in the modulation of function in both circuits. Indeed, stimulant medications, which block DA transporters to enhance extracellular DA, are a first-line treatment for ADHD. These medications modulate activity in these proposed basal ganglia and cerebellar thalamocortical circuits associated with symptoms and behaviors associated with ADHD, such as difficulty suppressing competing behaviors during goal-directed activity, impulsive behavior, poor sustained attention during complex tasks, and inefficient response to changing reward or learning contexts. The substantia nigra (SN) and ventral tegmental area (VTA) are central components of this circuit, and it is possible that early DA circuit dysfunction involving the SN is already present in young children with ADHD. This could be indicated if there are differences in cellularity of SN or VTA between medication naÃ¯ve ADHD and typically developing (TD) children before they are exposed to stimulants, which may affect cellularity in these regions. To establish whether there are existing diagnostic group differences, we employed a novel MRI method sensitive to *in vivo* neurite density. Method: The final participating sample consisted of 152 4-7-year-old medication naÃ¯ve children diagnosed with ADHD (dual clinician diagnosed) and 137 typical controls (M age = 5.50, SD = 0.87, and 69% male). All children were scanned in an MRI (3T Siemens Prisma) with a 102-direction multi-shell diffusion-weighted imaging acquisition. Restriction spectrum imaging (RSI; White et al., 2013) reconstruction of the diffusion signal was applied. The SN was identified using the Pauli atlas, and SN differences in restricted and hindered diffusion, which are sensitive to cellularity in grey matter (Palmer et al., 2022) were examined across age, with diagnostic group entered as a moderator. Results: In SN, we found a significant positive effect of age for restricted diffusion, but this effect was moderated by diagnostic group status (p = .02). Specifically, the slope for the ADHD group was significantly smaller than the TD group. In contrast, the age effect, which was also present in the VTA (p = .0004), was not moderated by group in this region (p = 0.33). Conclusions: Age-related differences in cellularity, evident in early adolescence using the RSI diffusion method (Palmer et al., 2022), are already indicated at earlier ages (4-7-years) in SN and VTA DA regions. The novel finding here, though, is that in

SN these age-related differences proceed differently in children with ADHD relative to TD children. This indicates an early emerging structural difference in the DA circuit for children with ADHD that can be detected with novel diffusion imaging methods.

2-D-15 - Generalizable multivariate neuroanatomical correlates of psychiatric problems in preadolescence

Bing Xu [1], **Henning Tiemeier** [2], **Ryan Muetzel** [1]

[1] Erasmus Medical Center Rotterdam, [2] Harvard T.H. Chan School of Public Health

Details

Introduction

Associations between brain structures and child psychiatric problems have been extensively investigated across different disorders. However, findings were inconsistent, showed modest effect sizes in specific brain regions, and were prone to poor replicability. This lack of regional convergence could be due to (*i*) the categorical nosology that most studies were based on, which omits the dimensional nature of many child psychiatric problems. (*ii*) conventional mass univariate methods that do not account for the likely multivariate nature of associations and the embedded burden of multiple testing correction. (*iii*) small sample sizes and a lack of rigorous external validation in an independent sample. We aim to address these gaps by applying multivariate machine learning techniques to delineate robust and generalizable associations between brain structures and child psychiatric symptoms in two large neurodevelopment cohorts, the Adolescent Brain Cognitive Development (ABCD) Study in the US and the Generation R Study in the Netherlands.

Methods

A total of 11,271 structural MRI scans from the multi-site ABCD Study (ages 9-to-10 years from 21 study sites) and the single-site Generation R Study (ages 9-to-12 years) were included. Each brain structural measure (cortical and subcortical volumes, cortical surface areas, and cortical thickness) was normalized and residualized by regressing out potential confounders. Psychiatric symptoms were assessed using the eight syndrome scales of the Child Behavioral Checklist (CBCL). The ABCD sample was randomly split into a training set consisting of 17 sites and a test set consisting of 4 sites, a procedure that was repeated 10 times to reduce sampling bias. We applied a multivariate machine learning technique: sparse canonical correlation analysis (SCCA), in the training sets of ABCD and test *out-of-sample generalizability* in the test sets of ABCD. Importantly, *out-of-study generalizability* was further tested by applying the model weights in ABCD directly to Generation R, which is a highly stringent (gold-standard) generalizability test.

Results

We identified one brain-behavior dimension that was highly generalizable in test sets (*out-of-sample*) of ABCD as well as in Generation R (*out-of-study*). This brain-behavior dimension captured the correlation between higher attention-dominated externalizing problems and widespread reduced cortical/subcortical volumes and cortical surface areas, especially in frontal and parietal lobes. This association was highly consistent when we implemented traditional CCA without sparsity, when using more fine-grained

measures (item scores of CBCL) of child psychiatric problems, and when removing the effects of head motion from the brain data. Moreover, the derived latent brain dimension was predictive of ADHD medication, child cognitive ability, and school achievement, with greater precision compared with total grey matter volumes of the brain.

Conclusion

By leveraging two independent large neurodevelopment cohorts, we identified one highly robust multivariate association between brain structural patterns and attention-dominated externalizing problems in the general population, which showed marked generalizability across different populations and study protocols. Our results showed the pervasiveness of reduced brain structures that are related to higher attention and social problems in preadolescence. Importantly, when using the gold-standard test, achieving a high level of generalizability is not common in existing brain-behavior association studies. This makes our results hold special values not only in illustrating the relationship of brain and child psychiatric problems, but also in providing methodological implications for replicable and generalizable multivariate prediction models. Future studies could extend the investigation into different development periods and the predictive values for diagnosis and disease trajectory in clinical samples.

2-E-33 - Differences in intra- and interhemispheric white matter connectivity in children with down syndrome and autism

Dea Garic [1], **Rebecca Grzadzinski** [1], **Khalid Al-Ali**, **Robert Mckinstry** [2], **Kelly Botteron** [3], **Natasha Marrus** [2], **Stephen Dager** [4], **Annette Estes** [5], **Guido Gerig** [6], **Heather Hazlett** [7], **Martin Styner** [1], **Joseph Piven** [7], **Robert Schultz** [8], **Juhi Pandey** [9], **Tanya St. John** [5], **Mark Shen** [7]

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Details

Background: Down syndrome (DS) is the most common genetic cause of intellectual disability, with a prevalence rate of 1 in 700 live births. Despite this, our understanding of white matter (WM) connectivity in DS remains limited, with only about six diffusion weighted imaging studies with matched controls conducted to date. Most reports are in adults with DS, who have widespread reductions in WM integrity as indexed by fractional anisotropy (FA). Only one study has examined WM microstructure in children with DS compared to typically developing (TD) children, with results suggesting lower FA particularly in the bilateral uncinate (UNC) and right inferior longitudinal fasciculus (ILF). The modest sample size of that study (n=10 DS, aged 2-4 years) requires further investigation.

Another limitation of previous WM microstructure studies in DS is the reliance on diffusion tensor imaging (DTI), which is unable to parse out crossing fibers and disentangle microstructural characteristics (e.g., myelination, axonal and neurite density). With multishell diffusion acquisition, it is possible to generate more sensitive microstructural data from High Angular Resolution Diffusion Imaging (HARDI) and Neurite Orientation and Dispersion Imaging (NODDI) models.

We included another comparison group, children with autism, since DS and autism have significant shared symptomatology but potentially divergent brain development, with DS typically associated with decreased brain volume, while autism has been linked to early brain overgrowth. By leveraging data from concurrent clinical cohorts scanned under identical imaging protocols in the Infant Brain Imaging Study, we aim to compare WM structural differences across multiple diffusion models in children with DS, autism, and typical development.

Methods: The sample consisted of 103 children (DS=25, autism=27, TD=51) between the ages of 7 to 12 years (*M*=9.85, *SD*=1.06). Nine major intrahemispheric fiber pathways were examined: bilateral frontotemporal arcuate (arcuate FT), temporoparietal arcuate, cingulum, parietal corticofugal, fornix, inferior fronto-occipital fasciculus (IFOF), optic radiation, ILF, and UNC. Two interhemispheric pathways were examined: splenium and tapetum. Analysis of variance models were conducted to first examine group differences on average DTI, HARDI, and NODDI values in core intrahemispheric WM (aggregate of all nine intrahemispheric pathways per hemisphere), then for each tract individually. All analyses covaried for age, sex, and intracranial volume. Significance values were adjusted for multiple comparisons using False Discovery Rate.

Results: The DS group had lower FA, generalized FA (GFA), axial diffusivity (AD), and higher orientation dispersion (ODI) in left core intrahemispheric WM than both the autism and TD groups. The right hemisphere had similar patterns, but only AD reached significance. Core intrahemispheric group differences were driven by differences in the bilateral IFOF, left ILF, right UNC, and right arcuate FT. The fornix was observed to have a unique pattern, with higher MD, RD, AD, and lower ODI in the DS group, which will be further discussed. On the other hand, interhemispheric connectivity showed an opposing pattern: children with DS had higher FA, GFA, and neurite density (NDI) in the tapetum compared to other groups. This same pattern was also observed in FA and NDI of the splenium. No significant differences were found between the autism and TD groups.

Conclusion: Taken together, results suggest that children with DS have a pattern of less coherent intrahemispheric connectivity, but denser neuronal packing and greater WM integrity within interhemispheric pathways, compared to children with autism and TD. These findings provide early insight into WM development in school-aged children with DS and have the potential to further elucidate microstructural differences than what has previously been observed through DTI models alone.

2-F-41 - Educational Environment is Related to White Matter Development

Ethan Roy [1], **Amandine Van Rinsveld** [1], **Ariel Rokem** [2], **Jason Yeatman** [1], **Bruce Mccandliss** [1], **Leo Sugrue** [3], **Andreas Rauschecker** [3], **Pierre Nedelec** [3]

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Details

Introduction

Students who are fortunate to attend high quality schools demonstrate better performance across academic domains including reading and math. Furthermore, educational intervention studies have shown that changes in the educational environment can drive both learning and lead to changes in

white matter properties (Huber et al., 2018). In contrast, demographic factors, such as parental income and education, have been shown to relate to white matter development. We used longitudinal data from the ABCD dataset to explore whether the educational opportunities afforded to an individual relates to the development of white matter tissue properties above and beyond other demographic factors.

Methods

We used data from the Stanford Education Data Archive (SEDA), which provides measures of the quality of each participant's educational context. SEDA uses standardized test scores from nearly every school in the United States to generate achievement scores for each school relative to the national average. This score can be thought of as the quality of educational opportunity afforded by the school. We performed a median split using SEDA scores to classify each participant as belonging to relatively high or low quality educational environments.

We also leveraged the preprocessed longitudinal diffusion MRI data available in the ABCD dataset. Tractography was performed on these data using DIPY (Garyfallidis et al. 2014) and tractometry was performed using pyAFQ (Kruper et al., 2021). We first conducted univariate comparisons of the diffusion kurtosis imaging metrics between SEDA groups across a left-lateralized network of white matter tracts that have been linked to academic skills, as well as their right lateralized counterparts. We then trained a machine learning model (XGBoost; Chen & Guestrin, 2016) on diffusion and demographic data to explore high-dimensional predictions of SEDA scores. Finally, we constructed longitudinal growth models to examine the relationship between SEDA scores and change in fractional anisotropy.

Results

A comparison of white matter properties across SEDA score groups revealed group differences in diffusion properties, as well as correlations between white matter properties and SEDA scores. Furthermore, machine learning models suggested that the addition of white matter features to the model slightly increased the explained variance in SEDA scores, above and beyond what is explained by other demographic factors alone. We then leveraged the longitudinal ABCD data to explore intraindividual change in the white matter while controlling for parental education, income, and broader demographic factors. Not surprisingly, growth models replicate past findings that show developmental changes in the white matter as a function of age. However, these models also revealed a significant age by SEDA interaction in a series of left-lateralized bundles that have been implicated in reading and math skill in the past. Decomposing this interaction revealed that white matter development is accelerated in the left arcuate, SLF, and ILF for individuals in schools with higher SEDA scores, even when controlling for known demographic effects.

Conclusions

The present analysis found both cross-sectional and longitudinal links between the quality of an individual's educational environment and their white matter in a large, diverse sample. Multivariate models suggested that a chil's educational environment is related to white matter development above and beyond the influence of other demographic factors. Furthermore, growth modeling suggested the rate of white matter maturation in the left arcuate, left SLF, and left ILF is higher in individuals from schools with higher SEDA scores. Together, these findings suggest that the quality of an individual's

school environment may lead to measurable differences in white matter properties and that differences in educational quality shape developmental trajectories in white matter.

2-G-44 - Associations of Mother-Child Closeness, Adolescent Symptomatology and Structural Brain Networks

Sunghyun Hong [1], **Felicia Hardi** [1], **Scott Tillem** [1], **Leigh Goetschius** [1, 2], **Jeanne Brooks-Gunn**, **Vonnie Mcloyd** [1], **Nestor Lopez-Duran** [1], **Colter Mitchell** [1], **Luke Hyde** [1], **Christopher Monk** [1]

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Details

Introduction: Mother-child closeness is an essential aspect of positive parenting that reflects the quality of the caregiver-child relationship. Prior research suggests that greater mother-child closeness is associated with lower rates of adolescent internalizing symptoms, yet multi-informant approaches to examining closeness across multiple time points in population-based samples are lacking. Moreover, while some preliminary studies have explored the relationship between positive parenting and the brain, no research has investigated the neural correlates of mother-child closeness. Caregiving practices are critical to support the development of neural structures, specifically white matter structures that facilitate information transfer in the brain. Such investigations can advance our understanding of potential biological mechanisms relating to mother-child closeness and adolescent mental health. Our study consisted of two aims. First, we examined the associations between mother-child closeness and internalizing symptoms in a population-based sample. Second, we investigated the associations between mother-child closeness, neural network architecture, and internalizing symptoms in a subsample.

Methods: In the first analysis (N=3872 from The Future of Families and Child Wellbeing Study), we examined whether mother-child closeness is linked to adolescent internalizing symptoms. Then, in a subgroup of the full sample (Study of Adolescent Neurodevelopment; N=237), we examined whether mother-child closeness was associated with adolescent internalizing symptoms and white matter structural network organization. Mother-child closeness was assessed by averaging mothers' and children's self-reported ratings of their level of closeness with each other at ages 9 and 15. Adolescent internalizing symptoms were measured using latent variables constructed from children's self-reported depression and anxiety at age 15. Structural network organization was assessed by applying graph analysis on diffusion MRI-based white matter connectomes at age 15. The analysis focused on topological properties of structural networks using measures of global network efficiency (how quickly information transfers from one end of the network to the other), transitivity (how nodes are clustered together), and modularity (how easily it is for the network to be subdivided into segregated groups). All analyses were adjusted for covariates, including average household income from birth to age 15, maternal marital status at birth, maternal educational status and depression at age 15, children's sex at birth, race, and pubertal development at age 15.

Results: There was a negative relationship between mother-child closeness and adolescent internalizing symptoms. Greater mother-child closeness was associated with lower internalizing symptoms (full sample: $\hat{I}^2 = -0.234$, $p < 0.001$; sub-sample: $\hat{I}^2 = -0.171$, $p = 0.008$). There was a positive relationship

between mother-child closeness and two network metrics. Greater mother-child closeness was associated with greater global network efficiency ($\hat{I}^2 = 0.186$, $p = 0.009$) and greater transitivity ($\hat{I}^2 = 0.189$, $p = 0.008$), but not with modularity. There were no associations between network metrics and internalizing symptoms.

Conclusion: Our study utilized a population-based sample to investigate the link between mother-child closeness and internalizing symptoms, followed by examining its association with whole-brain neural network architecture in a sub-sample. Greater mother-child closeness is associated with lower internalizing symptoms in adolescence. Additionally, greater mother-child closeness is related to greater global efficiency and transitivity. Our findings are the first to indicate that differences in structural network organization may emerge from parent-child closeness. Future studies with larger neuroimaging data are necessary to generalize these findings.

2-M-92 - Reports of the death of brain-behavior associations have been greatly exaggerated

Carolina Makowski [1], **Timothy Brown** [1], **Weiqi Zhao** [1], **Donald Hagler** [1], **Hugh Garavan** [2], **Tom Nichols** [3], **Terry Jernigan** [1], **Anders Dale** [1]

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Details

Magnetic resonance imaging (MRI) has been a popular and useful non-invasive method to map patterns of brain structure and function to complex human traits. A more ambitious challenge is to define features of the developing brain that predict cognitive, social, or emotional traits, and thus uncover opportunities to improve behavioral outcomes. Recently published observations in a sample of thousands of children cast doubt upon these prospects, particularly for prediction of cognitive traits from resting state functional MRI (fMRI), which seems to account for little behavioral variability. Here we compare the sample sizes required to detect reproducible brain-behavior associations across imaging modalities using both univariate and multivariate methods. We demonstrate that by applying multivariate methods to high-dimensional brain imaging data, we can capture lower dimensional patterns of structural/functional brain architecture that correlate sufficiently robustly with cognitive phenotypes to be reproducible with only 42 individuals for working memory-related fMRI, and between ~50-75 for structural/diffusion MRI. Power is further enhanced when empirically modeling the task fMRI time series data, with only 36 individuals required. Dimensionality reduction of empirically-modeled task fMRI data also allowed us to obtain a finite number of separable spatio-temporal components predictive of general cognition, which yielded larger effect sizes than any individual univariate association and more interpretable patterns of brain-behavior associations (e.g., dorsolateral-prefrontal and parietal activation linked to cognitive performance). These results point to an important role for neuroimaging in translational neurodevelopmental research and showcase the ability to measure meaningful and reproducible brain-behavior associations without the need for thousands of individuals.

2-N-98 - Development of Functional Systems In 0-2 year-olds

Jiaxin (Cindy) Tu [1], **Michael Myers** [1], **Chad Sylvester** [2], **Evan Gordon** [1], **Timothy Laumann** [1], **Omid Kardan** [3], **Eric Feczko** [4], **Trevor Day** [4], **Oscar Miranda-Dominguez** [4], **Lucille Moore** [4], **Damien Fair** [4], **Monica Rosenberg** [5], **Christopher Smyser** [1], **Jed Elison** [4], **Adam Eggebrecht** [2], **Muriah Wheelock** [2]

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Details

Objective: The brain is organized into different systems that serve distinct functions in healthy adults, and are often used for dimensionality reduction in functional connectivity (FC) studies to understand brain-behavior associations. To conduct such brain-behavior research, the system models used to partition the brain should fit well to actual system-level divisions in the data. However, at the earliest stages of post-natal development, adult models of brain systems may not be appropriate. Several groups, ours included, have developed functional atlases with age-specific delineation of brain systems, but no prior research has benchmarked the improvement, if any, these system parcellations provide as models for infant brain organization compared to their adult counterparts. Here, we assess the confidence of each spatial location belonging to its assigned system(Yeo et al. 2011) based on infant FC at 0-2 years old to measure the goodness of fit of the different adult and infant system parcellations.

Method: We used the vertex-wise FC in 32k fsLR space from infants and neonates scanned during natural sleep from the Baby Connectome Project (BCP, 8-29 months grouped in 5 bins, Howell et al. 2019) and Early Life Adversity, Biological Embedding (eLABE, gestational age 38-45 weeks) datasets. Results from the Washu120 young adult dataset (Gordon et al. 2016) were also included as a comparison to the infants and neonates. We considered various systems-level parcellations developed from the adult (19-32 years, Laumann et al. 2015), infant (8-26 months, Kardan et al. 2022) and neonate (gestational age 38-45 weeks, Sylvester et al. 2022) FC . We used the silhouette index (SI; Rousseeuw 1987) measure to quantify the confidence of each spatial location belonging to its assigned system. The SI at each vertex i compares the mean intra-cluster distance (a_i) and the mean nearest-cluster distance (b_i): $SI_i = (b_i â€“ a_i) / \max(a_i, b_i)$. In our case, the distances were measured as 1-Pearson's correlation between functional connectivity maps from seed vertices and the clusters were the systems. The resulting SI lies between -1 and 1 and a high SI indicates that the vertex is well-matched to its assigned system compared to other systems. A high mean SI indicates that the data have been well-clustered.

Result: First, we found that neonate, infant, and adult FC were all best represented by the system parcellation it is defined in (mean SI~0.2) and not by the system parcellation from other age groups (mean SI~0). Second, we found that the confidence for adult system assignments (mean SI) increased across ages from 9 to 25 months. Third, we found that the mean SI varied greatly across systems with three major patterns of development: 1) visual, motor, retrosplenial, salience, dorsal and ventral attention systems were adult-like (mean SI>0) by 1 year and some of the systems can be even more segregated from other systems (higher mean SI) than their Washu120 adult counterparts; 2) the default, parietal memory, and frontoparietal association systems were rapidly developing from one to two years after birth, but still less segregated (lower mean SI) than their Washu120 adult counterparts; 3) the cingulo-opercular and auditory systems were the slowest to mature and remained far from adult-like (mean SI<0) in organization by 2 years old. Lastly, we showed that core regions previously reported to have a high consensus of adult systems across individuals (Dworetsky et al. 2021) highly overlap with the regions with SI>0 to adult systems in the neonate and infant data (~0.70-0.75 in overlap coefficient across two datasets).

Conclusion: We found that resting-state system organization can be very different across newborn, infancy, and adulthood stages. We also observed a diversity in developmental trajectory of different resting-state systems from 0 to 2 years old and identified stable system 'coresâ€ which had similar

system-organization throughout the lifespan.

2-P-109 - Characterizing striatal dopamine-related neurophysiology in rewarded response inhibition in youth at risk for problematic substance use

Ashley Parr [1], **Finnegan Calabro** [1], **Will Foran** [1], **Douglas Fitzgerald** [1], **Susan Tapert** [2], **Kate Nooner** [3], **David Goldston** [4], **Michael Debellis** [4], **Duncan Clark** [1], **Beatriz Luna** [1]

[1] University of Pittsburgh, [2] University of California, San Diego, [3] University of North Carolina Wilmington, [4] Duke University

Details

Little is known about the relationship between the neurodevelopment of dopamine (DA) systems and substance use behavior. Differences in response inhibition and striatal reward sensitivity have been shown in adolescents with increased substance use vulnerability (Tervo-Clemmens et al., 2017, 2020), and we have recently shown that striatal tissue iron, reflecting DA availability (Larsen et al., 2020), contributes to frontostriatal development (Parr et al., 2021) and to individual differences in rewarded response inhibition in adolescence, with stronger effects of rewards in individuals with *high* tissue iron relative to *low* iron (Parr et al., 2022). We will leverage this template to understand the role of striatal neurophysiology in rewarded response inhibition in adolescents at risk for problematic substance use.

The National Consortium on Alcohol and NeuroDevelopment in Adolescence (NCANDA) study combines neuroimaging with assessments of executive function and substance use in a large, multisite, longitudinal cohort (ages 12-21 at baseline). Indices of striatal tissue iron were obtained via time averaged and normalized T2* weighted images (nT2*w) for the Duke and Pittsburgh sites (300 participants (55% F), up to 5 visits; 1152 sessions). Executive function was assessed using the anti-saccade task (reward and neutral conditions). Linear mixed effects models investigated relationships between nT2*w, anti-saccade, and binge drinking (Hasler et al., 2022).

In confirmation of prior studies (Peterson et al., 2018), nT2*w indices of DA-related striatal neurophysiology increased throughout adolescence into adulthood (B = .09, t =2.70, p =.007). Preliminary results suggest that adolescents with *high* nT2*w endorsed higher levels of binge-drinking relative to *low* (B = -.42, t =-2.39, p =.02). Anti-saccade performance improved across adolescence (B = .38, t =8.45, p <.001) and was modulated by rewards (B = .25, t =6.04, p <.001; reward M =.81, SE =.008; neutral M =.76, SE =.009), and binge drinking was associated with enhanced rewarded anti-saccade performance (B = .35, t =1.94, p =.05; binge drinking M =.88, SE =.01; non- M =.78, SE =.01), potentially reflecting increased reward sensitivity.

We provide novel *in vivo* evidence that individual differences in DA-related neurophysiology may support increased reward sensitivity, which may contribute to higher incidences in binge-drinking. Future work will examine longitudinal relationships between neurobiological factors and deviations from normative development that predict substance use into adulthood.

Saturday, September 9, 2023

3-C-14 - Data-driven identification of neurobiological phenotypes during threat learning in youth exposed to childhood trauma and associations with psychopathology

Stephanie Decross [1], **Margaret Sheridan** [2], **Nim Tottenham** [3], **Katie McLaughlin** [1]

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Details

Objective: Childhood trauma (CT) alters patterns of neural activation and connectivity during threat conditioning in ways that contribute to psychopathology. Multimodal measures of brain function (e.g., activation, connectivity) offer complementary information about the neural basis of threat learning, and are typically analyzed separately. However, aspects of environmental experience and psychopathology may be more related to complex combinations of neural activation and connectivity profiles than single indicators. Additionally, group-level analytical approaches considering neural metrics separately fail to capture considerable individual variability within groups. Unsupervised machine learning techniques enable the simultaneous analysis of measures of interest, e.g., neural activation and connectivity, while addressing meaningful variability by identifying latent structures of similarity across all participants. This study leverages a data-driven approach to characterize differing profiles of neural functioning and describe the associations of these profiles with CT and psychopathology.

Methods: 147 youth (aged 8-16 years) with and without exposure to CT underwent a differential threat conditioning procedure during an fMRI scan. Dynamic patterns of learning were described by the habituation rate of activation of regions-of-interest to CS+>CS- over the blocks of the task, as previously. Functional connectivity was assessed with generalized psychophysiological interaction analyses. Right amygdala habituation rate (AHR) and right amygdala-hippocampus connectivity (AHC) were the selected neural measures for the present analysis, as both previously exhibited differences as a function of CT and were associated with psychopathology in separate analyses. A k-means clustering analysis was performed over AHR and AHC. A chi-squared test examined the distribution of CT-exposed youth over the clusters, and multiple regression was used to examine associations with psychopathology.

Results: Various fit statistics converged upon 3 as the optimal number of clusters. All 3 clusters displayed statistically unique mean values of AHR and AHC. Cluster 1 (‘Reactive Profile’) comprised those with increasing reactivity and medium connectivity levels; cluster 2 (‘Extremes Profile’) comprised those with the most habituation and least connectivity; and cluster 3 (‘Adaptive Profile’) comprised those with medium habituation and the greatest connectivity. CT-exposed youth were overrepresented in the Extremes Profile, and very overrepresented in the Reactive Profile. Cluster membership predicted psychopathology, such that the Extremes and Reactive Profiles were associated with greater levels of depression, panic, generalized anxiety, externalizing, and PTSD symptoms than the Adaptive Profile, and did not differ between themselves.

Conclusions: Neurobiological phenotypes during threat learning may be identified by allowing data-driven analyses to cluster participants with similar profiles of neural activation and connectivity. Importantly, CT was significantly associated with two differing phenotypes, highlighting individual

variability following environmental exposure to threat. Both CT-related phenotypes were associated with transdiagnostic psychopathology, suggesting multiple neurobiological pathways to psychopathology. Some CT-exposed youth were clustered in the Adaptive Profile, suggesting a potential pathway to resilience. Differences in psychopathology were not identified between the CT-associated profiles in the present analysis. However, data visualizations (e.g., of PTSD symptoms) suggest that with even more highly powered studies, further clinically-relevant differentiation may be detected. Future work should move towards simultaneously analyzing multiple modalities of neural data in large samples to further elucidate the complex interplay of neural systems and how such patterns relate to environmental experience and psychopathology.

3-E-33 - Differential developmental contributions of limbic and motor connectivity underlying fine motor function in preschool-age children with and without ADHD: a longitudinal study.

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Details

Objective: While diagnosis of attention-deficit/hyperactivity disorder (ADHD) is primarily characterized by symptoms of hyperactivity and inattention; it is highly associated with fine motor delays and difficulties. Fine motor development in the preschool age is well characterized on a clinical level, but its neural underpinnings are not well understood. In this study, we employ a longitudinal approach to examine development of structural connectivity and fine motor skills and examine their association and how it differs in children with ADHD.

Methods: This study employed linear mixed-effects models to characterize developmental (i.e., age-related) changes in fine motor function (e.g. overflow, as measured by the PANESS instrument), and structural connectivity using diffusion tensor imaging (DTI). Data were drawn from a longitudinal study of preschool-age children with and without ADHD, with an overall sample of 127 children and adolescents (ages 4-7 at start of study) either with an initial diagnosis of ADHD (n=72, 29 girls) or typically developing (TD) controls (n=55, 23 girls) with MRI scans collected at a single site. There were a total of 376 time points, from which there were 208 usable DTI scans across 94 subjects. DTI data were run through FSL TBSS pipeline, and ROIs were defined from JHH DTI atlas. Outliers removed on a within-model basis (residual >2.5sd from mean), fit using natural splines, with Holm test for multiple comparisons (consistent with methods from Simmonds et al., 2014).

Results: Consistent with prior studies, developmental increases in fractional anisotropy (FA, higher values reflect greater integrity of white matter tracts) were seen broadly across the brain. Neuroimaging analyses revealed differences in development of connectivity by diagnosis, with some regions (corpus callosum, internal capsule, corona radiata) showing greater early developmental FA increases (age 4-7y) in ADHD than controls. Further, associations were seen in the interaction of age, diagnosis, and fine motor function. In limbic circuitry (cingulum), early developmental increases in FA were associated with better fine motor function in ADHD group, and poorer function in TD group. In contrast, in motor circuitry (internal capsule), the TD group showed that FA development during this time was associated with better fine motor function, while the opposite association was seen in ADHD.

Conclusions: These findings suggest differences in the development of motor circuitry in preschool-age children with ADHD. However, differences in fine motor development in ADHD seem to be underpinned by a dissociation in the development of motor and limbic circuitry, such that connectivity with the limbic system supports fine motor development in controls but not in ADHD.

3-E-34 - A shifting role of thalamocortical connectivity in the emergence of large-scale functional brain organization across early lifespan development

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Details

Introduction. How does the brain acquire specific functions across different areas (i.e., functional specialization), and how do functionally specialized areas organize major processing architectures such as cortical hierarchy across development? While the interplay between intrinsic (i.e., genetic patterning) and extrinsic (i.e., sensory experiences relayed through thalamic connections) mechanisms have been, for long, considered critical for such developmental processes during the embryonic stages, our understanding of the postnatal brain development is still limited. Given thalamocortical circuitry (established during early development) plays a fundamental role in sensory processing and continues to evolve throughout the lifespan, it may play a critical role in shaping functional organization throughout postnatal development. Accordingly, in this study, we examined the developmental effects of thalamocortical connectivity on large-scale functional brain organization across infancy, childhood, adolescence, and young adulthood.

Methods. First, we employed connectopic mapping to comprehensively chart the gradually changing functional relationship between the thalamus and the neocortex in two large-sample developmental cohorts: developing Human Connectome Project (HCP) cohort consisting of 195 infants (39.7 Â± 3.0 weeks), and the HCP development cohort comprising 603 participants (14.8 Â± 3.9 years). We then employed mechanistic approaches, such as genetic transcriptomic association analysis and developmental brain simulation based on generative network modeling, to interpret the developmental changes. Through thalamus-centered (e.g., core and matrix genes) and whole-brain (i.e., Allen Human Brain Atlas) analyses, we comprehensively delineated subcortical-cortical gene influences, and then leveraged generative network modeling to simulate brain development. Finally, perturbing the network simulations allowed us to identify the age window significantly contributing to the emergence of large-scale cortical hierarchies.

Results. We found that the development of thalamocortical connectivity showed diverging patterns across age, indicating a developmental change in the relationship between the thalamus and macroscale cortical functional organization. During infancy, thalamocortical connectome topology showed strong anchors in low-level sensory regions while the other end was spread out across undifferentiated higher-

order cortical regions, indicating that the thalamocortical connections lay the basis for the development of cortical hierarchy. We also found a significant interaction with cortical genes involved in developmental processes during infancy, but not childhoodâ€“young adulthood. However, during childhood to adolescence, these thalamic projections undertake a unique role of differentiating between internally- and externally-oriented functional processes, suggesting the emergence of mature functional systems. Specifically, the salience network forms a stable anchor that differentiates between external-oriented networks such as dorsal attention, visual and sensorimotor networks on one gradient, and the default mode network on the other gradient. Moreover, this differentiation reflected the distinct patterns of underlying thalamic projections based on the relative density of â€˜core' and â€˜matrix' cells. Finally, we demonstrated that the thalamocortical connectivity is a major player in scaffolding the emergence of a continuous internal-external functional brain stream (i.e., 'functional gradientâ€ by Margulies, et al. PNAS 2016) and modular structures using generative network modeling. Specifically, our perturbation analysis revealed its highest influence in later age groups (i.e., above 12 years), particularly in the development of cortical hierarchy, including the internal processing areas such as the default mode network.

Conclusion. Our findings provide compelling evidence of the active role of thalamocortical connectivity in shaping large-scale functional brain organization, emphasizing its significant impact across the early developmental stages. These results may provide new insights into developmental neuroscience, as well as clinical conditions that are related to atypical interaction between intrinsic and extrinsic mechanisms, such as autism and schizophrenia. Additionally, our study challenges the prevailing cortico-centric models of large-scale functional brain organization by highlighting the importance of examining subcortical brain structures, particularly the thalamus.

3-E-43 - Connectivity Between Striatum and Task Positive Networks is Modulated by Long-term Stimulant Exposure in Childhood ADHD, an ABCD study

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Details

Background

Stimulants (methylphenidate and amphetamines) are the first-line pharmacological treatment for Attention-Deficit/Hyperactivity Disorder (ADHD) and their acute administration attenuates symptoms via upregulation of striatal dopamine activity. An emerging area of research uses resting-state functional connectivity (rs-FC) to test the neural correlates of stimulant exposure and points to potential modulatory effects on rs-FC. However, progress is stymied by relatively small sample sizes and methodological heterogeneity, with little known about the effects of long-term exposure. We explored striatal-cortical rs-FC correlates of long-term stimulant exposure in youth with ADHD and their relation to symptom improvement across two years. Advantages of our approach include a large sample size as well as a focus on long-term outcomes, both made possible by use of data from the Adolescent Brain Cognitive Development (ABCD) study.

Methods

We selected children (n=202; 77 F; mean age at baseline=9.9 years [sd=0.65]) from the ABCD study with moderate to severe ADHD symptoms at baseline (based on the Kiddie Schedule for Affective Disorders and Schizophrenia and T score>=60 on the Child Behavior Checklist ADHD Problems Scale) who had complete data and were recommended by the ABCD study for rs-FC data analysis. Using pretabulated rs-FC data, in which striatal seeds were 6 ROIs from the ASEG atlas and cortical networks were 10 networks from the Gordon atlas, we constructed Bayesian hierarchical models in which change in striatal-cortical rs-FC across two years (2-year follow-up baseline) predicted stimulant exposure (n=89), controlling for head motion, gender, and socioeconomic status. Given the comorbidity and polypharmacy in the sample, sensitivity analyses tested the specificity of initial results and tested for associations with amount of stimulant exposure. Lastly, for striatal-cortical connections associated with stimulant exposure, we explored correlations with ADHD, externalizing, and internalizing symptom improvement.

Results

Bayesian hierarchical models revealed strong evidence, as defined by 0 falling outside the 95% credible interval for an estimated effect, for associations between stimulant exposure and change in 2 striatal-cortical functional connections at rest, which demonstrated specificity in two sets of control analyses. These were left caudate-frontoparietal network (Est.=-5.13, sd=1.86, 95% QI=[-8.86,-1.58]) and left putamen-ventral attention network (Est.=-2.94, sd=1.19, 95% QI=[-5.35,-0.63]). Additional associations emerged which were strong but weakened when analyses were limited to children exclusively exposed to stimulants, including with left putamen-cinguloparietal network (Est.=2.00, sd=0.73, 95% QI=[0.61,3.48]) and left nucleus accumbens-dorsal attention network (Est.=-4.13, sd=1.96, 95% QI=[-8.05,-0.34]). We did not identify any associations with the amount of stimulant exposure, however, there was an interaction between exposure and rs-FC change for left putamen-ventral attention network when predicting ADHD symptom improvement at the 2 year follow-up, controlling for baseline symptoms (Est.=5.22, sd=2.47, 95% QI=[0.47,10.22]). Post-hoc tests indicate this was driven by the non-exposed group, for whom left putamen-ventral attention network rs-FC attenuated over 2 years for children whose symptoms no longer met clinical criteria (t(110)=2.2, p=.030).

Discussion

Results contribute to the burgeoning literature on the modulatory effects of stimulants on rs-FC, and our study is among the first to investigate the effect of chronic stimulant exposure. Specifically, results reveal the stimulant effect on the longitudinal rs-FC changes between left caudate and putamen and canonical task-positive networks, such as frontoparietal and ventral attention networks. More broadly, the study highlights the diversity and particularity of questions that can be addressed using large multi-site datasets such as ABCD.

3-I-80 - Lateralization of activation in the superior temporal gyrus for speech processing in sleeping infants is predictive of their language skills in kindergarten: a task-based fMRI study.

Jin Wang [1], **Ted Turesky** [2], **Megan Loh** [1], **Ja'kala Barber** [1], **Victoria Hue** [1], **Escalante S. Elizabeth** [2], **Adrian Medina** [1], **Nadine Gaab** [1, 2]

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Details

Using functional magnetic neuroimaging (fMRI), prior studies have observed that infants already exhibit left-lateralized brain activation in the superior temporal gyrus (STG) for speech sentence processing even during sleep. Using electroencephalogram (EEG), other studies have found that electrophysiological responses to oddball speech sounds in infancy are prospectively associated with language and literacy outcomes at preschool and school age. However, EEG does not provide spatial accuracy for brain function and the speech sounds in those studies were limited to a few syllables. Little is known about whether brain activity in STG localized by task-based fMRI for speech sentence processing, a more naturalistic task, in sleeping infants is associated with subsequent language outcomes. To address this gap, the current study involved 59 3-12-month-old infants who underwent fMRI while listening to forward- versus backward-speech during natural sleep. Of these, 25 were subsequently assessed on language skills in preschool/kindergarten. We observed that neither the amplitude of brain activation in the bilateral STG nor standardized behavioral measures were associated with subsequent language skills in kindergarten. However, the left-lateralization index of brain activation in STG consistently predicted various aspects of language skills, including expressive language, receptive language, and phonological awareness. Overall, our findings provide the first evidence suggesting that brain indices evoked by language tasks in sleeping babies during fMRI can be a useful tool and may be more sensitive than behavioral measures in predicting later language skills.

3-I-81 - Longitudinal associations between language network characteristics in infant brain and school-age reading abilities are mediated by early-developing phonological skills

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Details

Background: Reading acquisition is a prolonged learning process relying on sound and early language development starting in utero. Behavioral longitudinal studies have demonstrated that infant language abilities were prospectively associated with preschool/kindergarten language skills, which in turn related to school-age reading performance. The advances of pediatric neuroimaging techniques facilitate the characterization of the neural network mechanisms underlying language development in infancy. However, it is still unknown how the early-emerged language network scaffolds long-term reading acquisition.

Objective: To examine whether and how the FC characteristics of the language neural network in infancy are associated with individual differences in children's language and preliteracy skills in kindergarten and subsequent reading abilities.

Methods: Our research question was addressed using a seven-year longitudinal dataset, spanning infancy to elementary school ages. Seventy infants (32 females) completed resting-state fMRI scanning during natural sleep (mean age = 9.4 $\pm$3.6 months) and were followed until kindergarten (mean age = 5.7 $\pm$0.7 years), where their oral language, phonological processing skills, and rapid automatized naming (RAN) abilities were assessed behaviorally. Of this larger cohort, thirty-nine (20 females; mean age = 7.7 $\pm$0.8 years) were subsequently seen in second grade and assessed on their word reading abilities. The intrinsic functional organization of the infant language network was first probed using the hierarchical

clustering. Correlation and mediation analyses were subsequently performed to evaluate prospective associations between infant language network characteristics and school-age language and reading abilities.

Results:

1. A modular architecture (Q = 0.30) was identified for the infant language network, which included three modules: a) an inferior frontal (IFG) module comprising bilateral inferior frontal gyri and their orbital part; b) a middle frontal (MFG) module consisting of bilateral middle frontal gyri; and c) a temporoparietal (TPG) module involving bilateral middle temporal and angular gyri.
2. Longitudinal behavior analyses showed that phonological processing skills and RAN abilities at the kindergarten time point were significantly correlated with word reading abilities at the elementary school time point.
3. FC of the IFG module within the infant language network was positively associated with phonological processing skills at kindergarten age and word reading abilities at elementary school while controlling for infant scan age, head motion, nonverbal IQ, home literacy environment, and family socioeconomic status. Moreover, keeping the covariates consistent, mediation analyses further revealed a significant mediation role of kindergarten-age phonological processing skills on the relationship between the infant FC and school-age word reading abilities.

Conclusion: The current study demonstrates that the functional characteristics of the infant language network are linked to kindergarten-age phonological processing skills, and further support later reading development. Our findings shed light on the scaffolding role of the early-emerging language neural network in supporting the development of core language/preliteracy skills and laying the foundations for subsequent reading acquisition.

3-J-85 - Neural synchrony during parent-child spatial problem-solving interaction: Role of parent verbal and gesture strategy

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Details

Synchronous interactions between parent and child are fundamental for children's development. Most prior work examined synchronous interactions focused on the relations to children's social cognition development (Nguyen et al., 2020) or emotional outcomes (Feldman, 2007a, Feldman, 2017). However, such interactions played a vital role in children's cognitive development as well (Casey et al., 2000; Mahy et al., 2014; Rueda et al., 2004; Hoeft et al., 2007; Redcay et al., 2008). The challenge of exploring how synchronization affects children's cognitive development lies in constructing a natural interaction scenario that requires the participation of cognitive abilities. fNIRS (functional near-infrared spectroscopy)-based hyperscanning, which measures neural data from all participants simultaneously using multiple devices, offers the opportunity of setting a natural interaction in the laboratory. In the current study, we apply fNIRS-based hyperscanning in a cooperative spatial task (tangram puzzle) and do

the video recording for the whole session. Two main brain areas from both hemispheres, the dorsal lateral prefrontal cortex (dlPFC) which is relevant to problem-solving, and the temporoparietal junction (TPJ) area which is relevant to social mentalization, are covered using 8 by 8 fiber distribution through fNIRS. During the task, two participants are asked to cooperate with each other to solve a tangram puzzle together. Our goal in the current study is to explore how different parental strategies in this cooperative spatial task relate to different neural synchrony patterns. Therefore, we categorized parental strategies into two categories: verbal support and gesture support (Clingan-Siverly et al., 2021), and did the behavioral coding based on the videotape. After running the preprocessing to remove noise, we run the wavelet transform coherence (WTC) to represent the neural synchrony patterns underlying different conditions and strategies. We shuffled the dyads and ran WTC among random pairs (two participants coming from different families) as the control group. The results revealed higher WTC scores in regular pairs than in random pairs ($F(1, 287) = 99.2$, $p < 0.001$, Î·2 = .15ï¼‰ and the random pair is not related to the cooperation ($r = -.292$, $p = 239$). In other words, the elevated interpersonal neural synchrony came from real cooperation and interaction instead of doing the same task. Then, we aligned the behavioral data with the neural data to conduct strategy-based analysis. The effect of the strategy was significant and neural synchronization of the gesture strategy was significantly different from the no-strategy. When we zoomed into specific gesture strategy events, we found that the WTC score increased by comparing before, during, and after the gesture event, which meant the neural synchronization went up with the unfolding of the gesture strategy ($F(2, 26) = 0.001$, $p = 0.004$), controlling for overall WTC differences. From the spatial perspective of synchronous patterns, the highest levels of synchrony came from the channel pair based on dlPFC of the parent. This may reveal that during a cognitive relevant interaction, parent strategy plays a role and the child process information input given by the parents to help themselves develop cognitive abilities. Overall, from the current study, we explored the dynamic change of neural synchrony during a cooperation cognitive task and the results showed that neural synchrony was higher in cooperation, went up with the unfolding of strategy, and showed up in a particular brain area.

3-K-91 - Early Life Stress Blunts the Neuroimmune Association of C-Reactive Protein and Nucleus Accumbens Activation During Adolescent Reward Processing

Justin Yuan [1], **Saché Coury** [1], **Tiffany Ho** [2], **Ian Gotlib** [1]

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Details

Early life stress (ELS) is associated with an increased risk of developing psychopathology in adolescence. Converging lines of evidence have demonstrated that ELS affects immune function and neural circuits underlying reward processing. Importantly, elevated levels of systemic inflammation have been found to be associated with blunted responses to reward in the ventral striatum, which includes the nucleus accumbens (NAcc), in both clinical and typically developing samples. It is unclear, however, if exposure to ELS exacerbates this association; and if these patterns are evident in adolescence. Here we tested whether exposure to ELS during childhood moderates the association between systemic inflammation and neural activation in adolescents as they completed a monetary reward processing task.

Our sample included 105 adolescents from the community who were participating in a longitudinal study of psychobiological mechanisms of exposure to ELS (mean age=16.01 years; SD=1.45 years;

range=13.07-19.86 years; 59F/46M). ELS during childhood was assessed at the onset of the study when participants were a mean age of 11.5 years using the Traumatic Events Screening Inventory for Children (TESI-C), an interview that asks participants about their prior exposure to over 30 types of stressors. Participants' responses were coded for objective severity and a cumulative score of ELS severity was calculated for each participant. Current levels of systemic inflammation were assessed using a dried blood spot protocol where participants provided a blood sample that was assayed for circulating levels of C-reactive protein (CRP). Participants also underwent a functional magnetic resonance imaging (fMRI) scan during which they completed a monetary incentive delay (MID) task, which probes neural responses during the anticipation and outcome of rewards and losses. We modeled participants' neural activation in the NAcc during two phases of the task: anticipation of reward > neutral and outcome of reward > neutral. Parameter estimates of activation were extracted using a bilateral anatomical NAcc mask derived from the Harvard-Oxford atlas (50% threshold). We tested whether participants' exposure to ELS significantly moderated the association of CRP levels with NAcc activation during the contrasts, controlling for assay batch, BMI, age, sex, race, MRI scanner upgrade, and previous Covid infection. Significance was set to a multiple comparisons-corrected a=0.025 for each contrast.

We found a significant interaction between participants' cumulative exposure to ELS and their CRP levels on NAcc activation during the outcome of reward contrast (B=-0.31; 95% CI=[-0.53,-0.09]; t(87)=-2.82, p=0.006). Specifically, in youth with lower ELS exposure, higher levels of CRP were associated with higher levels of NAcc activation during outcome of reward. Conversely, in youth with higher ELS exposure, higher levels of CRP were associated with lower levels of NAcc activation during outcome of reward. The interaction effect of ELS and CRP on NAcc activation during the anticipation of reward was not significant.

We found that exposure to ELS in childhood significantly moderated the association of inflammation with NAcc activation during outcome of monetary reward. Adolescents with low ELS exposure had a positive neuroimmune association, suggesting that in typically developing adolescents, higher levels of systemic inflammation are associated with activation of reward processing regions. Conversely, high ELS exposure was associated with a blunted relation between inflammation and activation in reward regions. This negative association is consistent with previous neuroimmune findings in both typically developing and clinical populations. Our findings highlight the importance of considering environmental influences during sensitive periods of development and suggest that maladaptive outcomes associated with exposure to ELS are due, at least in part, to altered immune function.

Poster Abstracts

Poster Session 1

Thursday, September 7, 2023

A- Attention

1-A-1 - Chronic home radon exposure is associated with altered neural and behavioral indices of attention

Haley Pulliam [1], **Christine Embury** [1], **Hannah Okelberry** [1], **Danielle Rice** [1], **Anna Coutant** [1], **Ryan Glesinger** [1], **Tony Wilson** [1], **Brittany Taylor** [1]

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Details

Background: Radon is a prevalent, naturally occurring gas which contributes to radiation within the environment and is the second-leading cause of lung cancer worldwide. Other environmental toxins have been linked to disadvantageous neural outcomes including impaired cognitive functioning in children and adolescents. However, radon has seldom been examined for its effects on the developing brain. This study aimed to investigate the effects of chronic home radon exposure on top-down neural processes of attention in youths. **Methods:** 47 participants (aged 6-14 years) completed a Simon interference task during MEG and radon levels were measured in their homes. Time-frequency analyses of the MEG data indicated increased theta (3-6Hz, 150-550ms) and gamma activity (78-96Hz, 100-350ms), as well as decreased alpha (8-12Hz, 400-600ms) and beta activity (14-18Hz, 200-450ms) during the task relative to baseline. Source reconstruction of each oscillatory band was performed, and subtraction maps comparing task condition (Simon-control) were computed to explore attentional interference effects. We used whole-brain correlations to explore associations between home radon exposure and interference-related oscillatory dynamics, controlling for the effect of age. **Results:** Youths with greater radon exposure exhibited aberrant oscillatory activity in widespread cortical areas related to attentional processes spanning predominantly right frontoparietal areas (rs = -.569-.576). To explore the functional relevance of these neural aberrations, we computed a series of mediation analyses to determine the extent to which neural indices of attentional interference mediated the effects of radon exposure on behavioral performance during the task. We found that neural interference in the alpha band in the right DLPFC mediated the effect of radon exposure on conditional accuracy differences (Î² = -.208, 95% CI[-.416, -.057]), such that youths with greater radon exposure did not adequately recruit the right DLPFC (Î² = .520, p < .001), which was associated with a greater behavioral interference effect (Î² = -.400, p = .026]. In contrast, conditional differences in gamma activity in the middle cingulate seemed to serve as a compensatory mechanism. Specifically, greater gamma interference in the middle cingulate mediated the effect of exposure on accuracy (Î² = .374, 95% CI[.144, .796]), such that youths with more

radon exposure recruited this region to a greater degree during the Simon condition (Î² = .606, p < .001), which subsequently predicted a reduced behavioral interference effect (Î² = .617, p < .001). **Conclusion:** Herein, we demonstrated that youths with greater exposure were not recruiting expected regions associated with higher order cognition while instead recruiting other areas more strongly to compensate for their performance in the task. The data suggest disrupted cortical processing in attentional networks related to radon exposure in children and adolescents, which have direct implications on observable behavioral performance.

1-A-2 - Mechanisms of visual spatial attention in reading in children

Mahalakshmi Ramamurthy [1], **Jason Yeatman** [1], **Grace Adebogun** [1], **Katelyn Osuna** [1, 2]

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Details

Background: Shifting and focusing attention is a key mechanism in the extraction of sensory information, to allow for adaptive behavior. Reading is a perfect example: spatial attention must shift precisely from one location to the next in order to select letters or words in sequence. The interplay between the development of attention and reading ability has yet to be measured in an ecologically valid paradigm in children. In our previous work we reported the role of covert attentional mechanisms in reading in skilled readers (adults: 18-40yrs, n=22). Here we extend the same paradigm to evaluate the effect of visual spatial attention in a letter identification task in children between 6 to 12yrs (n=19).

Methods: A string of 6 letters was presented briefly (120ms) and participants were asked to report a post-cued letter from one of the six positions, from 12 letter choices. Attention was manipulated by introducing two types of pre-cues: exogenous (50ms, peripheral, uninformative) and endogenous (150ms, central, informative). On valid trials, the pre-cue and post-cue sides match; on invalid trials they mismatch, and on neutral trials both sides of the fixation are pre-cued. Eyes were tracked to ensure fixation while encoding.

Results: Similar to adults, children showed a significant cue effect for both exogenous (valid>invalid) and endogenous cues (valid>neutral). Notably, the benefits were greatest at the longest cue to target onset interval (600ms) for endogenous cues (similar to adults) but showed no difference between 50 and 100ms for exogenous cues, unlike adults who showed a temporal time course, with exogenous cue benefits peaking at the shortest cue-target interval of 50ms. On neutral trials, we observed a W-shaped serial position function where encoding accuracy (') varied as a function of letter position with higher accuracy for outermost positions (1,6) compared to the middle crowded positions (2,5) [Outer - middle: Endo âˆ†' = 1.36; Exo: âˆ†' = 2.54], this is also similar to adult participants reported in our previous work. Interestingly, the difference in encoding accuracy between the outermost and middle positions was significantly reduced with a valid endogenous cue (âˆ†' = 0.127; t= 3.461, p=0.00078) but not with an exogenous cue (âˆ†' = 1.83; t = 1.669, p=0.09).

Conclusions: Our results demonstrate that although exogenous and endogenous cue benefits are of comparable magnitude, in children, they exhibit differential functional utility. These findings are similar to what we reported in adult participants. Together our findings suggest that the developmental effects of visual spatial attention are mainly manifested as an increase in the magnitude of cue benefits and a

more robust temporal dynamics of these effects, specifically in the exogenous system, however it is remarkable that the function utility of these attention effects in the context of specific task are consistent across development. We hypothesize that endogenous cues enable uniform encoding of elements within a string and therefore might be a key mechanism for the development of reading ability.

1-A-3 - Visuo-spatial Attention Development is Modulated by Local Computations in the Dorsal Stream

Patricia Hoyos [1], **Anna Lyn Williams** [1], **Edan Daniel Hertz** [1], **Sabine Kastner** [1], **Jesse Gomez** [1]

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Details

Pivotal to all aspects of human cognition is attention, our ability to selectively focus on a signal and filter out irrelevant noise. As a species reliant on vision, humans continuously use visuo-spatial attention. However, how such an ability emerges during childhood and the neural correlates that underlie the protracted development of visuo-spatial attention are not well known. This is a striking gap in human neuroscience considering the prevalence of Attention Deficit/Hyperactivity Disorder (ADHD). We created two novel, child-friendly videogames designed to help us understand how visuo-spatial computations develop in the dorsal stream, comprised of visual regions known to control attention allocation in space. In the first game called 'Cartoonotopyâ€, participants fixate at the center of the screen as a colorful cartoon-filled sliding bar sweeps across the visual field. This allows us to map the receptive field of the population of neurons within a voxel (a 3-D pixel unit in a Magnetic Resonance Image) as the area of visual space from which it receives information (e.g., its window to the world). In the second game, 'gopheRFieldâ€, participants fixate while catching gophers emerging anywhere from a grid of gopher holes in the periphery. This allows us to quantify how each voxel's receptive field window dynamically shifts in response to the allocation of visuo-spatial attention to the periphery. Thus far, we have collected data from n=10 adults (mean age of 27.3), and n=2 children, with data collection ongoing. In our adult population, we find that the allocation of attention to the periphery significantly increases the receptive field window's size and eccentricity (distance from the center of the visual field), particularly in higher-order regions of the dorsal stream that are more specialized for visuo-spatial attention control ($p<0.005$). We find a similar trend in the children's data that we have begun to analyze. However, we hypothesize that development will significantly modulate receptive field properties and their dynamics. Previous literature indicates that visuo-spatial attention undergoes significant development as children get older. This developmental trajectory impacts the acquisition of skills that heavily rely on visuo-spatial attention, like reading (Hoyos et al., 2020). By studying the development of the attention network, we will provide useful benchmark data for future studies in children with ADHD and dyslexia, offering translational insight as to why there is a high comorbidity between the two disorders.

B – Brain connectivity

1-B-4 - Impact of Perceived Hostility on Triple Network Model Connectivity in Children and Adolescents

Danielle Rice [1], **Jake Son** [1], **Mikki Schantell** [1], **Giorgia Picci** [1], **Hannah Okelberry** [1], **Anna Coutant** [1], **Grace Ende** [1], **Yu-Ping Wang** [2], **Julia Stephen** [3], **Vince Calhoun** [4], **Gaelle Doucet** [1], **Brittany Taylor** [1], **Tony Wilson** [1]

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Details

Title: Impact of Perceived Hostility on Triple Network Model Connectivity in Children and Adolescents

Introduction: The emergence and increased prevalence of psychiatric disorders in children and adolescents continues to be widely studied, including the role of social factors such as emotional support and social distress and its influence on brain connectivity throughout development. However, research related to perceived hostility in youth and its impact on long-term changes in cross-network connectivity is limited. This longitudinal study utilized the triple network model of psychopathology as a framework to study how perceived hostility impacts the longitudinal trajectory of connectivity between the salience network (SN) and frontoparietal network (FPN), and the SN and default mode network (DMN).

Methods: Resting state fMRI data were collected yearly at three timepoints from 93 participants (ages 9-15) and processed using the DPABI Toolbox. We computed SN-FPN and SN-DMN connectivity using the Yeo-7 atlas and estimated a latent growth curve model to explore longitudinal connectivity changes. Participants also completed the Emotion Battery of the NIH Toolbox, which measured a range of domains including the Perceived Hostility fixed form (Ages 8-17 v2.0) measure. The main analysis was conducted using MPlus to test a model including age and sex as control variables, and perceived hostility as the predictor variable.

Results: In the baseline growth model without predictors, we found no systematic change in SN-FPN connectivity over time (slope=0.027, p=.293). However, we observed significant modulation after including perceived hostility as a predictor, such that greater perceived hostility was associated with increases in SN-FPN connectivity over time (b=.010, p=.012). Similarly, we did not find systematic changes in SN-DMN connectivity over time (slope=.022, p=.423), although including perceived hostility in the model altered its trajectory such that higher perceived hostility was associated with increases in SN-DMN connectivity over time (b=.009, p=.024).

Conclusions: Perceived hostility alters connectivity among critical networks for psychopathology over time in children and adolescents, suggesting that the degree of social distress related to perceived hostility may impact the longitudinal trajectory of key brain networks and modulate the risk for psychopathology as adolescents enter young adulthood.

1-B-5 - A hierarchical comparison of structural connectomes in major depressive disorder versus controls in two large population samples

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Details

Major Depressive Disorder (MDD) is considered to be associated with structural dysconnectivity in the brain. As such, network science is increasingly used to understand the pattern of disruption in MDD. Hubs (regions with the most connections) are central to brain connectivity and are frequently implicated in brain disorders. However, it remains uncertain if MDD is driven by structural deficits that are disproportionately concentrated in hubs or distributed more generally across brain connections. Previous studies were limited in sample sizes and there is a lack of robust replication. We utilised two large adult population cohorts: UK Biobank (UKB, N=5104) and Generation Scotland (GS, N=725) as discovery and replication samples, respectively, to investigate MDD case-control differences in brain network architecture. Graph theory analysis was conducted across three hierarchical levels global, tier (nodes were grouped into four tiers based on degree) and rich club (connections between hubs), and local. Network-based statistics (NBS) were also used to study group differences at the region-to-region connection level. In UKB, significant reductions in network efficiency were observed in MDD cases globally (Cohen's *d*: -0.08, pFDR: 0.033) and across all tiers (Cohen's *d* range: -0.07 to -0.08, pFDR: 0.02). No differences in rich club organisation were identified. Locally, reductions in nodal efficiency of hubs, mainly those involved in emotion regulation and reward processing, were observed in MDD cases (Cohen's *d* range: -0.08 to -0.1, pFDR range: 0.013 to 0.035). No differences were identified at the connection level using NBS. Similar effect sizes were observed for these associations in GS but were not statistically significant in the lower-N replication sample. Collectively, these results suggest that connections between hubs remain robust in MDD, but the overall reduction in structural connectivity is a result of the accumulation of subtle but widespread impairments in connections surrounding hubs and non-hubs. Given that adolescence is the peak period for the onset of MDD, It is of interest to replicate the above analysis in adolescent cohorts, such as the ABCD study, to see if brain features of vulnerable adolescents are similar to that in adults.

1-B-6 - Influence of age on selective attention and multispectral brain connectivity

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Details

Introduction: The development of selective attention in children and adolescents is an important process that promotes the ability to accurately and quickly complete tasks. While previous work has elucidated changes in brain power during this sensitive developmental period, studies focusing on age-related changes in dynamic functional connectivity are relatively limited. In this work, we investigate

spectrally-specific functional connectivity changes in youth by harnessing the excellent spatial and temporal precision of magnetoencephalography (MEG).

Methods: MEG data were collected from 96 children and adolescents (ages 6-13) during a modified Flanker task and were preprocessed and transformed into the time-frequency domain. A data-driven approach was used to identify significant time-frequency windows for beamforming. Time-resolved theta (4-7 Hz), alpha (8-14 Hz), and gamma (66-78 Hz) windows were imaged using a beamformer and compared using a paired t-test (i.e., incongruent vs. congruent). Significant brain regions from this statistical map were subject to whole-brain connectivity analyses (for each condition separately), then subtracted to generate whole-brain interference connectivity maps. These maps were then subject to whole-brain correlations with age, while controlling for power at both seed and source regions.

Results: Reaction time was significantly correlated with age such that reaction time decreased with increasing age. Furthermore, the reaction time interference effect (i.e., incongruent - congruent) was significantly correlated with age such that older participants exhibited a greater interference effect. Connectivity in the theta band between the prefrontal and midcingulate cortices, the alpha band between the frontal eye fields and dorsolateral prefrontal cortex, and the gamma band between the inferior frontal and dorsolateral prefrontal cortices was significantlycorrelated with age. For alpha, connectivity increased with increasing age, while for theta and gamma connectivity decreased with increasing age among each node pair.

Conclusions: These findings suggest that region and spectrally-specific connectivity changes occur throughout this critical period of development across a network of regions that have been implicated in selective attention. This work contributes to the growing body of literature that examines MEG-based connectivity changes in children and adolescents.

1-B-7 - Early adolescents with an anxiety disorder have reduced amygdala to nucleus accumbens structural connectivity

Alyssa Griffith [1], **Josiah Leong** [1], **Ethan Ellis** [1]

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Details

Anxiety disorders and their medication can alter adolescent brain development. This project targeted the structural white-matter connection from the amygdala to the Nucleus Accumbens (NAcc) in early adolescents (9-10 years old). We sourced Diffusion Magnetic Resonance Imaging (DMRI) and anatomical T1 MRI data from the Adolescent Brain Cognitive Development (ABCD) study. We identified 3 groups of adolescents: (1) those with a clinical level of anxiety who did not take any medication (n=550), (2) those with anxiety who took a Selective Serotonin Reuptake Inhibitor medication (SSRI; n=31), and (3) controls on no medications (n=3,443). Comparative axon-tracing studies establish a unidirectional glutamatergic projection from the BasoLateral nucleus of the Amygdala (BLA) to the NAcc. We targeted these 2 brain areas with FreeSurfer's subcortical segmentation, then performed constrained spherical deconvolution-based probabilistic tractography between the areas, and finally extracted diffusion metrics along the anatomical trajectory of the BLA-NAcc tract. We found reduced Fractional Anisotropy (FA) of the BLA-NAcc tract across all adolescents with an anxiety disorder compared to controls. Adolescents with

unmedicated anxiety not only had lower BLA-NAcc tract FA, but also smaller volume of the BLA. Further, BLA-NAcc tract FA correlated with greater BLA volume in these adolescents. Finally, BLA-NAcc tract FA and BLA volume correlated with less severity of anxiety symptoms. These findings identify structural white-matter connectivity and volumetric reductions in adolescents with unmedicated anxiety, link connectivity to volume, and find an effect of both modalities on symptom severity. The results open the question of precedence: do changes in the BLA-NAcc connection precede or follow volumetric changes of the end regions? Future analyses of longitudinal data from the ABCD study can chart the normative growth curves of structural connectivity and volume, then measure the effect of anxiety disorders and their medications on structural brain development.

1-B-8 - Longitudinal assessment of brain functional networks across the birth transition: a pilot study

Details

Background:

Birth is the most significant transitional event in human life. During gestation, rapid neural proliferation, migration, and even regression occur alongside axonal growth and synaptogenesis[1, 2]. After birth, the brain enters phase of dramatic outgrowth and expansion. There is a surge axonal myelination, dendritic arborization, and functional synaptic contacts rapidly accrue[3]. Studies using resting-state functional connectivity MRI (rs-fcMRI) have identified nascent resting-state networks (RSNs) in infants and older fetuses[4-6], and it is thought that these networks follow a typical sequence of primary to higher-level and short- to long-range emergence as they develop[7-9]. However, the massive reorganization of large-scale functional circuits over the birth transition is under-studied, and yet could provide fundamental insight into developmental biology and the origins of many human behaviors.

Methods:

Eleven infants who completed both the fetal scan (27-37 weeks of gestational age) and infant fMRI scan (12-16 weeks after birth) of the Perinatal Imaging of Neural Connectivity (PINC) cohort were included in the present analysis. Image processing included brain extraction, motion correction and scrubbing, optimal combination of multiple echoes, normalization, ICA and CompCor denoising, and smoothing (4mm) for both fetal and infant scans. Functional connectivity was estimated between 16 regions of interest (ROIs) including bilateral visual cortex, cerebellum (CER), cuneus, supplementary motor cortex (SMA), thalamus, medial prefrontal cortex, putamen (PU), and anterior insula (aINS). We also conducted the group-level Independent Component Analysis (ICA) for each age group (fetal and infant).

Results:

Results show enhanced interhemispheric and emerging dorsocaudal connections after delivery. All subjects show significantly increased functional connectivity ($p < 0.0004$) between SMA and CER, between bilateral PU, and between bilateral aINS. Notably, the cerebellum, a key region for motor coordination, developed FC to cerebral motor regions through the visual cortex only after delivery. At

the network level, there is also a shift from a more fragmented network in the fetal brain to a more connected and clustered network in infants.

Conclusions:

This study provides longitudinal support for the hypothesis that brain develops following a "local to distributed" pattern across the birth transition. Next steps are to increase the sample size using the whole PINC dataset (scans n > 450) and to map the developmental trajectory of brain functional networks and graph features over the birth transition. It will also be interesting to examine how perinatal environmental factors interact with this growth trajectory. Such work will provide fundamental insight into the developmental of brain neurocircuitry at the beginning of human life, and assist future studies seeking to isolate atypical brain network pattern in clinical research samples.

Reference

1. Bystron I, Blakemore C, Rakic P. Development of the human cerebral cortex: Boulder Committee revisited. Nature Reviews Neuroscience. 2008;9(2):110-22.

2. Stiles J, Jernigan TL. The basics of brain development. Neuropsychology review. 2010;20(4):327-48.

3. Petanjek Z, JudaÅ¡ M, Å imiÄ‡ G, RaÅ¡in MR, Uylings HB, Rakic P, KostoviÄ‡ I. Extraordinary neoteny of synaptic spines in the human prefrontal cortex. Proceedings of the National Academy of Sciences. 2011;108(32):13281-6.

4. Gao W, Alcauter S, Smith JK, Gilmore JH, Lin W. Development of human brain cortical network architecture during infancy. Brain Structure and Function. 2015;220(2):1173-86.

5. Grayson DS, Fair DA. Development of large-scale functional networks from birth to adulthood: A guide to the neuroimaging literature. Neuroimage. 2017;160:15-31.

6. Thomason ME. Development of brain networks in utero: Relevance for common neural disorders. Biological psychiatry. 2020;88(1):40-50.

7. Fransson P, SkiÃ¶ld B, Horsch S, Nordell A, Blennow M, Lagercrantz H, Ã…den U. Resting-state networks in the infant brain. Proceedings of the National Academy of Sciences. 2007;104(39):15531-6.

8. Thomason ME, Grove LE, Lozon Jr TA, Vila AM, Ye Y, Nye MJ, Manning JH, Pappas A, Hernandez-Andrade E, Yeo L. Age-related increases in long-range connectivity in fetal functional neural connectivity networks in utero. Developmental cognitive neuroscience. 2015;11:96-104.

9. Fair DA, Cohen AL, Power JD, Dosenbach NU, Church JA, Miezin FM, Schlaggar BL, Petersen SE. Functional brain networks develop from a ‘local to distributedâ€ organization. PLoS computational biology. 2009;5(5):e1000381.

1-B-9 - Evaluating resting-state fMRI Methods Using Simulated Timeseries Data

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Details

Abstract: Thousands of participants are required to effectively study relationships between resting-state functional connectivity and mental health in youth. However, as these datasets increase in size they also increase in complexity. Datasets like the Adolescent Brain Cognitive Development (ABCD) study, for example, recruited 11,572 participants across 21 sites and require increasingly complex methods for statistical inference. Simulated data provide a ground truth against which fMRI analytical methods can be evaluated. Therefore, we developed Nebuchadnezzar, a tool for constructing realistic, simulated fMRI timeseries data from existing neuroimaging datasets. To validate Nebuchadnezzar, we simulated fMRI timeseries data based on connectivity maps for cognition and study site in ABCD. We then used conventional resting-state analysis methods to recover connectivity maps from the simulated data and compared these maps to the original ABCD connectivity maps to evaluate simulation accuracy.

Methodology: Nebudchadnezzar takes one or more connectivity maps as its input and embeds them within fMRI timeseries for a cohort of simulated participants. Each connectivity map is decomposed into the difference between two positive definite covariance matrices using eigendecomposition. Then, for each covariance matrix, a random timeseries is simulated from its corresponding multivariate normal distribution using the Cholesky decomposition. The random timeseries are added together according to per-participant mixing proportions from a randomly generated design matrix to obtain simulated fMRI timeseries for each simulated participant.

In the study, we first generated input connectivity maps for cognitive ability and for study site using the ABCD ARMS1 population (N=3000) from the ABCD-BIDS Community Collection (ABCC). Second, the connectivity maps were entered into Nebuchadnezzar for data simulation with varying numbers of participants and timepoints (n = 560, 1040, 1520, 2000, or 2480 participants or timepoints). Third, linear regression analysis was performed using the simulated fMRI data and simulated design matrix to recover connectivity maps for cognition and site. Fourth, the recovered connectivity maps were compared to the input connectivity maps using edgewise correlation; larger edgewise correlation coefficients corresponded to greater similarity between the input and recovered matrices. Finally, for each combination of timepoints and participants, 1000 simulations were performed to create a distribution of edgewise correlations.

Results: With 2480 simulated participants and 2480 simulated timepoints, the average edgewise correlation between the simulated and experimental connectivity maps were r=0.92 for cognition and r=0.79 for site. Edgewise correlation decreased as either the number of simulated participants or simulated timepoints decreased. With 560 simulated timepoints and 560 simulated participants, the average edgewise correlation decreased to r=0.87 for cognition and r=0.70 for site.

Conclusions and Future Directions: Simulated fMRI timeseries are a useful tool for testing complex analytical methods against a known ground truth. Nebuchadnezzar generated realistic, simulated fMRI timeseries based on real connectivity maps from ABCD, achieving an edgewise correlation of up to r=0.92 between the input connectivity map and the connectivity map recovered from the simulated data. Furthermore, by simulating datasets with varying numbers of participants and scan lengths, we were able to reproduce the positive relationship between study size and replicability seen in real fMRI studies. Thus, simulated data may also prove to be a useful supplement to conventional power analysis. We plan to test Nebuchadnezzar on the UK Bio Bank and other brain wide association studies in order to test and refine our code before release to the scientific community.

1-B-10 - Polyneuro risk scores reflect treatment effects in medication-naive children with ADHD

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Details

Attention-deficit/hyperactivity disorder (ADHD) treatment guides currently recommend psychostimulant medication as a first-line treatment option due to the efficacy in reducing the core symptoms of the disorder. However, medication effects are highly variable among individuals, with some experiencing little to no improvement in symptomatology, and others encountering adverse side effects that hinder continued use. Moreover, clinical subtypes of ADHD (e.g., inattentive, hyperactive, combined) have not proven predictive of treatment response, leading to a common practice of trial-and-error to find an effective medication/dosage. Recently, functional magnetic resonance imaging (fMRI) modalities have been proposed as a promising alternative to the trial-and-error method of medication selection. A reliable marker of intervention effect could offer clinicians insight to modify treatment plans more quickly rather than waiting extended periods for robust behavioral effects. In this study, we leveraged our new polyneuro risk score (PNRS) approach combined with Precision Functional Mapping (PFM) to assess its sensitivity, within individuals, to methylphenidate (MPH) administration in a medication-naive cohort of children diagnosed with ADHD. The ability to quickly monitor responders versus non-responders with a brain based marker (i.e., PNRS) has the potential to accelerate the identification of optimal treatment in patients.

Here, the PNRS framework (Byington & Grimsrud et al., 2023) was utilized to analyze high-quality resting-state fMRI data (FD<0.2mm, 8min) from the Adolescent Brain and Cognitive Development study (N=6574). We calculated the weighted contribution of each connection to various cognitive/behavioral outcomes that are known to be affected by ADHD: general ability, executive function, learning & memory, emotion dysregulation, as well as a composite score of ADHD symptoms. The connection weights for each behavior were ranked after split-half cross-validation, and then used to estimate the PNRS in an independent PFM cohort of youth diagnosed with ADHD and typically developing (TD) participants matched in several demographics (N=60, M age=9.99). This randomized, double-blind study involved two sessions of resting-state fMRI and go-no-go (GNG) task-based fMRI, with the ADHD group receiving either MPH or a placebo before each session. The TD group did not receive drug or placebo. For each participant, a PNRS per behavior was calculated for each session, and a repeated measures ANOVA was performed to assess differences in PNRS related to the intervention. GNG task performance was then utilized to identify medication responders and non-responders and determine if these subgroups had differences in PNRS responses.

PNRS were stable across sessions for the TD individuals (test-retest reliability values between 0.39 and 0.81). While we observed similar stability *across* participants for most outcomes in the ADHD individuals, we also found change *within* participants consistent with the intervention. Thus, we categorized ADHD individuals into responders and non-responders based on improved performance on the GNG task and found significant differences in PNRS between the two groups. We found that individuals categorized as responders had corresponding, consistent change in PNRS, while those who were non-responders did not - highlighting the sensitivity of PNRS to the intervention. These findings were most pronounced in the PNRS associated with executive function (EF).

The PNRS framework demonstrates sensitivity to changes in brain circuitry due to MPH administration, particularly in EF, where the change in PNRS corresponded to the change in behavior observed during the GNG task. This suggests that the PNRS framework combined with PFM has the potential to measure intervention effects within individuals, and may serve as a reliable quantitative approach as opposed to the current standard of trial-and-error for medication evaluation.

1-B-11 - Maternal blood pressure during pregnancy and offspring autonomic nervous system brain connectivity

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Details

Objective: High blood pressure, or hypertension (HTN), is a major risk factor for cardiovascular disease, and one in ten women experiences a form of HTN while pregnant. HTN in pregnancy increases risk of fetal demise and prematurity, and can be associated with poor perinatal outcomes including fetal growth restriction, preterm birth, and stillbirth. Offspring exposed to hypertensive disorders of pregnancy are at elevated risk for developing HTN and cardiovascular disease. The ANS is critical regulating blood pressure, which starting prenatally, and involves input from higher order brain regions (e.g., prefrontal cortex) after 30 weeks gestation. Connections between the ANS and cortex help

interpret environmental stressors and generate physiologic responses, but few studies consider higher order brain relative to brainstem regulators of ANS in early life. Further, how HTN affects early regulation in offspring has not be studied. As such, this study aims to evaluate relationships between maternal ANS modulation during pregnancy via blood pressure and offspring ANS brain development.

Methods: This study sample consists of 50 mother-offspring dyads. Continuous blood pressure was collected from the mothers in their third trimester of pregnancy during a standardized physiological protocol. Blood pressure signals were digitized and passed to a microcomputer. Then custom-written software detects the time and magnitude of each systolic peak and diastolic trough, resulting in a blood pressure time series.

Infant fcMRI scans of the women's offspring occurred between 2-6 weeks of postnatal age. With three layers of ear protection applied, the infant was fed, swaddled, and once asleep, he/she placed and secured on the scanner bed. Images in 6 resting state scans were acquired and averaged off-line to allow for rescanning one of the acquisitions if the infant moved. Infant fcMRI data were transformed to the 2 week (+/- 2 weeks) old template from the NIH Normal Brain Development Study using a concatenation of three registrations. Data was slice time and motion corrected, and images were iteratively smoothed.

Brain regions of interest (ROI) are the hypothalamus, dorsal anterior cingulate, dorsal medial frontal cortex, and amygdalae because of their involvement in regulation. The time course of a ROI were computed as average time course across all voxels in the ROI, and this was correlated with time course for every other voxel in the gray matter to create a map of r-values, reflecting seed-to-whole-brain connectivity. These r-values are transformed to z-values yielding a map for each participant representing the strength of correlation to the seed region.

Analytic Plan: Linear regression with the ROI connectivity map as the dependent variable and maternal blood pressure during pregnancy as the predictor variable will be used. A model for each of the ROI connectivity maps will be repeated. $P<0.05$ corrected will be considered significant.

Preliminary Results: Preliminary data showed that newborns exposed to maternal hypertensive [n=11] compared to normotensive [n=20] levels of blood pressure, had increased connectivity between the right amygdala and the dorsal medial frontal cortex and anterior cingulate.

Conclusion: This study will demonstrate the influence of exposure to a hypertensive in utero environment on offspring brain development, and further elucidate intergenerational mechanisms that impact the development of ANS regulation in early infancy.

1-B-12 - Impact of fetal inflammation on fetal functional connectivity

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Details

There is strong evidence to suggest that prenatal inflammation is a significant risk factor for neurodevelopmental or psychotic disorders in offspring. The belief is that inflammation during pregnancy can alter fetal brain development, with long-term consequences for offspring health and development. Previous research has demonstrated that newborns born to mothers with higher levels of prenatal interleukin-6, a biological indicator of maternal inflammation, show differences in functional connectivity in salience, dorsal attention, medial temporal, and subcortical networks. This prior study was conducted in a community sample of healthy mothers, and thus, suggests that even moderate inflammation experienced by a mother during pregnancy may affect brain outcomes in her child during infancy. However, to date, if and how prenatal inflammation is related to the fetal brain is still unknown.

The current study aims to fill this gap. Pregnant mothers (N = 138; 89% racial/ethnic minority) were recruited during the second and third trimester of pregnancy, and inflammation was assessed based on placental histology rather than measurement of a single cytokine at one timepoint in maternal blood. Placental tissues were examined by expert pathologists and scored for chronic placental inflammatory lesions, including chronic chorioamnionitis, villitis of unknown etiology, and chronic deciduitis. Resting-state imaging data were acquired in fetuses between 19.43 and 39.29 weeks of pregnancy.

Hypothesis testing will be performed both at the subnetwork level (between and within neural subsystems) and at the global level using a Graph theoretical approach. The network-level approach will apply a consensus procedure (infomap) that produces an optimal model comprised of approximately 14â€“16 distinct fetal networks distributed across cortical, subcortical, and cerebellar regions of interest. Once networks are defined, Spearman rank correlation followed by enrichment permutation tests will be applied to determine whether the number of connections (edges) that yield significant prenatal inflammation effects within each network pair is greater than expected by chance. Models will test the impact of prenatal inflammation on global network topography (graph metrics) and on between- and within-network resting state functional connectivity.

We expect higher intrauterine inflammation to predict reduced global efficiency and to disturb connectivity of the cerebellum, striatum, posterior cingulate, medial prefrontal cortex and insula as well as brain regions that comprise default mode and dorsal attention networks. If these results are observed, this would support the idea that the neural regions most sensitive to prenatal inflammation are those associated with behavioral impairment in existing literature. This would suggest that the increased risk for developmental disorders in children exposed to infection before birth may be due to neuroinflammatory events that occurred while they were still in the womb.

1-B-13 - Timing-related effects of prenatal opioid exposure on neonatal functional connectivity

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Details

Objective: Prenatal opioid exposure (PODE) impacts infant brain development with documented long-term consequences. Functional magnetic resonance imaging (fMRI) studies of youth and neonates with PODE reveal aberrant brain functional connectivity. Further, PODE is related to elevated risk of negative outcomes, including deficits in behavioral and emotional regulation. Despite ample evidence in animal

models demonstrating that the timing of PODE during the prenatal period significantly impacts offspring outcomes, most human fMRI studies use a binary categorization to assess drug exposure (i.e., presence of opioid use at any point during pregnancy). This severely limits the ability to detect prenatal opioid timing effects, which could have differential impacts on the brain's functional architecture. Given that large-scale brain networks start to form prenatally with the strength of long-range connectivity increasing linearly with advancing fetal age, the salience network is likely to be most affected by third trimester exposure to opioids. We hypothesize that the mechanism by which PODE alters salience network connectivity in the infant brain is shaped by prenatal opioid exposure timing factors.

Methods: Subjects included neonates with PODE (n=42), neonates with prenatal exposure to other drugs excluding opioids (PDE, n=39), and drug-free controls (CTR, n=28). Two-week rsfMRI scans were acquired during natural sleep. The Timeline Follow Back (TLFB) calendar/interview was conducted to assess prenatal frequency of opioid and other drug use in each trimester. The primary measure of interest will include prenatal opioid exposure timing (by trimester). Data collection and preprocessing is complete for this sample; the analysis plan (detailed below) will be complete by Flux.

Analysis Plan: Hypothesis-driven seed-based functional connectivity analyses will be conducted. For the salience network, the core region of interest (ROI) will include the right anterior insula. For this ROI, the timeseries extracted from processed residuals in standard space will be correlated with that of every other voxel in the brain. Resulting correlation measures will be normalized using Fisher's *Z* transformation prior to statistical comparisons. Group-level connectivity maps will be generated for each seed using one-sample *t*-tests. Quantitative ANOVA comparisons will be conducted using voxelwise multivariate modeling (AFNI's 3dMVM) to detect clusters with significant group differences after correcting for multiple comparisons at the whole-brain level (cluster-corrected at $p<.05$ with a voxelwise cutoff of $p<.001$). Control variables will include gestational age at birth, gestational age at MRI, birth weight, and sex. For each identified cluster, *post hoc* comparisons will be conducted using Tukey's test to identify significant differences between each pair of groups (i.e., PODE vs CTR, PDE vs CTR, PODE vs PDE). PODE-specific effects will be identified as clusters showing significant differences between PODE vs CTR and between PODE vs PDE. Within the PODE group, moderating effects of timing will be examined by building on the voxelwise multivariate model. Specifically, PODE timing will be added separately as a main effect.

Hypothesis: The PODE group is expected to show reduced connectivity in frontoparietal regions of the salience network. Third trimester exposure will be related to more severe reductions in connectivity.

General Implications: It is currently unknown how timing of PODE may impact early neurodevelopment. Ultimately, this work will contribute to a better understanding of brain mechanisms underlying developing cognitive systems and how functional connectivity of the brain may be altered by adversity associated with prenatal exposures. Elucidating how timing of PODE impacts neurodevelopment will inform personalized treatments to optimize outcomes in affected infants.

C – Brain function

1-C-14 - Spatial processing of limbs suggests viewing experience across development drives functional organization of visual cortex

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Details

Human visual cortex develops regions selectively involved in perceiving and recognizing ecologically important visual stimuli such as people and places. Located in the ventral temporal lobe, these regions are organized consistently relative to cortical folding, a phenomenon thought to be inherited from how centrally or peripherally these stimuli are viewed with the retina, which is referred to as the eccentricity theory of cortical organization. Face regions, viewed with central vision (low eccentricity), are located laterally on the Fusiform gyrus, while place regions, viewed with peripheral vision (high eccentricity), are located more medially in the collateral sulcus. While this center-periphery theory of cortical organization successfully predicted the emergent location of a novel representation for a new visual category learned during childhood, PokÃ©mon, whether or not this theory can describe the visual properties of all category-selective regions is not yet clear. In particular, a limb-selective region located lateral to face-selective regions of the Fusiform should, according to this theory, pool information from the central visual field. This, however, is in contrast to how bodies and limbs are typically experienced: with peripheral vision. Are the spatial computations of this limb-selective region thus dictated by the way limbs are visually experienced across development, or will its spatial computations be dictated by their cortical position according to the eccentricity theory? In Experiment 1, we implement naturalistic eye tracking in n=27 young adults viewing Hollywood films to demonstrate that bodies and limbs are statistically much more likely to be viewed with peripheral vision ($p<0.0001$). To determine if the way that the limb-selective region in visual cortex samples visual space matches these viewing patterns, in Experiment 2 we performed receptive field (RF) mapping in n=25 young adults during functional magnetic resonance imaging (fMRI) to evaluate which portion of the visual field evokes responses from limb-selective voxels. We find that receptive fields in the limb region sample the peripheral visual field significantly more than face regions ($p<0.005$), that is, they're more eccentric. While consistent with the way that limbs are visually experienced during development, this defies the eccentricity theory of visual cortex development. In Experiment 3, using a large receptive field dataset from the Human Connectome Project (HCP, n=181 young adults), we expand upon the eccentricity theory and demonstrate that the limb region is actually at a cortical transition point between two halves of a larger parabolic eccentricity gradient, with one gradient extending ventrally, and a previously-undescribed one extending laterally towards the middle temporal gyrus. While this new theory parsimoniously describes visual cortex organization, it is still possible that limb-selective receptive fields sample from the central visual field earlier in development but lose their central coverage to face-selective regions which expand during childhood and take-over the limb-selective region. Thus, in Experiment 4, we performed receptive field mapping in n=20 children and through ongoing analyses will differentiate between two possibilities: 1) the peripheral spatial sampling of the limb region is developmentally stable, or 2) becomes more peripheral with development. In conclusion, these data have provided an alternative framework of cortical organization that accounts for the wiring of visual cortex and visual experience, offering a refined model relating how developmental experience is mapped onto cortical representations in vision.

1-C-15 - Exploring Aperiodic Activity in the Bucharest Early Intervention Project.

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Details

Background

Electroencephalographic (EEG) neural oscillations have been extensively investigated as crucial indicators of brain activity in psychopathology. However, the aperiodic activity, which is characterized by non-rhythmic fluctuations in the EEG signal, also offers significant insights into the neural mechanisms underlying psychopathology (e.g. Karalunas et al., 2021). Aperiodic activity, defined by an offset and a slope, has been proposed as a marker of brain maturation, reflecting alterations in the excitatory-inhibitory (E:I) ratio and exhibiting susceptibility to change throughout life (Donoghue et al., 2020; McSweeney et al., 2023). Currently, there is limited understanding regarding the alterations in aperiodic activity that occur over the course of an individual's life, particularly during adolescence, a time when the brain undergoes significant structural transformation and maturation processes. Here we examine developmental changes in aperiodic activity in the Bucharest Early Intervention Project (BEIP).

Methods

Participants included abandoned children from Romanian institutions, who were randomly assigned to foster care (foster care group, FCG; *n* = 68) or to continued institutional care (care-as-usual group, CAUG*; n* = 68), and a never-institutionalized group (NIG; *n* = 135). Resting-state EEG data were collected at six time points spanning from 20 months to 16-years of age. At baseline, 30-, 42-, and 96 months, a lycra Electro-Cap with 14 electrodes was used. At 12 and 16 years, a 64-channel HydroCel Geodesic Sensor Net was used. To ensure consistency, we selected the same 12 scalp sites (F3, F4, Fz, C3, C4, P3, P4, Pz, O1, O2, T7, and T8) at all time points. Aperiodic activity (offset and exponent) was extracted using the specparam1 algorithm (Donoghue et al., 2020a) from the FOOOF python package, employing a modified version by Wilkinson et al. (in prep) that is optimized for younger populations. After data preprocessing, cleaning, and exclusion of improperly fitted files, the final dataset included EEG data at 20 months (Baseline, N=154, 49% girls), 30 months (N=140), 42 months (N=128), 96 months (N=140), 12 years (N=146), and 16 years (N=117).

We conducted ANOVAs to test the effects of Age, Gender and the Groups. The first ANOVA tested the interaction between Age (BL, 30M, 42M, 96M, 12Y, 16Y) and Gender (Male vs Female). Two additional ANOVAs tested the interaction between Age and Institutionalization groups: (1) FCG vs CAUG, (2) Ever-Institutionalized Group vs NIG.

Results and Discussion

Our findings revealed no substantial differences between the Care as Usual and the Foster Care groups or between the Ever Institutionalized and community controls (all $p > 0.05$ for main and interaction effects of Institutionalization). However, there was a main effect of Age for both the offset ($F(1,5) = 41.55$, $p < 0.001$) and the exponent ($F(1,5) = 5.21$, $p < 0.001$) and a significant interaction between Gender and Age for the offset ($F(1,5) = 2.67$, $p < 0.05$). The offset was as age increased, having a significant reduction from 96 months-old to 12 years-old ($p < 0.05$) and from 12 years-old to 16 years-old ($p < 0.05$). The exponent had an increase from 42 months-old to 96 months-old ($p<0.05$), and a decrease from 12 years-old to 16 years-old ($p<0.05$). Males had lower offset compared to females only at 12 years-old of age ($p < 0.05$).

The more pronounced reduction in aperiodic activity during adolescence might indicate a period of significant neural reorganization, which could possibly involve synaptic pruning and the strengthening of neural connections essential for adult cognitive and emotional functioning. Sex hormones can lead to distinct neural trajectories for males and females during adolescence. Overall, these results emphasize the importance of examining aperiodic activity in the context of age and gender to better understand the neural mechanisms underlying brain maturation and functional organization.

1-C-16 - Evoked brain responses to repetition, deviance, and omission of tactile stimuli in a sequence in premature neonates

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Details

Sensory prediction (SP) is the ability to anticipate future stimulations on the basis of previous sensory inputs, a core feature of cognitive development. It optimizes cognitive resources and regulates sensory processing through repetition suppression (RS) when a stimulus becomes irrelevant, or repetition enhancement (RE) to relevant or unexpected stimuli. Impaired SP could be a key to understanding the emergence of Neurodevelopmental Disorders (ND). NDD are associated with sensory deficits, such as tactile hypo- or hypersensitivity, and authors proposed that altered SP and RS may be early mechanisms leading to cognitive impairments found in autistic or attention deficit syndromes. In prematurely born infants, who have an increased risk of NDD, recent studies also revealed altered RS and SP, supporting this hypothesis. The aim of this work is to describe the evoked brain responses to somatosensory stimulus repetition, deviance, and omission in premature neonates with different degrees of prematurity, hence different risks of subsequent NDD. Indeed, the earlier these children are born, the more exposed to brain injury, iatrogenic pain, and inadequate stimulation they are, and the more susceptible is their brain.

Using 128-channel electroencephalography (Magstim EGIÂ®) we measure the event-related brain activity of preterm neonates at 35 weeks of corrected gestational age (GA) during a tactile oddball/omission paradigm. The protocol contains 290 trials: 200ms-long vibrations that feel like moving up or down the forearm. The first and last 40 stimuli are identical (standards) and used to assess RS. In between, stimuli are organized in 30 contiguous blocks of seven stimuli, containing five standards, one deviant (vibration direction is reversed), and one omission each, in pseudo-random order. To date we have acquired 45 usable data sets, aiming at 90, *i.e.,* 30 in each GA group: early prematurity (birth before 30 weeks GA), moderate prematurity (between 30 and 33 weeks GA), and late prematurity (after 33 weeks GA).

Preliminary results show RS in the somatosensory cortex of early and moderate preterms. We do not observe RS in late preterms but their response to standards is lower than in other groups at all times of the protocol. More analysis is necessary to determine whether this is due to a much quicker RS across repetitions, suggesting the benefit of being born closer to term, or a constant low response with no repetition effect. Deviant stimuli elicit a positive mismatch response in the somatosensory cortex of early preterms, and a negative one in late preterms. The response of moderate preterms stands in between. In

the frontocentral area, results show a mismatch positivity in early preterms and negativity in moderate and late preterms. Therefore, the morphology of this marker appears directly linked with neurodevelopmental risk. A very similar pattern is observed on the post-omission standard (the first standard stimulus presented after an omission), indicating that both deviance in nature and deviance in timing elicit a mismatch response that varies with NDD susceptibility. The frontal area also showed activity depending on the group during the omitted stimulus time itself, showing that a prediction was formed in all three groups.

These results provide evidence of sensory prediction and top-down regulation of somatosensory cortex activity in premature neonates, and it shows that the associated brain activity, measured at the same corrected gestational age for all neonates, differs depending on their degree of prematurity at birth. Future investigations will be necessary to determine if this is due to GA at birth itself, or to post-natal exposure to adverse events. These results support the hypothesis that neonatal markers of neurodevelopmental risk can be evaluated using functional brain measures of sensory processing.

1-C-17 - Cortical maturation and functional selectivity of face- and body-processing regions in children and adolescents

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Details

Objectives:

Previous research has highlighted cortical thinning as a key process of maturation across the brain during development. Recent work, however, has suggested that apparent thinning of the visual ventrotemporal cortex (VTC) in adults compared to children may emerge from greater myelination leading to different image intensities and a â€˜shift' in the grey-white boundary in MR images. In addition to microstructural changes, there is evidence for changes in the functional selectivity of VTC across development, with reduced selectivity in fusiform face area (FFA) in children relative to adults. Here, using ultra-high field 7T MRI, which affords higher resolution compared to previous studies, we assessed what functional and structural changes underlie the maturation of face- and body-selective regions in VTC across childhood and adolescence by combining multimodal imaging data.

Methods:

A total of 42 children and adolescents aged 8 to 18 years of age were recruited for the present study. A high-resolution MP2RAGE structural scan (TR/TE=6000/2.7ms; resolution =0.65x0.65x0.65mm; TA=10min 46 secs) and whole-brain EPI gradient-echo functional scan (TR/TE=2000/30ms; resolution= 1.5x1.5x1.5mm; 87 slices; TA=9min 18sec) were acquired on a 7T Siemens Magnetom scanner. Retrospective correction of head movement was used during image acquisition of the MP2RAGE to mitigate blurring of the high-resolution data at 7T in addition to correction for B1 inhomogeneities. The functional scan presented blocks of images of faces, bodies, houses, and chairs.

Functional data were analysed in FSL. The Faces > Houses and Bodies > Chairs contrasts were used to identify the functionally-defined regions-of-interest (fROIs) FFA and fusiform body area, with a z-statistic image threshold set to 3.

The MP2RAGE scan was processed through the FreeSurfer [version 7] recon-all pipeline using the high-resolution option, which includes brain extraction, intensity normalization, and generation of white and pial surfaces. Vertex-wise estimates of cortical thickness and functional selectivity were averaged within a given fROI. Myelination was assessed using quantitative R1 mapping (i.e., 1/T1), using the MP2RAGE sequence, where higher R1 values indicate higher myelination.

Results:

We found that face-selectivity of the fusiform cortex increases across late childhood and adolescence but found no increase in body-selectivity across these ages, consistent with previous research. Our proxy for myelination (R1) demonstrated that myelination increased with age in both the fusiform cortex's face- and body-selective regions. Contrary to expectations, cortical thickness in these regions did not decrease with age, but there was a significant negative relationship between cortical thickness and myelination in FFA that was independent of age. Neither myelination nor thickness of fROIs were related to their functional selectivity.

Conclusion:

Overall, our results provide insight into the structural and functional development of the face- and body-selective fusiform cortex in childhood and adolescence. Specifically, we identified cortical myelination as a key aspect of maturation across these stages of development. Cortical thickness did not decrease with age but myelination was related to cortical thickness in face-specific fusiform cortex. We found no evidence to suggest that functional selectivity of these regions is underpinned by differences in myelination and cortical thickness during development. Further research on myeloarchitecture and histology of face- and body-selective fusiform cortex is needed to elucidate microstructural change across developmental stages and their relationship to function and behaviour.

D- Brain structure

1-D-18 - The structural development of discrete thalamic nuclei from late childhood to early adulthood

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Details

Background:

The thalamus is a subcortical brain region with extensive and reciprocal connections across the cortex. It contributes to a variety of functions including relays of sensory information, decision making, and cognitive control. Converging evidence suggests that these heterogenous functions are subserved by

distinct thalamic nuclei. To date, few if any studies have examined the structural and functional development of these nuclei in humans. In this study, we assessed age-related variations in thalamic nuclei volumes from late childhood through early adulthood using both cross-sectional and longitudinal methods.

Methods:

Longitudinal data were collected from 197 healthy individuals ages 9-23 across five waves over a 12-year period. Whole brain volumes were acquired on a 3-Tesla Siemens Trio/Tim Trio Scanner. The scanner was upgraded in the middle of the second assessment wave. The volumes of twenty-five bilateral thalamic nuclei were extracted using FreeSurfer 7.2.0, and eighteen of these were selected or combined based on their established functional associations. Nuclei were combined across hemispheres. We first used a cross-sectional approach to evaluate age-related variations using data from the second post-scanner-upgrade assessment wave (total n=168). Quality checks were done manually for all participants and double checked using statistical outlier detection. After removing participants with significant head motion or segmentation errors, the sample consisted of 153 individuals, with a mean age of 18.48 years (SD = 3.96). General linear models were utilized to predict whole thalamic and thalamic nuclei volumes from age while controlling for biological sex, total intracranial volume, and scanner upgrade effects. Tests were corrected for multiple comparisons using False Discovery Rate adjusted p values.

Results:

Cross-sectional analyses reveal no significant linear effect of age on overall thalamic volume ($p = .350$). However, increasing age was associated with smaller volumes of the mediodorsal (MD; $p = .022$), reunions (Re; $p = .008$), and medial geniculate (MG; $p = .022$) nuclei and larger volumes of the ventromedial (VM; $p = .007$) and parafascicular (Pf; $p = .019$) nuclei. None of the other thirteen nuclei showed significant age-related effects. Moreover, these nuclei are functionally distinct. Whether these age-related variations contribute to individual differences in neurocognitive development is also being investigated within the sample.

Conclusions:

These findings are among the first to identify unique patterns of development in thalamic nuclei from late childhood to young adulthood. We show that although the overall thalamus is not undergoing significant change during this time, the MD, Re, MG, VM, and Pf are still developing. Given the role of these regions in higher order cognition, sensory-motor skills, and autonomic regulation, these findings provide a novel context for understanding adolescent cognitive and behavioral development. We next plan to use hierarchical linear modeling techniques to replicate this set of analyses with longitudinal data, providing the opportunity to investigate developmental trajectories within subjects over time.

1-D-19 - BOBs (Baby Open Brains) Repository: An Open-Science Repository of Segmentations for Human Infants

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Details

Objective: Longitudinal early-life neuroimaging studies, like the Healthy Brain Cognitive Development (HBCD) study (Volkow, 2021), require processing pipelines that can work across the human lifespan. In particular, efforts to perform surface-based analysis require the extension of processing tools like Freesurfer (Fischl, 2012) into the infant domain (Zollei, 2020). Efforts toward such extensions remain limited by the availability of manually-corrected and Freesurfer-compliant segmentations of anatomical MRI data (Rodrigues, 2015). High quality segmentations require considerable effort and expertise, and would therefore benefit from review in an open repository. Furthermore, different segmentation protocols vary by neuroimaging subfields. Inherently, these protocols do not differ in validity. Therefore multiple segmentations need to be maintained in order to properly contextualize findings for respective subfields. Therefore, we constructed the Baby Open Brains (BOBs) repository to provide a community-wide resource for maintaining infant segmentations.

Methods: The Baby Connectome Project (BCP) was curated based on anatomic data quality (n=80 total) of which 73 infants aged 0-8 months were selected for data processing. All data were pre-processed using the DCAN-infant pipeline (Hendrickson, 2022), and the spatially normed MNI Infant, AC-PC-aligned T1 and T2 were used to guide segmentations. Initial segmentations were constructed in one of two ways, either using ANTS joint label fusion (JLF; Wang, 2012), or using the BIBSnet algorithm (Hendrickson, 2022) trained on a subset of the final segmented data. Initial segmentations were then provided to markers, who were guided by an expert rater to correct the cortical (grey/white matter) and subcortical segmentations. All segmentations were reviewed and approved by the expert rater prior to upload. Segmentations were version controlled via datalad (Halchenko et al., 2021) to ensure data provenance. Version controlled data were uploaded to OpenNeuro, (Markiewicz et al., 2021) which hosts BOBs repository for accessibility. BrainBox (Heuer et al., 2016) can be used to both view, comment, and refine segmentations, enabling continuous improvement. A subset of JLF and manual segmentations (n = 38) were then re-run through the DCAN-infant pipeline and the output volumes were compared to assess structural differences between automated approaches and the manual segmentations.

Results: Manual corrections show substantial improvement over prior available approaches for automated infant segmentations. Comparisons of T1/T2 identified unmyelinated white matter and gray matter shows substantially better annotation compared to automated approaches across infant age ranges. For the subset of manual data used for quantitative comparison, JLF volumes, compared to manually corrected volumes, show significantly inflated gray matter ($T=4.68$, $p<0.001$, $DSC=0.868$) and deflated white matter ($T=8.13$, $p<0.001$, $DSC=0.85$) estimates.

Conclusions: The BOBs repository will enhance researchers' ability to construct, improve, and test infant pipelines that incorporate expert-reviewed segmentations. In addition, we will continue to refine our 0-8 month segmentations, while extending into subsequent 1, 2, and 3 year olds. The entire community can add new segmentations, as well as view, comment, edit, and/or improve current human infant brain segmentations. Studies like HBCD will find such repositories critical for ensuring best standards and practices for data processing.

1-D-20 - Anterior pituitary volume mediates associations between pubertal hormones and changes in dysregulation symptoms in youth

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Details

The anterior pituitary gland (PG) is a potential locus of hypothalamic-pituitary-adrenal (HPA) axis functioning, with documented links between dehydroepiandrosterone (DHEA) levels and anterior PG volumes. Beginning in adrenarche, the anterior PG plays an increasing role in the major influx of DHEA, with normative volumetric increases in PG documented during the pubertal window. Given the known role of the PG in stress responses, a growing literature has provided some evidence for correspondence between PG volume and mental health disorders, including internalizing symptoms during adolescence. Though mixed, some findings suggest that larger whole PG volume may be associated with elevated or clinical levels of mental health symptoms. However, there is increasing speculation that the anterior and posterior PGs should be separated, as they are functionally and structurally distinct. That is, the posterior pituitary is involved in oxytocin and vasopressin secretion, while the anterior pituitary is involved in facilitating production of pubertal and stress hormones. Importantly, specific links between DHEA levels, anterior pituitary volume, and psychopathology have not been established in developmental samples. Thus, the current study sought to examine the mediating role of anterior PG volumes on the relationship between DHEA levels and changes in a potent transdiagnostic symptom subtype (i.e., dysregulation) during adolescence. In a community sample of 114 youth (9-17 years; M_{age} = 12.87 (SD = 1.88); 51% female), salivary DHEA and high-resolution T1-weighted MRI scans were collected. The anterior and posterior PGs were manually traced by trained raters with excellent inter-rater reliability (ICCs = .93-97). Participants also completed the Child Behavior Checklist to assess dysregulation symptomology

(subscales: anxious/depressed, attention problems, aggression) at the time of the MRI and hormone collections and one year later. Difference scores in dysregulation symptoms were calculated between the two timepoints to evaluate symptom changes. Results from structural equation modeling suggested that anterior, but not posterior, PG volume significantly mediated the associations between DHEA levels and dysregulation symptoms such that greater DHEA predicted larger anterior PG volumes, which in turn predicted increases in dysregulation ($\hat{I}^2$ = 0.08, *b* = 0.06, 95% CIs (0.02 0.20). All variables were corrected for age and sex, and brain volumes were corrected for total intracranial volume. These findings corroborate and extend prior work linking DHEA, pituitary volume and anxiety symptoms in adolescents. The results convey that there is specificity in associations between pubertal hormones, PG volume, and developmental psychopathology that are consistent with the functional role of the anterior PG. This study has implications for future studies by providing the key insight that anterior and posterior PGs should be examined separately in order to fully disentangle HPA-axis mediated effects on risk for psychopathology during puberty.

1-D-21 - Hypothalamic volume and body mass index in the ABCD study

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Details

Introduction Childhood obesity represents a major public health challenge. The importance of hypothalamic nuclei in the regulation of energy balance is well established in animals yet remains understudied in humans. As a first step towards addressing this knowledge gap, we tested the hypothesis that hypothalamic volume was associated with BMI in a large representative sample of adolescents at baseline (mean age=9.9 years; n_{base}=10,710) and two-year follow-up (mean age=12.0 years; n_{2y}=6,227).

Methods Whole hypothalamus and its associated subunits were segmented using a neural network-based approach (FreeSurfer *mri_segment_hypothalamic_subunits*) and spot inspected for accuracy. ComBat harmonization was used to account for site effects while preserving variance in sex, age, and BMI. Parsimonious cross-sectional linear mixed effects analysis nesting for family structure and adjusting for sex, age, and intracranial volume was used to test the association between hypothalamic volume and BMI. A second model was used to additionally consider the potentially confounding factors: area deprivation index, parent education, parent income, puberty score, reported race and ethnicity. A third and fourth model considered effect sizes over and above two prominently reported neural correlates of BMI in the ABCD sample (nucleus accumbens cellularity, and an elastic net defined multimodal brain wide association score). Finally, in recognition of the distinct role of the arcuate nucleus in regulating energy balance, we tested for subunit specificity (inferior tubular volume) in the relationship between hypothalamic volume and BMI.

Results At baseline, hypothalamic volume was positively associated with BMI ($\hat{I}^2$=2.3 [1.9 2.7], t=11.9, $p<10^{-15}$, n=10,710, R^2=1.3%). This relationship remained significant and increased in effect size at the 2-year follow-up ($\hat{I}^2$=2.3 [2.0 2.7], t=11.4, $p<10^{-15}$, n=6,227, R^2=2.0%). Potentially confounding factors had little impact on the strength of these associations as both remained highly significant at ($p<10^{-15}$) with

relative decreases in effect sizes (R^2) of only 19% and 5%, respectively. Further, the effect size of the association between hypothalamic volume and BMI is larger than and persists ($p<10^{-15}$) when adjusting for nucleus accumbens cellularity (10% and 3% reduction in R^2baseline and 2-year follow-up, respectively). While the association remained significant ($p<10^{-8}$) at baseline and two-year follow-up after adjustment for a multimodal brain wide association score, the effect size of the association was meaningfully dampened (>50%) suggesting shared variance between hypothalamic volume and a distributed brain wide network associated with BMI. Finally, inferior tubular volume was significantly associated with BMI over and above that of whole hypothalamus volume (R_{base}^2=0.2%; $p_{base}<10^{-4}$; R_{2y}^2=0.3%; $p_{2y}<10^{-5}$) attributing specificity to a subunit heavily implicated in energy balance.

Conclusion Taken together, the above findings highlight the relative importance of the hypothalamus for regulating energy balance in humans. Importantly, because the hypothalamus is believed to underly satiety in this context, and because satiety is distinct from more well understood networks associated with feeding behaviors (e.g., reward, salience, interoception, inhibition), this work addresses an understudied niche in the neurocircuitry underlying human obesity risk.

1-D-22 - Replicable associations of brain morphology with anxiety and depression symptoms in adolescents from two large population-based samples

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Details

Introduction. Brain morphological variation has been implicated in the pathogenesis of anxiety and depression, primarily in subcortical areas and the prefrontal cortex. Yet, inconsistencies in the literature have been reported and investigations have been predominantly limited to adults, clinical samples, and regions of interest (ROIs), meaning the brain-wide neuroanatomical characteristics of youth psychiatric symptomatology remain unclear. Here, we tested the association of depression and anxiety symptoms with brain morphometry, at an ROI and vertex-wise level, in adolescents from the general population.

Methods. We leveraged the worl's largest cohorts of pediatric neurodevelopment: the Generation R (GenR) and Adolescent Brain Cognitive Development (ABCD) studies, for a total of 7,442 adolescents (11-to-17-years-old; N_{GENR} = 1,997; N_{ABCD} = 5,445). A cross-sectional design was used. Brain morphological data were obtained from MRI scans and summarized into ROIs (amygdala and hippocampus volume, caudal middle frontal, lateral and medial orbitofrontal, rostral middle frontal, superior frontal cortical area and thickness) and vertex-wise area and thickness. Symptoms of anxiety and depression were assessed using the syndrome and DSM-V-oriented scales from the Child Behavior Checklist (i.e., anxious-depressed symptoms, anxiety, and affective problems), which were based on parent reports. Multiple linear regression models were used to test the association of these phenotypes with ROIs. Vertex-wise linear regressions were run for each vertex's area and thickness. Models were adjusted for age, sex, ethnicity, parental education, puberty, and site (ABCD only). Results were meta-analyzed across cohorts to identify replicable associations.

Results. Meta-analysis of ROI results revealed associations for both anxiety and affective problems (DSM-V scales) with the lateral and medial orbitofrontal, and rostral middle frontal surface area (**Figure 1**). Affective problems were additionally related to the amygdala and hippocampal volume as well as the caudal middle frontal and superior frontal area (**Figure 1**). These associations survived multiple testing corrections (FDR < 0.05), and most of them presented similar effect sizes across cohorts (**Figure 1**). Combined anxious-depressed symptoms (syndrome scale) related to the rostral middle frontal area (estimate = -0.00004; SE = -0.00002; *p*-value = 0.014), but not after multiple testing corrections. No associations were found with any of the phenotypes for cortical thickness. Meta-analysis of vertex-wise analyses showed similar patterns, with no associations for cortical thickness with any of the phenotypes, and associations in surface area only for affective problems. Clusters for affective problems confirmed ROI analyses: associations were primarily located in the rostral middle frontal and orbitofrontal cortices. Additionally, new areas of associations were found: the inferior and middle temporal, superior parietal, precentral, and cingulate regions. Of note, analyses in each cohort independently yielded results that were seemingly inconsistent across studies and did not reveal several aforementioned regions of associations.

Conclusion. In this large study, which leveraged two cohorts and both *a priori* and data-driven analyses, we highlight three important points. First, despite anxiety and depression being closely related phenotypes, they likely present unique neural correlates in adolescence. Second, the lower cortical surface area at frontal, temporal, and parietal regions, and smaller subcortical volumes, might underlie differences in key functions in individuals with depression (e.g., decision-making, social behaviors, memory encoding). Third, the increased power gained from meta-analyzing allowed the identification of robust and replicable regions of associations that would have otherwise not necessarily been found.

Figure 1. Statistically significant results for affective problems with regions of interest from the meta-analysis and each cohort independently.

Note. ABCD = The Adolescent Brain Cognitive Development Study; CI = confidence interval; GenR = The Generation R Study; Meta = meta-analysis. Estimates are unstandardized.

1-D-23 - Dynamic effects of sex on global brain volumes across the human lifespan

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Details

Background: Biological sex can affect neurobiology, potentially contributing to sex-biases in the prevalence and presentation of many psychiatric illnesses (BÃ¶lte et al., 2023; DeCasien et al., 2022; Gur

& Gur, 2016). Yet the association between biological sex and brain structure has been hotly debated, with studies reporting a range of significant and null findings (DeCasien et al., 2022; Eliot et al., 2021; Williams et al., 2021). These discrepancies may partially result from study-level differences in sample size and ages, as well as statistical techniques used to model age effects. 'Brain chartsâ€ models of brain morphology across the human lifespan derived from Magnetic Resonance Imaging (MRI) can overcome these limitations by directly quantifying sex's effect on brain structure at the population level (Bethlehem et al., 2022). Crucially, these models can be adapted to quantify how sex-effects vary over the lifespan, reflecting sex-specific biological processes that may impact brain growth and aging. Here we utilize a brain chart framework to test the hypothesis that sex moderates the normative effect of aging and to uncover sex's dynamic associations with brain anatomy across the lifespan.

Methods: MRI data were provided by the Lifespan Brain Chart Consortium (Bethlehem et al., 2022). Current analyses utilized a large, global subsample of 62,339 individuals (31,551 female) ages 0-100 years who were scanned across 74 primary studies. T1-weighted MRI scans (and T2-weighted scans when available) were preprocessed and segmented primarily using FreeSurfer (versions 5.3 or 6.0), producing volumes for four global tissue types: cortical gray matter, white matter, subcortical gray matter, and ventricles. Brain charts were constructed for each global volume using Generalized Additive Models for Location, Scale, and Shape (GAMLSS) which explicitly model mean, variance, and skewness of the outcome distribution using generalized gamma distributions (Stasinopoulos & Rigby, 2008). We fit separate models to assess the main effect of sex on lifetime global volumes ('sex-stratifiedâ€ models), as well as the added explanatory value of age-varying sex effects ('sex-flexibleâ€ models). All models included a main effect of age, fit non-linearly using fractional polynomials, as well as random and main effects to control for scan site and segmentation software, respectively. We compared sex-stratified and sex-flexible model fits for each tissue type using likelihood ratio tests.

Results: GAMLSS models produced robust brain charts of global tissue volumes across the lifetime, accounting for the main and age-varying effects of sex on brain structure. For each tissue class, sex significantly moderated the nonlinear effect of age on median volume, with sex-flexible models explaining individuals' volumes better than sex-stratified models (all p-values < 0.001, Cohen's w for interaction term: 0.03 - 0.07). Cumulatively, sex was associated with small differences in median global brain structure volumes (Cohen's w for main and age-varying sex effects: 0.12 - 0.18). Models were generally consistent with an earlier age of peak volume in females, with the largest sex-bias observed in subcortical gray matter volume (female = 16.1 years, male = 18.9 years).

Conclusions: Across all four global volumes, sex significantly moderates the normative effect of age, demonstrating that the shape of brain growth trajectories differs systematically between females and males. Future work is needed to uncover whether these differing trajectories contribute to sex-biases in psychopathology. These results provide an important proof-of-concept for normative models of human brain structure to account for sex's dynamic effects across the lifespan.

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1-D-26 - Uncovering a sulcal link to reasoning performance in lateral parietal cortex

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Details

The lateral parietal cortex (LPC) is crucial for human cognition, including spatial processing, reasoning, and visual orientation. While primary (large and deep) sulci in LPC have been extensively studied, the relationship between smaller, late-developing LPC tertiary sulci and cognition remains largely unexplored. Understanding the role of tertiary sulci in cognitive functions may provide valuable insights into the neuroanatomical basis of cognitive development. Previous research has established a link between the depths of tertiary sulci in lateral prefrontal cortex (LPFC) and reasoning ability in children and adolescents (Voorhies et al., 2021). While it is well-known that both LPFC and LPC are critical for reasoning, tertiary sulci have been largely overlooked and it is still an open question if, mirroring LPFC, there is a relationship between tertiary sulcal morphology and reasoning in LPC.

To fill this gap in knowledge, we studied the relationship between LPC sulcal anatomy and reasoning performance in 79 children and adolescents (*M*_age = 12.48, *SD*_age = 3.48, aged 6.44 - 18.75 years). We manually identified sulci in the LPC and examined their depth in relation to Matrix reasoning task performance. Our investigation yielded three main findings:

First, we identified 12 non-tertiary and 5 tertiary sulci in LPC, including 4 new tertiary sulci: the ventral (sLocs-v) and dorsal (sLocs-d) supralateral occipital sulci, as well as the ventral (pAngs-v) and dorsal (pAngs-d) posterior angular sulci. Each new sulcus is located in a consistent position between the superior temporal and intraparietal sulci along a dorsal-ventral axis traversing the superior portion of the occipital lobe into the angular gyrus. Along this axis, we found higher sulcal incidence rates ventrally compared to dorsally (sLocs-v: 93.7% left, 98.7% right; sLocs-d: 60.8% left, 58.2% right; pAngs-v: 21.5% left, 26.6% right; pAngs-d: 3.8% left, 8.9% right)

Second, a data-driven, model-based approach identifies a relationship between the depths of 9 non-tertiary and 4 tertiary sulci and reasoning performance. Interestingly, in the LH, but not the RH, the model identifies that the depths of two of these newly identified sulci predicted reasoning performance (sLocs-v ($\hat{I}^2$ = -0.86); sLocs-d ($\hat{I}^2$ = 0.35)).

Third, model comparisons showed that including the depths of the identified sulci resulted in a lower AIC and higher adjusted $R\hat{A}^2_{CV}$ than models with either age alone or all LPC sulci: (1) age + depth of the specific sulci identified by the model (LH: AIC = 116.9, adjusted $R\hat{A}^2_{CV}$ = 0.37; RH: AIC = 123.8, adjusted $R\hat{A}^2_{CV}$ = 0.38), (2) age only (LH: AIC = 123.8, adjusted $R\hat{A}^2_{CV}$ = 0.31; RH: AIC = 128.5, adjusted $R\hat{A}^2_{CV}$ = 0.36), and (3) age + depth of all LPC sulci (LH: AIC = 164.3, adjusted $R\hat{A}^2_{CV}$ = 0.38; RH: AIC = 182.2, adjusted $R\hat{A}^2_{CV}$ = 0.38).

This study is the first to explore the relationship between morphological features of manually defined LPC sulci and reasoning performance in children and adolescents. Our results highlight the importance of considering sulcal anatomy - especially the smaller, shallower, and more variable sulci - to understand individual variability in cognition. These findings contribute to our understanding of the neural basis of cognitive development and emphasize the need for further investigation of the role of sulcal anatomy. Finally, longitudinal research is needed to determine whether variability in LPC sulcal anatomy is predictive of reasoning during development or also into adulthood.

1-D-27 - Structural brain development of speech networks in young children at-risk for speech disorders.

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Details

Children with Attention-Deficit/Hyperactivity Disorder (ADHD) are up to three times more likely to display speech and language problems compared to typically developing children. Among the broad categories of language impairment, disorders of speech articulation are the most prevalent, which includes deficits in the repetition of monosyllabic and bisyllabic utterances. These children may have dysfunction in brain regions and pathways of the comprehensive neural network implementing speech articulation. Crucial regions implicated in the motor control and implementation of effective speech are lateral inferior frontal regions, and medial frontal regions including pre-supplementary motor area (pre-SMA) and the anterior cingulate gyrus. The connectivity of these lateral inferior frontal and medial frontal cortical regions have also been identified as potentially important for speech. This connectivity is supported by a fiber pathway known as the frontal aslant tract (FAT). To investigate the role of these brain regions and the role of the FAT in the structural development of networks supporting speech, we examined a diffusion weighted imaging (DWI) data set in young children (4-7-years). Method: The final participating sample consisted of 48 4-7-year-old children diagnosed with ADHD (dual clinician diagnosed) and 47 typically developing (TD) controls (M age = 5.51, SD = 0.81, and 74.7% male; 49.5% TD). All children were scanned in an MRI (3T Siemens Prisma) with a 102-direction multi-shell DWI acquisition. The RSI model was applied to measure structural development of gray matter, which allowed us to implement a more complex reconstruction of the diffusion signal that parsed out the hindered normalized total signal fraction (HNT) and the restricted normalized total signal fraction (RNT). White matter connectivity was measured using a standard DTI model. The model indexed four different metrics: fractional anisotropy (FA), axial diffusivity (AD), radial diffusivity (RD), and mean diffusivity (MD). In addition to DWI metrics, data were collected on the Syllable Repetition Task (SRT), a validated measure of phoneme articulation. Results: Differences in the cellularity of gray matter predicted performance on the SRT differentially across ADHD and TD groups in the middle anterior and anterior cingulate gyrus for both HNT and RNT (p = .04), with only the TD group showing a significant association (p < .05). Additionally, across both groups performance on the SRT was associated with AD in the white matter pathway projecting from the left supplementary motor area (SMA) to pars opercularis, a subcomponent of the FAT (p = 0.04). Conclusions: In young children (4-7-years), performance on a phonemic articulation task is associated with cellularity in middle and anterior cingulate as measured by HNT and RNT, and in microstructure of the left FAT measured with DTI. In cortex, the association was

stronger for the TD group, suggesting microstructural differences in networks supporting speech development across TD and ADHD.

1-D-28 - Characterizing changes in brain structure from infancy to school age in moderate-to-late preterm and term-born children.

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Details

Objective: Preterm birth (< 37 gestational weeks') has been linked to alterations in brain structure and function, implicating cognitive, motor and socio-emotional domains, with the majority of findings based on infants born before 32 weeks. Relatively less is understood about the brain development of infants born moderate or late preterm (MLP), who comprise ~85% of preterm births, and are not routinely offered developmental surveillance despite mounting evidence that they are at higher risk of developmental problems. The current study aims to characterize changes in regional cortical and subcortical measures in MLP and term-born children between infancy and 9 years of age.

Methods: Infants born MLP (32â€“36 gestational weeks', n=201) and at term (â‰¥ 37 gestational weeks', n=200) were recruited and MRI scanned at term-equivalent age (TEA, 40 Â± 2 weeks' gestational age) and again at 9 years of age. Using compatible surface-based neonatal and adult parcellation software (MCRIB-S, FreeSurfer), cortical volume, thickness, surface area, curvature and folding indices and subcortical volumes were calculated in 66 cortical and 14 subcortical regions, respectively. Statistical analysis involved assessing the birth group differences in structural measures at TEA, with an interaction term for sex. False discovery rate-corrected p-values are presented to account for multiple comparisons across brain regions and measures. Subsequent analyses will include 9-year structural measures and changes in measures between TEA 9 years.

Results: Preliminary analysis of structural measures at TEA (MLP n=136, FT n=48) revealed that cortical thickness and surface area were most sensitive in identifying birth group differences, with smaller surface area and thicker cortex in structures across frontal, temporal, parietal and occipital lobes, and in the cingulate cortex in MLP compared with FT born infants ($P_{FDR} < 0.05$). The MLP group displayed reduced volumes across structures in the frontal lobe, but increased volume across the temporal lobe. Lower cortical folding and curvature was also found in MLP infants in structures across frontal, temporal, parietal, occipital lobes and in the cingulate cortex and insula. In structures where there was evidence that group differences were influenced by sex (interaction $p < 0.05$), birth group differences were largely found in males but not females.

Findings from subsequent analyses assessing 9-year structural measures and changes in measures between TEA 9 years will be presented.

Implications: By characterising changes in structural measures between infancy and school-age, this work will provide novel insights into the development of cortical and subcortical structures across time, and with greater spatial specificity than prior studies in this high-risk population.

1-D-29 - Evaluating informant discrepancies in anxiety symptoms as predictors of amygdala volumes using a latent profile analysis approach: a pre-registered study

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Details

Anxiety co-occurs in up to 82% of autistic youth. Previous work has found mixed results regarding the presence of an association between amygdala volumes and anxiety symptoms in autistic youth. These discrepancies may be due to difficulties in the measure that is used when assessing anxiety or due to differences in parent versus child (self) report. Additionally, in a nonautistic sample of youth, informant (parent versus child) was identified as a moderator of anxiety-amygdala associations, such that an association was observed (smaller amygdala volumes) only when the child reported high anxiety levels (Warnell et al., 2018). Thus, assessing informant discrepancy or lack thereof may provide insight into the mixed findings regarding amygdala-anxiety associations and also provide insight into potential subgroups of youth that parent or self-report may be better assessing anxiety symptoms. Therefore, the current study aimed to 1) assess the presence of informant discrepancies in parent versus self-reported anxiety symptoms utilizing a latent profile analysis approach (LPA) and 2) examine whether the profiles that emerge are differentially associated with amygdala volumes in both autistic and nonautistic youth.

Participants will include at least 113 autistic and nonautistic adolescents aged 8 14-years-old recruited from two larger longitudinal studies (one completed, *n* = 59; one with ongoing data collection, predicted *n* = 54 at time of Flux conference) with a useable structural MRI scan and anxiety measure. Participants and their parents completed the Screen for Child Anxiety Related Emotional Disorders (Birmaher et al., 1999) to assess anxiety symptoms and an IQ test (Kaufman Brief Intelligence Test, Second Edition) at a behavioral visit prior to participating in the MRI scan. Participants in the autistic group met either on the Autism Diagnostic Observation Schedule, Second Edition or Autism Diagnostic Interview, Revised version for a diagnosis of Autism Spectrum Disorder.

Data Analytic Plan: First, a LPA will be used in order to classify participants into separate profiles based on shared patterns of responses (Masyn, 2013). We hypothesize that 4 profiles will emerge: 1) high anxiety reported by both parent and child, 2) high anxiety reported by parent and not child, 3) high anxiety reported by child and not parent, and 4) low anxiety reported by both parent and child. Specifically, the LPA will be run in MPlus version 8 with full information maximum likelihood estimation to account for missing data. The optimal number of profiles will be determined by comparing fit indices (i.e., AIC, BIC, AWE, CAIC, aLMR, BF, and BLRT) of increasing profiles and stopping when the fit indices are not within statistical guidance or have too few participants. Once the final number of profiles has been determined, group (autistic, nonautistic), FSIQ, age, and gender will be considered as covariates after identifying the latent profiles. Next, to assess differences in amygdala volumes across profiles, model constraints will be computed based on pairwise difference tests. We hypothesize that unique associations will be observed depending on whether there is agreement or not, such that the profile with parent and child agreement will be associated with amygdala volumes; although we have no hypothesis about the direction given inconsistencies in previous work (e.g., larger in autistic youth and smaller in nonautistic youth).

1-D-30 - Vertex and voxel-wise association between cortical morphology and attention in adolescents

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Details

Objective: Previous studies have focused on associating attention and cortical morphology in specific regions, but now we have the computational power to model these associations across the entire brain. Additionally, we compare different modes of measuring behavior across two measures and see if there are distinct patterns across the measures.

Methods: Using data from the ABCD study release 4.0, we used linear mixed effects models to associate structural MRI measures of cortical thickness and cortical surface area along with diffusion MRI measures of gray and white matter with attention as measured via two different methods, the caregiver-answered attention subscale of the Child Behavior Checklist (CBCL) and the flanker inhibitory control and attention test of the NIH Toolbox. Statistical analyses used FEMA which allows for models to be run at each vertex or voxel across the entire brain.

Results: Vertex-wise analysis of cortical thickness and surface area appears to show similar patterns of association in the frontal lobe across the two measures, when mean cortical thickness and total surface area are not included in the model, but this pattern largely disappears when mean thickness and total surface area are added to the models. For the diffusion MRI metrics, patterns across the cortex, particularly in the frontal lobe, appear to be matched across the two measures of attention. Results have not yet been acquired for voxel-wise analysis of either the sMRI or dMRI measures, but we intend to run the same models as the vertex-wise analysis just on the voxel-wise level.

Conclusions: Cortical area and thickness association patterns are seemingly due to a size effect as the pattern seemingly disappears when total area and mean thickness are added to the model. While noise is a concern for gray and white matter in the cortex, these patterns are seemingly quite strong. Looking at voxel-wise associations in the future, we are curious to see if sMRI patterns are less size dependent deeper in the brain. Additionally, we expect the dMRI patterns will hold in further voxel-wise analysis.

1-D-31 - Relationships between emerging reading abilities and white matter features across childhood

Meaghan Perdue [1], **Bryce Geeraert** [1], **Catherine Lebel** [1], **Deborah Dewey** [1]

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Details

Numerous studies have linked reading ability to white matter integrity, but recent large studies have failed to replicate findings using diffusion tensor imaging. Advanced diffusion weighted imaging (DWI) models may be more sensitive to individual differences in reading ability and reveal associations with specific features of white matter structure (Koirala et al., 2021; Meisler & Gabrieli, 2022). In addition,

inhomogeneous magnetization transfer imaging (ihMT) provides myelin-specific metrics that can help distinguish whether white matter associations with reading are driven by features of fiber organization, myelination, or both.

We will investigate associations between reading ability and specific features of white matter structure using advanced DWI models and ihMT in children aged 4-11 years. We will examine global and tract-level measures of white matter to determine if effects are specific to reading-related tracts. We will also examine potential age-related changes in relationships between white matter and reading. We predict that reading ability will be associated with more efficient white matter structure (indexed by higher fiber density, cross section and myelination) in tracts associated with reading. We expect that reading will be more strongly associated with dorsal and bilateral tracts in younger children, and with left hemisphere inferior tracts in older children, reflecting maturation of the reading network.

Approximately 345 datasets from 109 children (ages 4-11) will be included from a longitudinal study of brain development (Reynolds et al., 2020). Data collection is complete.

DWI, ihMT, and T1-weighted anatomical scans were acquired on a 3T GE MR750w scanner with a 32-channel head coil. Scan sequence details have been previously reported (Geeraert et al., 2018; Reynolds et al., 2020).

Reading ability was assessed using the Woodcock Reading Mastery Test (Woodcock, 2011), administered on the same day as the MRI scan. Reading ability will be quantified as a composite of raw scores on the Word Identification and Word Attack subtests.

DWI processing is underway using multi-shell multi-tissue constrained spherical deconvolution in *MRTrix3* (Tournier et al., 2019). Tracts of interest will be segmented using TractSeg (Wasserthal et al., 2018) and mean apparent fiber density, fiber cross section, and combined fiber density and cross section will be extracted for each tract. Tracts of interest will include the arcuate fasciculus, superior longitudinal fasciculus, inferior longitudinal fasciculus, and inferior fronto-occipital fasciculus in each hemisphere. We will also extract global white matter metrics from the whole-brain tractogram.

Voxel-wise quantitative ihMT (qihMT) values have been calculated as an index of myelination (Geeraert et al., 2018). qihMT maps will be warped to each subject's DWI image and mean qihMT values will be extracted from each tract of interest, and the whole brain white matter mask.

We will examine relationships between reading and white matter using linear mixed effects models. Each white matter metric will be tested in a separate model with reading score as the dependent variable, white matter metric, sex, age, and white matter*age interaction as fixed effects, and subject as a random effect. If white matter*age interactions are identified, we will use functional concurrent regression to examine relationships between white matter structure and reading over time.

This research may enable us to identify novel and specific links between reading ability and white matter macro- and micro-structure during a crucial period of reading development, and to examine how these brain-behavior relationships may change over the course of learning to read. Findings will provide a model for future research investigating white matter features in children with reading disabilities, paving the way for investigation of neurobiological and genetic causes of reading disabilities.

1-D-32 - Investigation of the association between estradiol levels and brain structure and function in early adolescent females.

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Details

Background:

During adolescence, about one-third of young people are diagnosed with internalizing disorders like depression and anxiety, with these disorders being more common in females than males. Sex difference in incidence rates may be related to pubertal factors, such as the influence of pubertal hormones on brain development. While some studies have examined the correlation between estradiol levels and brain structure in adolescents, more research is needed to test associations between estradiol levels and both brain structure and function in adolescents, particularly during early adolescence when hormone levels begin to surge.

We aim to use the Adolescent Brain Cognitive Development (ABCD) study baseline (9-10 years) and two-year follow-up (11-12 years) imaging and hormone data to investigate associations between gonadal hormones (estradiol, testosterone) and brain structure and function.

Methods proposed: We will use a machine learning algorithm called linear elastic-net regression to investigate associations between hormone levels and brain structure (gray matter volumes, cortical thickness and white matter microstructure) and function (resting-state connectivity, emotional n-back task-related function). Structure and function data from all regions across the whole brain (using the FreeSurfer Desikan parcellation) and white matter tracts (using DTI atlas) will be extracted. For each analysis (described below), data will be randomly partitioned into training and test data. Then, using the MATLAB package GLMnet, a ten-fold, cross-validated elastic-net regression with a nested 20-fold cross-validation framework for hyperparameter tuning for alpha (Î±) and lamda (Î³) will be applied to the training set for feature (i.e., region) selection. Generalisability will be measured by applying the best fit model from the training set to the testing set.

For each modality, a model will be developed (i.e. a separate elastic net regression model will be run for structural, diffusion, resting state, EN-back functional task; n_{model} = 4) to determine which regions are associated with hormone levels (separate models run for estradiol and testosterone). Features which passed the threshold of explaining atleast 1% of the variance in hormones in the test data will be included for the further analysis. In next step, all the significant features from each modality will be modeled together in the same model along with covariates (age, sex, body mass index, site,). We will also include

interactions between each feature and age, to establish whether associations between hormones and brain structure/function differ by age (from 9 to 12 years).

Progress: We have completed cleaning hormone data following the protocol developed by Herting et al. (2021). The estimated count of participants to be included in the elastic-net models will be n1=2213 having oestradiol and all imaging data, n2=4637 having testosterone and all imaging data. In addition, we have decided on a machine learning pipeline for our models.

Anticipated completion by the congress: We are hoping that by the end of the July, we will have completed running all the machine learning models, thus able to discuss findings from all analyses during the congress. This will be one of the only studies to investigate associations between estradiol and brain development in early adolescent females, and the first study to investigate multiple imaging modalities and associations with hormone levels in 9-to-12-year-olds. The analysis results will be presented in the Flux congress for the first time.

1-D-34 - Are Centile Scores of Structural Brain Phenotypes Associated with Internalizing Symptoms during Adolescence?

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Details

BrainChart, an available interactive open-source software tool, allows researchers to extract normalized, referenced centile scores based on lifespan brain MRI trajectories (Bethlehem, Seidlitz, White et al., 2022). Drawing from three longitudinal samples, this study will characterize the relationship between brain morphology centile scores (represented cumulatively as their deviation from the median) and variation in internalizing symptoms among adolescents. We will test whether there is a relationship between concurrent BrainChart centile deviation and level of internalizing symptoms, whether change in an individual's centile deviation is related to internalizing symptoms, and whether a change in centile deviation occurs before or after an increase in internalizing symptoms. We will also determine whether these relationships vary by age. As of the date of the submission, we have completed the preregistration and accessed the data for two of the three longitudinal samples. No analysis has been conducted yet, though they will all be completed by Flux.

1-E-36 - Neural response to reward moderates associations between victimization and suicidality in sexual minority adolescents

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Details

Background: Sexual minority youth (SMY) are more than four times as likely to attempt suicide than their heterosexual peers (Johns et al., 2020). Interpersonal models of suicide underscore social experiences as a primary risk factor for suicidal behavior, and Minority stress theory posits that in SMY, high rates of identity-based social victimization may be responsible for health disparities like suicidality (Joiner, 2009; Meyer, 2003). Contextualized within adolescence, a period of hypersensitivity for social stimuli (Foulkes and Blakemore, 2016), these identity-based victimization experiences may drive enhanced vulnerability to social stressors through altered functional connectivity. Existing research demonstrates alterations in functional reward neurocircuitry associated with both social experiences and suicidal thoughts and behaviors (Nelson and Guyer, 2011; Tyspes et al., 2019). Still, research delineating how adolescent social environment and functional circuitry interact to confer risk for suicidality is fundamentally lacking. We address this gap by examining whether neural reward systems moderate the influence of victimization on suicidal ideation.

Methods: 65 participants (N=65, 38% sexual and gender minority (SGM) adolescents) ages 13-22 (mean=17.3, SD=2.70) completed self-report measures of suicidal ideation (Suicidal Ideation Questionnaire), victimization (Marshall Victimization Scale), and a monetary reward task-based fMRI. The eight 'critical itemsâ€ of the SIQ most able to predict suicidality as identified by previous work were utilized (Boege et al., 2014). During image pre-processing, significant activation to reward > neutral outcome (p_{FWE}< 0.05) was determined within an anatomically derived 'rewardâ€ mask. SPM was used to extract BOLD signal of a priori reward ROIs (dmPFC, LVS, RVS). Linear models assessed the relationship between victimization and suicidal ideation and the potential moderating effect of neural response to reward.

Results: SMY reported greater victimization (p=0.01) and suicidal ideation (p=0.04) than heterosexual youth. Victimization was positively correlated with suicidal ideation (r = .13, p=.04). Dorsal medial prefrontal (dmPFC) activation in response to reward moderated the association between victimization and suicidal ideation (p=.008), such that those with both decreased dmPFC activation and greater victimization reported greater suicidal ideation.

Conclusions: These data suggest that exposure to victimization combined with certain neural response to reward, specifically lower dmPFC activity in response to win outcome, is associated with greater suicidal ideation in critical items predictive of future behavior. This suggests that less engagement of dmPFC, a region responsible for regulating executive and emotion responses to positive stimuli, in the setting of victimization stress, may play a role in suicidal thoughts and behaviors. An important next step will be to further evaluate how these identity-based social threat experiences interact with and potentially contribute to, neurodevelopment in emotion regulation areas, conferring risk for suicidality.

1-E-37 - Oscillatory theta activity during a selective attention task scales with polygenic risk for Attention Deficit Hyperactivity Disorder (ADHD) in youth

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Details

Background. One of the most commonly diagnosed disorders in childhood is Attention Deficit Hyperactivity Disorder (ADHD). Recent studies using the research domain criteria (RDoC) framework have utilized polygenic risk scores (PRS) for ADHD to identify the key brain circuits in normative populations. PRS are numerical representations of an individual's genetic susceptibility that utilizes information from multiple genetic variants to estimate an individual's likelihood of developing a certain condition or trait.
Methods. A total of 41 participants between the ages of 9-16 years-old completed the Connors 3rd edition questionnaire and provided saliva samples, which genome-wide genetic variants of individuals were extracted from. Using the Psychiatric Genomics Consortium (PGC) ADHD dataset, weighted PRS associated with ADHD were calculated for each participant. Participants also underwent high-density magnetoencephalography (MEG) during performance of the flanker selective attention task. The resulting MEG data were transformed into the time-frequency domain and imaged per condition using a beamformer, which generated whole-brain oscillatory maps. Conditional maps were then subtracted to generate flanker interference maps per participant and oscillatory response. Whole-brain correlations were then conducted on each interference map using the PRS, controlling for age.
Results. MEG sensor-level analyses revealed significant theta (3-7 Hz, 0-350 ms) and alpha/beta responses (9-20 Hz, 200-600 ms) following the onset of visual stimuli. We then conducted whole-brain correlations between the ADHD PRS and neural interference maps for each participant per oscillatory response. For theta, peaks were identified in the right dorsolateral prefrontal cortex (DLPFC) and left cerebellum. However, we did not identify any significant relationships between ADHD PRS and alpha/beta activity across the cortex. Our key findings indicated that larger PRSs for ADHD were associated with stronger theta activity in the right DLPFC ($p<.0001$) and the left cerebellum ($p<.0001$). Further analysis revealed that stronger theta activity in the right DLPFC was tightly coupled to increased behavioral hyperactivity ($p=.045$) and faster reaction times ($p=.024$).
Conclusions. Our findings suggest that stronger theta oscillations in the right DLPFC and left cerebellum scale with polygenic risk for ADHD. Further, hyperactivity symptoms and reduced behavioral inhibition are correlated with stronger theta oscillations in the right DLPFC.

1-E-38 - White Matter Microstructure Remodeling Across the Transition to Fatherhood

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Details

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Background: Current research has established the unique role of fathers in a chil's development. However, few research studies have examined fathers' neurobiological changes and their relations to parenting and child outcomes. Studying fathers' neurobiological changes during the transition to parenthood may provide insight into early interventions for supporting parent and child well-being. Multiple adult brain studies have reported associated changes in white matter microstructure (WMM) and brain function in response to major life events. However, no studies have examined changes in WMM in expectant or new fathers. This study will address this gap by investigating longitudinal changes in WMM associated with the transition to parenthood in a cohort of first-time fathers.

METHODS: We collected diffusion-weighted imaging (FOV = 256 mm x 256 mm; T_E/T_R = 69/8100 ms; 70 axial slices; 2 mm^3 isotropic voxels; diffusion directions = 63) data on a 3.0 Siemens MAGNETOM Prisma^{fit} scanner at USC's Dornsife Neuroimaging Center. Participants were first-time fathers (*n* = 30) who underwent imaging when their female partners were approximately six months pregnant (prenatal) and again when their infants were six months of age (postpartum). Longitudinal whole brain changes in fractional anisotropy (FA) from the prenatal to postpartum periods were examined using DSI Studio. We also covaried for fathers' age, race, and educational attainment.

RESULTS: We found increased FA in multiple white matter tracts, including the left cingulum when comparing prenatal to postpartum periods (Figure 1).

CONCLUSION: Findings link the transition to parenthood in fathers with increased FA in brain areas supporting memory and emotional regulation. Findings provide unique insight into fathers' neurobiological vulnerabilities with a larger goal of supporting fathers' adjustment to parenthood. Findings provide the first evidence of structural remodeling in fathers' white matter during the transition to parenthood. Further analyses examining fathers' white matter changes and mental health are underway.

1-E-39 - Examination of iron content in the striatum from functional MRI in young children with autism spectrum disorder

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Details

Brain tissue iron is essential for multiple aspects of brain function, including oxidative metabolism, myelination, and neurotransmitter (e.g., dopamine) synthesis and function. Previous studies have suggested age-related increase in brain iron content in the deep gray matter structures (basal ganglia) across the first two decades of life, with iron concentration plateauing in early adulthood in normative development. Atypically low iron content in the basal ganglia has been associated with poor cognitive

outcomes in the context of iron deficiency in infancy. The only known study in young children with autism found reduced iron content in the striatum in toddlers with autism spectrum disorder (ASD) compared to typically developing (TD) children (Tang et al., 2022). Given the scarcity of such data in autism, it remains unknown how the maturational trajectory of iron content in the striatum deviates from normative development across the first years of life in ASD. The current study aims to examine (1) age-related effects in iron content in the striatum in preschoolers with ASD compared to TD peers and (2) the links between iron content and developmental skills in ASD and typical development.

Participants include young children with ASD (n=59, mean age: 39Â±15 months) and typically developing (TD) children (n=39, mean age: 35Â±16 months) enrolled in a longitudinal study of early brain markers of autism. All participants underwent standardized assessment of developmental skills using the Mullen Scales of Early Learning (MSEL). Two 6-minute resting state fMRI scans were acquired during natural sleep on a 3T GE scanner. The ASD and TD groups do not significantly differ on age and head motion (root mean square displacement). A subset of the sample for whom longitudinal fMRI and behavioral data are available will be used for exploratory longitudinal analyses. Iron content will be estimated with R_2*=1/normalized T_2* from fMRI data and extracted in the bilateral caudate, putamen, nucleus accumbens, and pallidum. For Aim 1, ANCOVA will be employed to test for effects of age, diagnostic group, and age-by-group interaction in each region of interest (ROI) while controlling for sex, head motion, gestational age at birth, and socioeconomic variables. For Aim 2, linear regressions will be conducted between iron content in each ROI and MSEL cognitive domain T scores. Corrections for multiple comparisons will be conducted using Benjamini-Hochberg False Discovery Rate (FDR) at $q < 0.05$. For Aim 1, we hypothesize to find age-by-group interaction effect on iron content, with the normative age-related increase observed (cross-sectionally) in TD children and a weaker age-related increase (a shallower slope) observed in children with ASD. We also expect to find lower iron content in the striatum in children with ASD compared to TD children (main effect of diagnostic group), replicating the results of the only other known study in young children with ASD. For Aim 2, we expect that lower iron content will be associated with lower developmental skills (as assessed by the MSEL) in all children, with and without ASD.

Data collection for this study is complete. The proposed analysis plan will be implemented and results will be presented at the Flux conference.

1-E-40 - Assessing the Effectiveness and Safety of a Digital Therapeutic for Symptoms of Depression in Adolescents: Protocol for a Randomized Controlled Trial

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Details

Introduction: Depression is a major and increasingly prevalent mental health problem among adolescents and young adults in the US. However, those needing care commonly encounter barriers, such as unavailability of health professionals and long waitlists. The development of treatments that increase accessibility to effective care may offer a solution to this problem. Digital health interventions,

like digital therapeutics, can provide a timely and cost-effective treatment alternative. In this parallel-group, superiority, randomized, controlled, single-blind (investigator) trial, we investigated the effectiveness and safety of a novel digital therapeutic (SparkRx) for symptoms of depression in adolescents (13-21 years). **Methods**: Participants were recruited through direct advertisement or provider referrals. During a virtual consent and onboarding call, potential participants completed eligibility screening and the Patient Health Questionnaire (PHQ-8), a self-report assessment of depression severity, along with other baseline assessments. Using a permuted block randomization schedule, 223 participants were randomly assigned (1:1) to use either SparkRx or a control app without therapeutic content in addition to their usual care for symptoms of depression during a 5-week intervention period. Stratification factors were baseline total PHQ-8 score (<15, â‰¥15) and current antidepressant medication use (yes, no). Participants completed the PHQ-8 weekly during the intervention period, at post-intervention, and at 1-month follow up. **Outcomes**: The **primary outcome** was depressive symptom severity at post-intervention as measured by total PHQ-8 score. The following **secondary outcomes** were computed using the total PHQ-8 score: a) proportion of participants meeting criteria for intervention response (50% symptom reduction in PHQ-8 score from baseline to post-intervention); b) proportion of participants meeting criteria for remission (PHQ-8 score <5 at post-intervention); c) depressive symptom severity at 1-month followup; d) proportion of participants meeting criteria for a clinically-meaningful reduction in symptom severity (â‰¥5 reduction from baseline PHQ-8 score to post-intervention). To ensure **safety and capture adverse events (AEs)**, study staff monitored participants' symptom deterioration and questionnaire data, in addition to freeform text entered into the SparkRx app. **Analyses**: The primary hypothesis that participants using SparkRx will have lower PHQ-8 scores at post-intervention than those using the control app will be tested using a mixed effect model with appropriate correlation matrix. Timepoint, intervention arm, timepoint by intervention interaction, baseline PHQ-8 score, and antidepressant medication status will be included in the model as fixed effects. To analyze the secondary outcomes, we will compute the number and proportion of participants meeting criteria for intervention response, remission, and clinically-meaningful reduction in severity at post-intervention, and compare rates between treatment arms using chi-square tests. We hypothesize that there will be higher rates of intervention response, remission, and clinically-meaningful reduction in severity in SparkRx users than in control app users. All tests will be two-tailed and a serial gatekeeping approach will be implemented to control for multiple comparisons. Rates of psychiatric serious AEs, irrespective of device relatedness, will be compared between SparkRx and control app users using Fisher's exact test.

Recruitment and enrollment into the study has concluded. Data analysis will begin once the final participant completes their follow-up assessment, and will be completed by Flux.

Notes: Claims have not been reviewed by the FDA with regard to SparkRx's safety or efficacy. In Oct. 2021, Limbix released SparkRx under FDA's Enforcement Policy for Digital Health Devices For Treating Psychiatric Disorders During the Coronavirus Disease 2019 Public Health Emergency.

1-E-41 - Testing the generalisability of transdiagnostic latent patterns in functional brain networks to a Norwegian sample of youth

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Details

Introduction

Replicability and generalisability of neuroimaging findings across samples remains a challenge in the field (Botvinik-Nezer & Wager, 2022). While it is becoming increasingly common to validate results using unseen data from the same sample, fewer studies attempt to validate their results across samples. Recently, wederived brain informed dimensions of psychopathology based on covariance in functional brain networks in a developmental clinical sample from the US (Voldsbekk et al., 2023). These dimensions recapitulated the psychopathology hierarchy, with a general psychopathology factor and increasingly narrow dimensions. Similar dimensions of psychopathology have been identified in a population-based sample of children, using measures of both brain structure and functional connectivity (Kebets et al., 2023), alluding to a generalisable link between brain measures and the psychopathology hierarchy. However, it remains to be clarified whether these patterns have predictive utility across samples.

Objectives

The current study aims to address this question of generalisability and predictive utility by investigating whether the previously identified link between functional connectivity (FC) and psychopathology can be detected in a Norwegian convenience-based sample of youth. Specifically, we aim to not only validate the association in a new sample, but also to investigate whether the identified latent pattern has predictive utility. Specifically, we will investigate whether a) the FC side of the latent pattern can be replicated in a new sample, and b) if this pattern can predict levels of psychopathology in the new sample.

Methods/Analysis plan

In the previous work, we used partial least squares (PLS) (Krishnan et al., 2011) to identify latent variables (LV) between FC and symptom scores obtained from the Child Behaviour Checklist (Achenbach & Rescorla, 2001). Each LV represent a distinct pattern that relates a weighted set of symptoms to a weighted set of FC connections (i.e., edges). The sample consisted of children and adolescents aged 5-21 (n = 1880, 62% male) from the Healthy Brain Network study (HBN) (Alexander et al., 2017). Brain networks were derived using the Schaefer parcellation (Schaefer et al., 2018), resulting in 4950 unique partial correlations (i.e., edges). This work identified five LVs linking distinct patterns of functional connectivity to the following dimensions of psychopathology: a general psychopathology factor, externalising-internalising, neurodevelopment, somatoform and thought problems, respectively.

In the current work, we will perform out-of-sample validation of these detected patterns in the BRAINMINT sample, an independent convenience-based sample of Norwegian youth aged 9-25. To do this, we will first estimate corresponding brain network edges in BRAINMINT resting-state fMRI data. Then, we will decompose the BRAINMINT FC edges by multiplying them with the imaging weights estimated in the HBN PLS analysis. Then, to establish whether the resulting FC maps in BRAINMINT overlap with those in HBN, we will correlate them and test their significance using permutations. Next, we will correlate the derived BRAINMINT FC pattern with symptom scores in BRAINMINT, to test the generalisability and predictive utility of the FC pattern in a new sample. To do this, we will correlate the connectivity loadings in BRAINMINT with symptom scores obtained from the Strength and Difficulties Questionnaire (Goodman, 1997). To assess the reliability of the associations between BRAINMINT connectivity loadings and symptom scores, we will run 1000 bootstraps using resampling with replacement.

General implications

This work aims to determine the degree to which the link between FC and psychopathology in a US developmental clinical sample can be extended to a Norwegian convenience-based sample of youth. The implication of this work is to establish the degree of generalisability and reproducibility of brain-behaviour associations across samples. This represents an important contribution to the neuroimaging field, in which reproducibility long has remained an untouched issue.

F- Education

1-F-42 - Rapid Online Assessment of Reading (ROAR): A platform for developmental cognitive neuroscience research at an unprecedented scale

Jason Yeatman [1], **Wanjing Ma** [1], **Liesbeth Gijbels** [2], **Carrie Townley-Flores** [1], **Julian Siebert** [1], **Jasmine Tran** [1], **Tonya Murray** [1], **Mia Fuentes-Jimenez** [1], **Mahalakshmi Ramamurthy** [1], **Adam Richie-Halford** [1]

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Details

Background: Few, if any, developmental disorders have a single, consistent phenotype. Knowledge of different phenotypes, along with reliable measures to characterize those phenotypes, is critical for understanding the confluence of factors that contribute to developmental differences. Deep phenotyping is the precise and comprehensive analysis of phenotypic variation and is the foundation of precision medicine. Here we describe development and validation of the Rapid Online Assessment of Reading (ROAR), a platform designed for deep phenotyping at an unprecedented scale.

Method: Prototyping, validation and norming studies were done based on longitudinal data from 7,000 participants spanning 4-40 years of age. ROAR (https://roar.stanford.edu) was initially conceptualized as an online alternative to time consuming and resource intensive standardized reading assessments and, as such, included measures of single word recognition (ROAR-SWR), phonological awareness (ROAR-PA), and sentence reading efficiency (ROAR-SRE). Here we expand the platform to target vocabulary, visual

processing, and executive functions. Each ROAR measure is designed to be a) lightly gamified and engaging across a broad age range, and b) completely automated such that a child can complete the measure in a web-browser without a test administrator. The ROAR platform integrates with the most common single sign-on and student identification systems used in schools facilitating collaborative research with schools, efficient data collection in large, diverse and representative samples as well as longitudinal tracking of participants completing multiple tasks.

Results: All three reading measures achieved exceptional reliability with reliability greater than or equal to standardized, individually administered assessments (greater than 0.90). In validation studies comparing the self-administered online ROAR measures to individually-administered reading assessments, concurrent validity was extremely high: (1) ROAR-SWR correlated with the Woodcock Johnson Letter Word Identification between r=0.91 and r=0.97 depending on the age of the sample; (2) ROAR-PA correlated with the Comprehensive Test of Phonological Processing (CTOPP) composite index between r=0.69 and r=0.80; (3) ROAR-SRE correlated with the Test of Silent Reading Efficiency and Comprehension (TOSREC) between r=0.82 and r=0.93. We further found that implementing a Javascript-based computer adaptive testing algorithm (jsCAT; https://www.npmjs.com/package/@bdelab/jscat) reduced testing time by 40% while maintaining the same measurement reliability.

By examining the correlation between measures of reading ability and measures of visual motion perception and multi-element encoding we tested the hypothesis that individual differences in rapid visual processing are related to reading development. We found moderate correlations (r=0.35 - 0.45) between visual measures and reading ability between kindergarten and high-school. This result confirms the relationship between visual processing and reading development in the largest, most demographically diverse sample to date.

Conclusions: Deep phenotyping depends on collecting a myriad of measures in a large, diverse and representative sample. Unfortunately, conventional methods bias samples towards university communities which rarely reflect the diversity of the region (or nation) and resource constraints mean that sample sizes are often insufficient to reliably determine effect sizes, non-linearities, and interactions in complex, multivariate models. The ROAR platform overcomes these challenges by providing a growing battery of completely automated, lightly gamified online measures with exceptional reliability and strong evidence of validity that can be used in online, laboratory, school, and community-based research.

1-F-43 - Premotor Cortex Activity During Spatial Cognition Partially Mediates the Relation between Socioeconomic Status and Academic Outcomes

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Details

The disparity of success between students from high and low socioeconomic backgrounds is a significant educational concern in the United States. This disparity is important to consider in science and math education where students from low socioeconomic status (SES) often score lower on standard achievement measures than their high SES peers. The relationships between SES, cognitive ability, and academic achievement have been shown to persist throughout childhood making this a concern across development. Research in math and science education has shown that visuospatial skills play a role in learning in these domains. Yet, visuospatial skills are often under-instructed, under-supported and under-valued in educational settings. Limited research has investigated the role of SES in visuospatial thinking. Furthermore, while research suggests that difference in activation in regions such as the posterior parietal cortex, occipital cortex and premotor cortex could play a role in success during visuospatial tasks, whether these neural correlates underlie SES differences has yet to be examined. Investigation into the neural correlates could help to elucidate potential strategy differences and provide a more mechanistic explanation to the behavioral differences seen in past research. The current study aims to investigate if there is an association between childhood SES (maternal education) and neural activity associated with spatial cognition, and whether the neural activity associated with spatial cognition mediates the relation between SES and science academic achievement. Data were collected as part of a project which investigated the impact of a geospatial course on high school students' spatial cognition. Neural correlates of visuospatial thinking were measured with functional brain imaging (i.e., fMRI) while participants (N = 43) completed the Mental Rotation Task (MRT). During each MRT trial (84 trials) participants indicated whether two rotated images portrayed the same 3-dimensional object. Mother's education and GPA for high school science courses were collected to measure SES and science academic achievement respectively. Mother's education was associated with increased activation in the premotor cortex when completing a spatial task. Mediation analysis revealed a significant indirect effect of SES on academic outcomes through left premotor cortex activity. The bootstrapped unstandardized indirect effect was 0.18, and the 95% confidence interval ranged from 0.056 to 0.35. Thus, the partial indirect effect was statistically significant ($p<.001$). Research has suggested that increased activity in the premotor cortex could indicate preparatory motor processes or motor imagery during the MRT. These findings suggest the educational relevance of this neuromarker such that SES-related neural differences in activation are associated with better science academic performance. Results from this study add to past research demonstrating that visuospatial skills present a key target to help improve students' STEM outcomes along the socioeconomic gradient. The results of this study may be informative to future interventions that are aimed at reducing the SES opportunity gap in science education.

G – Environment (Stress, SES)

1-G-44 - Developing best practices for inclusion in pediatric fNIRS research: Equity for participants with afro-textured hair

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Details

Neuroimaging research has a notoriously long history of under-representing minority populations, especially African Americans, in their samples which can lead to biased findings. The legacy of exploitation of African Americans in the name of 'scienceâ€ thus has led to lesser willingness of African Americans to participate in biological research (Crockett, 2013; Fish et al., 2020; Gamble, 1997). When

they are willing to participate, Black individuals are often systematically excluded from research due to historic discrimination and individual characteristics that do not work well with existing methodologies (e.g., neuroimaging methods). For this reason, cognitive neuroscience research samples tend to be non-representative of the population as a whole. Increased representation requires changes to both methodological and relational practices.

Functional Near Infrared Spectroscopy (fNIRS) is a cap-based neuroimaging technique that uses optical methods to index brain activity. Although fNIRS is well-suited for investigating naturalistic contexts with movement-prone pediatric populations, it is, unfortunately, often not well-suited to collect data from participants with afro-textured hair (i.e., coarse, coily) in an inclusive and respectful way(Ricard et al., 2022; Webb et al., 2022). This is because fNIRS signal quality requires an unobstructed path to the scalp, which may be difficult with coarser, denser hair types and textures. Because researchers are often not trained in best practices for working with afro-textured hair, many Black participants are turned away from cap-based neuroimaging studies (Rocheleau, 2023), resulting in mostly White and unrepresentative samples. Furthermore, while techniques are being developed for optimizing EEG hardware and signal in afro-textured hair, there is currently no published research examining best practices for fNIRS with afro-textured hair. Thus, the central aim of this work is to establish best practices for optimizing fNIRS signals with afro-textured hair, while simultaneously maintaining the long-term integrity of the hair when preparing it for fNIRS capping.

We began this investigation by adapting novel hair preparation techniques for EEG studies, as recommended by literature(Richardson, 2021) and personal consultation with experts in professional haircare. We first tested capping and signal optimization processes using a number of different hair preparation methods on adult participants: (1) straight back cornrows completed in the lab; (2) professional box braids; (3) professional locs; (4) blown-out hair strategically pinned; and (5) braids placed based intentionally in the target montage/configuration. We are currently extending the best methods to determine optimal practices for working with socioeconomically, racially, and ethnically diverse samples of preschool-aged children (i.e., child-friendly and time efficient methods). Results suggest some initial directions, but also indicate the need for further investigation for inclusive fNIRS practices, to ultimately yield more representative research samples. We intend for this work to increase awareness of the racial bias that is embedded into our neuroimaging practices, advocate for greater racial and ethnic diversity in neuroscience research teams (i.e., hiring researchers with lived experience with afro-textured hair to ensure inclusivity and representation), and change the way we approach working with diverse populations in an inclusive and respectful way.

1-G-45 - Brain-Environmental interactions: a time sensitive matter

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Details

Introduction: When we acquire resting-state (rs) neurophysiological dynamics to assess brain activation patterns, we typically control for sensory and perceptual environments during testing conditions. Here, we investigated how temporally-distal environmental inputs, specifically metal exposures, experienced up to several months prior to testing, affect rs functional dynamics. We implemented an interpretable

gradient boosting (XGBoost)-SHAP (Shapley Additive Explanation) model that integrates the information from multiple exposure biomarkers to predict rs dynamics in typically developing adolescents.

Methods: In 124 participants (53% females, ages: 13-25 years) enrolled in the Public Health Impact of Metals Exposure (PHIME) study, we measured concentrations of 7 metals (Manganese, Lead, Chromium, Cupper, Nickel, Zinc) in biological matrices (saliva, hair, fingernails, toenails, blood, urine) and acquired rs functional magnetic resonance imaging scans. Using graph theory metrics, we computed global efficiency (GE) in 111 brain areas (Harvard Oxford Atlas). We used a predictive model based on ensemble XGBoost to predict GE from metal biomarkers, adjusting for age and sex. Model performance was evaluated by comparing predicted versus measured GE using Pearson's correlation coefficient. SHAP scores were used to evaluate feature importance.

Results: Measured versus predicted rs dynamics from our model utilizing chemical exposures as inputs were significantly correlated ($p< 0.001$, $r = 0.36$). Lead, chromium, and copper contributed most to prediction of GE metrics.

Conclusions: Our results indicate that a significant component of rs dynamics, comprising approximately 13% of observed variability in GE, is driven by recent metal exposures. These findings emphasize the need to estimate and control for the influence of past and current chemical exposures in the assessment and analysis of rs functional connectivity. This work provides a method to accurately predict rs metrics and highlights the power of simultaneously using exposomics data and interpretable machine learning algorithms for discovering overlooked interactions between the brain and environmental exposure.

1-G-46 - White matter structure and psychopathology in previously institutionalized adolescents

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Details

Background

Previously institutionalized (PI) adolescents show increased risk for general psychopathology and externalizing behavior, although early assignment to foster care partially mitigates this risk [Wade et al., 2018]. Despite a growing interest in the development of psychopathology in PI adolescents, little is known of the neural correlates associated with altered trajectories of psychopathology in this population.

PI adolescents exhibit altered white matter (WM) development, and early assignment to foster care is associated with later WM structure [Sheridan et al., 2022, Bick et al., 2015]. Psychopathology during adolescence is also associated with WM microstructure and macrostructure [Grazioplene et al., 2020, Burley et al., 2021, Gilchrist et al., 2023].

Aims

1) In a cohort of PI adolescents, explore associations between psychopathology (P-factor and externalizing) and WM microstructure (Fibre Density, FD), macrostructure (Fibre Cross-section, FC), and a combined measure (FDC).

2) Compare brain-behavior associations between those with and without a history of institutionalization.

3) Explore effect of randomization to foster care on brain-behavior associations.

Methods

Data collected from 81 PI adolescents (Ever Institutionalized (EIG), 42 males, M_{age} = 16.65), including 41 randomized to Foster Care (FCG, 20 males, M_{age} = 16.61), and 40 with continued Care As Usual (CAUG, 22 males, M_{age} = 16.69); and 33 adolescents without a history of institutionalization (Never Institutionalized (NIG), 16 males, M_{age} = 16.9).

Psychopathology was measured with the MacArthur Health and Behavior Questionnaire, completed by teachers and caregivers, combined into a composite score. Data reduction methods produced general psychopathology (P) and externalizing (EXT) factors.

Diffusion imaging data were processed using fixel-based analyses, and whole-brain statistical models identified associations between psychopathology (P & EXT) and fixel metrics (FD, FC, and FDC), and group interactions. All models controlled for sex & age; models for FC & FDC also controlled for intracranial volume.

Results

Widespread positive associations were found between FDC and P-factor scores within EIG ($p<0.025$).

Brain-behavior associations with P-factor differed between EIG and NIG in several WM tracts, including the inferior longitudinal fasciculus, fornix, corpus callosum, corticospinal tract and cerebellar peduncles; NIG displayed a negative association between FDC and P-factor ($p<0.05$).

Brain-behavior associations with externalizing differed significantly between EIG and NIG within the right cingulum (cingulate portion): NIG displayed a negative association between FC and EXT ($p<0.05$).

No differences were found in brain-behavior relationships between FCG and CAUG.

Discussion

Within EIG, a positive association was found between P-factor and fixel metrics in widespread WM. Recent work indicates a shift from positive to negative associations between fixel metrics and P-factor over the adolescence period [Grazioplene et al., 2022], suggesting that PI 16-year-olds display associations between WM structure and P-factor typically seen in a younger age group, indicating more â€˜immature' brain-behavior associations.

PI adolescents exhibit altered associations between WM structure and psychopathology: 1) P-factor associations in several WM tracts that have been previously linked to psychopathology in the general population; 2) externalizing behaviors localized to the cingulum, a WM tract recently associated with childhood aggression [Grazioplene et al., 2020], in line with work implicating it in impaired attention and cognitive control [Bubb et al., 2018].

Current results increase our understanding of the neural correlates of adverse behavioral outcomes in the PI population. It is unclear whether these group differences are specific to the current age group, and whether PI individuals catch up to their peers by late adolescence. Future work could investigate these relationships in multiple age groups.

1-G-47 - Using TIDAL (Tool to Implement Developmental Analyses of Longitudinal data) to explore trajectories of adolescent psychiatric symptoms in the context of food insecurity and socioeconomic status

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Details

Objective:

Modelling trajectories of mental health symptoms is a crucial component in examining why, when and how mental health symptoms change over time, especially over sensitive periods of development such as adolescence. Food insecurity and low socioeconomic status are closely related risk factors for adolescent mental health problems such as depression. Identifying how these environmental stressors impact trajectories of early mental health symptoms is particularly important in the face of increasing global food prices and cost of living.

We present a new digital tool in development: Tool to Implement Developmental Analyses of Longitudinal data (TIDAL; https://tidal.shinyapps.io/tidalapp). TIDAL aims to reduce barriers to trajectory modelling, such as the need for expertise in complex statistics, data manipulation and reducing the need for costly resources. TIDAL currently implements multilevel modelling to map group- and individual-level trajectories of adolescent mental health symptoms and provides a simple interface to convert data from wide to long format. We plan to add additional features following consultation with clinicians, young people, people with lived experience and people without specialist statistical backgrounds to ensure that TIDAL will be accessible and easy to use. For example, extracting points of peak velocity in symptom change, age of maximum symptoms and area under the curve.

Methods:

TIDAL implements a multi-level growth curve framework and R Shiny to model mental health trajectories across development. The tool and code is open-source and publicly available on GitHub (https://github.com/AmeliaES/TIDAL).

Here, we demonstrate its utility by applying TIDAL to Growing Up in Scotland (GUS; ~5 16 years longitudinally) and Adolescent Brain Cognitive Development cohorts (ABCD; ~9 14 years longitudinally). Within GUS, we will model symptom subscales from the Strengths and Difficulties Questionnaire (SDQ) at 5 time-points. Trajectories will then be grouped by: area deprivation (Scottish Index of Multiple Deprivation; SIMD), equivalised household income and food insecurity at age ~5 years. Within ABCD, we will model scores from the Brief Problem Monitor (BPM) at 7 time-points. Trajectories will then be grouped by household income, area deprivation index and family experience of food insecurity at age ~9 years.

Aims:

We firstly aim to test feasibility of the tool in multiple cohorts. Secondly, we aim to examine whether early food insecurity associates with worse longer-term trajectories of mental health problems over adolescence. Thirdly, as socioeconomic status and food insecurity are so closely interlinked, we also aim to examine effects of household income and area deprivation on adolescent mental health trajectories.

1-G-48 - Person-oriented approaches identify distinct longitudinal associations of childhood adversity with adolescent functional brain networks and mental health

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Details

Background. Early adversity poses significant challenges for adolescent well-being, yet there are vital individual differences in patterns of risk and resilience. These individual differences are partly reflected by neural heterogeneity in emotion processing, which could be examined using person-oriented approaches. In contrast to conventional approaches that rely on averages, person-oriented methods that cluster individuals with similar profiles of adversity exposures can better account for the complex interplay of adverse experiences. This comprehensive approach of capturing childhood environments could, in turn, result in a more precise identification of individual differences in brain function. In a large diverse sample with a high prevalence of adversity (*N*=4,210) and a neuroimaging sub-sample (*N*=167), this study applied person-oriented approaches to disentangle commonalities and differences in brain function and mental health among groups of individuals exposed to similar adverse experiences.

Method. Latent profile analysis was applied to identify adversity groups based on exposures to maltreatment and other maternal, family, and neighborhood risks across ages 0-9 years. Next, in a subsample of the individuals during adolescence (M_{age}=15.87), person-specific functional connectivity networks were separately estimated for each adversity class using Confirmatory Subgrouping (CS)

GIMME. CS-GIMME was applied to neuroimaging data during emotion (faces) task and connectivity maps were estimated across three neural networks: the default mode (DMN), salience (SN), and frontoparietal (FPN). Density (i.e., the proportion of network-specific connections from the total number of connections) was then computed for each network. Finally, adversity class and functional network patterns were examined in association with internalizing and externalizing problems at adolescence using latent variables of multi-informant (parent and youth) reports.

Results. Individuals (*N*=4,210) were classified into four classes: low (29%), medium (47%), and high (11%) global adversity levels, as well as a group with markedly high maternal depression (13%). Youth internalizing and externalizing problems increased with greater risk, whereby children classified in the high-adversity class followed by the maternal depression class showed the highest levels of mental health symptoms in adolescence. In the subsequent subsample analysis (*N*=167), relative to the low and medium risk classes, individuals in both the high-adversity and maternal depression classes had the lowest SN density ($F(3,163)=8.443$, $p<.001$), and the highest FPN density ($F(3,163)=12.43$, $p<.001$). Moreover, individuals in the maternal depression class also had the greatest DMN density ($F(3,163)=5.115$, $p=.002$). In relation to mental health outcomes, decreased SN density was related to increased externalizing behaviors ($b= -.217$, $p=.005$). All associations remained after adjusting for multiple demographical covariates. Notably, the pattern of findings was not observed for resting-state functional neuroimaging data, highlighting the critical nature of emotion processing for these youth.

Conclusion. In a representative sample, youth exposed to greater childhood adversity across multiple domains and those exposed to maternal depression had more mental health problems in adolescence. These youth also had fewer SN connections, but relatively more FPN connections, potentially demonstrating altered emotion regulatory functions compared to youth with low or moderate childhood adversity exposures. Moreover, youth exposed to high maternal depression had the most DMN connections, suggesting potential links between maternal depression exposure and rumination (commonly linked to DMN activity) during an emotionally salient task. These longitudinal associations underscore the significance of early environmental influences for adolescent brain development and mental health.

1-G-49 - Effects of parental socioeconomic status on cortical sulcation in offsprings. An intergenerational study

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Details

Growing evidence supports that prenatal processes play an important role for cognitive ability (Raznahan et al., 2012; Walhovd et al., 2012). Such findings have driven the search for anatomical brain features in postnatal life that could serve as a proxy for fetal events. A very interesting candidate is the sulcal patterns, namely the qualitative spatial organization of the cortical folds. Indeed, the sulcal patterns are determined before birth (Dubois et al., 2008), are stable across the lifespan (Cachia et al., 2016), and influence the cognitive abilities in normal and pathological conditions (Cachia et al., 2021). The sulcal patterns therefore

offer a window on the fetal constraints on specific brain areas on cognitive abilities. Different theories, integrating multiple factors during fetal life, have been proposed to explain the link between sulcal patterns and cognitive abilities, but the exact mechanism is still a topic of intense debates and experimental/simulation studies. Because of the effect of socioeconomic status (SES) on prenatal development and cognition (Aizer et al., 2014 ; Farah et al., 2017), we tested the hypothesis that parental SES would have an effect on offspring sulcation. We focused on the Anterior Cingulate Sulcus (ACC) which have two distinct sulcal patterns that been repeatedly associated with cognition, including inhibition, reality monitoring, hallucinationsâ€¦

In this context, 141 healthy participants, 81 children (9-10 years) and 60 adolescents (16-17 years), were recruited from public schools in France. All participants were right-handed as determined by the Edinburgh Handedness Inventory, were born full-term, had no history of neurological disease, and had no cerebral abnormalities. This study obtained informed consent and ethical approval from the National Ethics Committee (Committee for the Protection of Persons, CPP) in children (ID-RCB 2015-A00383-46) and in adolescents (ID-RCB 2015-A00811-48 and ID-RCB 2018-A03203-52). Highâ€resolution isotropic 3T anatomical data were acquired with contiguous 1-mm axial slices for children and adolescents. The MRI were pre-processed with BrainVISA 4.2 software (http://brainvisa.info) using the Morphologist toolbox with standard parameters. The 3D reconstructions of the cortical folds were then used to visually classify the ACC into two sulcal patterns, "single type" or "double parallel type", based to the absence or presence of a (secondary) paracingulate sulcus following previous procedure (Cachia et al., 2014). The maternal and paternal SES was indexed by the mother's and father's number of years of education. The distribution of ACC sulcal pattern in the left and right hemisphere was analyzed using binary logistic regressions with parental SES along with gender (male vs female) and age group (children vs adolescents) as covariates. Maternal and paternal SES were highly correlated ($p < 2$ e-10) and were therefore analyzed in separate models. We found a main effect of the mother ($p=0.01$) and father ($p=0.04$) SES on the ACC sulcal pattern in the left hemisphere, 'singleâ€ type ACC being associated with higher maternal and paternal SES compared to 'double parallelâ€ type. There was no significant effect of parental SES in the right hemisphere ($p>0.6$). There was no age-by-ACC pattern interaction.

Our findings suggest that mother and father SES influence the sulcal pattern of their offsprings, which in turn could constrain their cognitive abilities. Of note, SES is a complex construct reflecting environmental factors but also genetic factors (Belsky et al. 2018). The study of cortical sulcation, a developmental mechanism during fetal life, could therefore provide new insights into the intergenerational transmission of inequality.

1-G-50 - Alterations in fear learning as a mechanism linking childhood exposure to violence with PTSD symptoms: A longitudinal study

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Details

Fear learning is a core component of conceptual models of how adverse experiences may influence psychopathology. Specifically, existing theories posit that childhood experiences involving higher levels of childhood trauma (i.e., exposure to violence) are associated with altered fear learning processes, while experiences involving deprivation are not. Several prior studies have found altered fear acquisition in youth exposed to trauma, but not deprivation, although the specific patterns have varied across studies. The present study utilizes a longitudinal sample of children with variability in adversity experiences to examine associations among childhood trauma, fear learning, and psychopathology in youth. The sample includes 170 youths aged 10-13 years (M=11.56, SD=0.47, 48.24% female). Children completed a fear conditioning task while skin conductance responses (SCR) were obtained, which included both acquisition and extinction phases. Childhood trauma and deprivation severity were measured using both parent and youth report. Symptoms of anxiety, externalizing problems, and post-traumatic stress disorder (PTSD) symptoms were assessed at baseline and again two-years later. Greater trauma-related experiences were associated with greater SCR to the threat cue (CS+) relative to the safety cue (CS-) in early fear acquisition, controlling for deprivation, age, and sex. Deprivation was unrelated to fear learning. Greater SCR to the threat cue during early acquisition was associated with increased PTSD symptoms over time controlling for baseline symptoms and mediated the relationship between childhood trauma and prospective changes in PTSD symptoms. Childhood trauma is associated with altered fear learning in youth, which may be one mechanism linking childhood trauma with the emergence of PTSD symptoms in adolescence.

1-G-51 - A Bayesian approach to identifying links between adversity exposure and neural patterns of threat and safety learning

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Details

The ability to distinguish between threat and safety is critical for survival. Adversity exposure is associated with altered threat and safety learning, and difficulty identifying threat (or lack thereof) may link adversity exposure with anxiety. Cross-species evidence points to adversity-related changes in the hippocampus and amygdala, regions central to threat learning. Given dynamic changes in this neural circuitry across ontogenesis, adversity at distinct developmental stages may differentially impact processes such as associative learning. Here, we took a data-driven approach to linking neural responses to learned threat and learned safety with adversity timing. We hypothesized that we would be able to classify threat and safety conditions from neutral baseline using neural activation. We predicted that submitting classifier beta coefficients to Bayesian Gaussian Infinite Mixture Modeling (BGIMM) would yield one class with a distinct pattern of neural engagement, which would also be associated with the greatest cumulative adversity exposure, and a second class with a separate pattern of neural engagement that would be associated with greater exposure to adversity during early childhood and early adolescence due to increased neuroplasticity at these stages.

117 young adult participants (67% F, 33% M; 22.8 Â± 3.3 years) completed a safety cue learning fMRI task and measures of adversity exposure and anxiety symptoms. Elastic net-penalized classifiers with 5-fold cross validation were used to predict condition based on whole-brain activation data within participants. Absolute values of bilateral hippocampal and amygdala beta coefficients across participants were submitted to BGIMM to identify latent classes of hippocampal and amygdala engagement. Separate zero-inflated Poisson regression models were used to test differences in adversity exposure during early childhood (ages 0-4), late childhood (ages 5-9), early adolescence (ages 10-14), late adolescence (ages 15-19), and young adulthood (ages 20-30). Ordinary Least Squares models were used to test differences in neural engagement and anxiety symptoms between latent classes. All models covaried for sex, age at session, family income, and years of education.

Task condition prediction accuracy was 81.0% Â± 4.6% for threat vs. baseline and 79.6% Â± 4.3% for safety vs. baseline, significantly higher than chance (*ps*<0.001). BGIMM yielded two viable classes of participants (*n*=29 and *n*=18) after discarding classes containing less than 10% of the overall sample. Relative to Class 2, Class 1 displayed greater left hippocampal engagement to threat, and lower right hippocampal engagement to safety. Class 1 also displayed higher left amygdala and lower right amygdala engagement to threat, and lower left amygdala engagement to safety. Class 2 displayed the inverse patterns (*ps*<0.05). Latent classes also differed in adversity exposure: Class 1 had higher exposure to adversity during early childhood (*p*=.022), whereas Class 2 had higher exposure to adversity in late adolescence, young adulthood, and total adversity exposure (*ps*<0.001) after correction for multiple comparisons. The classes did not differ in anxiety symptoms (*p*>.05).

In sum, classes differed in both patterns of subcortical engagement to threat and safety cues, and developmental timing of adversity exposure, suggesting that age of exposure may be a key factor in how adversity shapes neural representations of learned threat and safety into young adulthood. The latent classes did not differ in anxiety symptoms, suggesting that adversity-associated differences in neural computations underpinning threat and safety learning may not consistently overlap with anxiety-related changes. Parsing complex links between adversity and threat learning, these results highlight the importance of considering developmental timing when investigating relations between adversity, neural processes supporting associative learning, and mental health.

1-G-52 - Causal effects of a parenting program on resting-state graph properties of high-risk adolescents: a randomized clinical trial

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Details

Background: Sensitive creates a foundation for the infant's optimal long-term brain development. On the other hand, when parents are inadequate in their role as caregivers, the developing connectome shows an impaired developmental trajectory in limbic and regulatory brain regions. Although the effects of insensitive care have been widely studied with traditional analytical approaches, such as average activation patterns and seed-based connectivity analyses, they cannot capture complex patterns of communication between spatially distant brain regions. There is an increasing agreement that disturbed brain development can best be understood at the level of brain networks that can meaningfully

characterize the global organizational properties of networks and the role of each region in the network. Moreover, our understanding of how adversities shape brain outcomes is limited by correlational study designs that do not permit causal inferences.

Objective: To address these limitations, this study used network-based analyses and leveraged data from a prospective randomized clinical trial that examined the effects of a parenting intervention on resting-state activation of adolescents at risk for receiving suboptimal care.

Methods: Families were referred by Child Protective Services as part of a diversion from foster care program following allegations of neglect before infants turned 2 years old. Families were randomly assigned to receive the Attachment and Biobehavioral Catch-up (ABC) intervention or the control intervention, Developmental Education for Families (DEF) that had a similar length and structure to ABC, but a different intervention mechanism; DEF provided psychoeducation about developmental milestones, whereas ABC targeted maternal sensitivity, nurturance, and decrease in threatening behaviors. At age 13, participants returned to the lab for a 6 minutes long resting-state MRI scan (N_{ABC}=31; N_{DEF}=29). Children without a history of neglect were also recruited as a low-risk comparisons (N_{COMP}=35). Graph Theoretic GLM toolbox was used for all 4 stages of data analysis: data preprocessing, connectivity matrix and graph property calculation, and running the general linear model with intervention group (ABC vs. DEF vs. low-risk group) as the predictor of interest. Graph properties of interest included local and global network segregation (transitivity, clustering coefficient), integration (current flow global efficiency), centrality (communication betweenness centrality), hierarchical nature (hierarchical structure).

Results: We found significant intervention effects on clustering coefficient of a node in the left superior frontal gyrus and the right piriform cortex, such that the DEF group had significantly higher clustering coefficient in both regions than the ABC or the low-risk groups. We also found intervention effects on communicability distance in the anterior superior surface of the angular gyrus such that children in the DEF group had significantly lower communicability distance than the ABC or low-risk groups. Finally, DEF children showed higher current flow global efficiency and lower hierarchical structures than the ABC or the low-risk groups.

Conclusions: The results support the acceleration neuromaturation hypothesis suggesting that suboptimal care causally leads to increased efficiency in the global network and locally dense connectivity around the superior frontal and piriform cortices in the DEF but not in the ABC or low-risk groups. Moreover, lower communicability distance in the DEF group also suggests that the parietal cortex facilitates more intercommunication in the DEF group than in the ABC and low-risk groups. Given the role of these brain areas in understanding people's actions, personalization of emotions, and attention tasks, decision making, and risk-related tasks, ABC may causally support their age-appropriate neuromaturation during adolescence, 11 years after the intervention was completed.

1-G-54 - Contributions of Socioeconomic Disadvantage to White Matter Development from Infancy to Early Childhood

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Details

Background: The first two years of life are characterized by rapid white matter (WM) myelination and changes in WM fiber density and complexity. Specifically, there are marked changes in white matter microstructure (WMM) across a host of areas in the ventral and dorsal language pathways including in the superior longitudinal fasciculus (SLF), uncinate fasciculus (UF), and inferior fronto-occipital fasciculus (IFOF). Despite evidence that early-life socioeconomic disadvantage (SESD) is associated cross-sectionally with WMM, to date, no longitudinal studies have examined the contributions of SESD to early developmental changes in WMM.

Objectives: Consistent with previous findings that greater SESD is associated with lower fractional anisotropy (FA), and separately, findings that slower maturation of radial (RD) and axial diffusivity (AD) are associated with more advantageous developmental outcomes, this project aims to test the hypotheses that SESD at birth is associated with (1) lower FA, and higher RD/AD at birth, (2) slower increase in FA, and faster decrease in RD/AD.

Methods: Data will come from three waves (e.g., within one week of birth, ages two and three) of the Early Life Adversity and Biological Embedding study (eLABE) (N = 385 singleton infants at birth with available WM data). SESD will be assessed by income-to-needs ratios (i.e., household income divided by federal guidelines for poverty by family size) calculated from maternal-report at birth. WMM (i.e., FA, RD, AD) will be assessed in the left hemisphere in the SLF, UF, IFOF, and corpus callosum. Of note, data for the eLABE study has already been collected.

Analysis Plan: 12 separate hierarchical linear models nested within child will be used to examine contributions of SESD to baseline levels and change in FA, RD, and AD controlling for sex, birthweight, maternal stress at birth (i.e., Cohen perceived stress scale) and total cognitive stimulation in the home (i.e., StimQ Questionnaire). Multiple comparison corrections will be conducted within WMM index (e.g., FA).

Implications: These analyses inform how early WMM development is influenced by SESD in WM pathways crucial for language and other cognitive/emotion functions.

1-G-55 - Examining the role of environmental unpredictability and social support on autonomic regulation and organization

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Details

Individual differences in early experiences of unpredictability and social support are posited to shape developing physiological regulation (Del Guidice et al., 2011). Prior research has shown inconsistent links between such experiences and physiological regulation, which may be attributed to the limitations of traditional physiological measures (e.g., resting RSA). Emerging theoretical and empirical evidence suggests that physiological regulation may be better indexed by measures capturing the nonlinear organizational structures characteristic of interactive physiological regulatory systems (Berry et al.,

2019). Using preliminary data from a sample of 56 12-15-year-olds, this study explored whether dimensions of environmental unpredictability and social support were associated with traditional and novel indices of physiological self-regulation. Specifically, using cardiac data collected during a five-minute resting baseline, we calculated respiratory sinus arrhythmia (RSA) as an index of parasympathetic regulation, as well as a novel summary index (alpha) posited to quantify the degree of autonomic system flexibility and organization. Controlling for demographic covariates (age and sex), multiple regression analyses indicated that neither unpredictability (std. beta = -0.01; p = 0.95) nor social support (std. beta = 0.11; p = 0.47) was significantly associated with resting RSA. In contrast, greater unpredictability (but not social support) was significantly associated with temporal cardiac organizations (std. beta = 0.40; p = 0.01) suggestive of more flexible autonomic system dynamics. Future work aims to leverage repeated measures of these physiological indices collected during a behavioral task to examine whether unpredictability and social support may be associated with regulation in the context of a cognitive challenge. Findings contribute to the growing literature examining how early experience becomes biologically embedded.

1-G-56 - Longitudinal association between neighborhood safety and adolescent health: The moderating role of affective neural sensitivity

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Details

Sleep deprivation and heightened mental health symptoms during adolescence have become significant global health challenges (Kansagra, 2020; Kieling et al., 2011). Systematic review about social determinants of health highlighted the influence of neighborhood characteristics (including neighborhood safety) on adolescents' mental and physical health (Baranyi et al., 2021; Mayne et al., 2021). Despite emerging research (e.g., Ip et al., 2022), the role of adolescents' neural development in the association between neighborhood safety and adolescents' mental and physical health has remained understudied. Importantly, adolescents' neural reactivity to emotion may influence how they perceive and process cues about safety and threat from the environment (Guyer, 2020). Thus, using data from the ABCD study (Casey et al., 2018), the current study investigated the longitudinal association between neighborhood safety and adolescent's health (i.e., sleep, internalizing symptoms, externalizing symptoms), and the role of adolescents' neural reactivity to emotion in the link between neighborhood safety and adolescent health.

The study utilized baseline (T1), one-year (T2), and two-year (T3) follow-up data from the ABCD study, which includes a total of 7918 adolescents at T1 (51% male; mean age = 9.96 years; 57% White, 11% African American, 19% Latino, 2% Asian, 11% Other). At each wave, parents reported on perceived neighborhood safety (3 items; Î±s > .86). At T1 and T3, parents reported adolescents' sleep disturbance, internalizing symptoms, and externalizing symptoms (Î±s > .78). Adolescent's neural reactivity to emotion was measured at T1 using the emotion n-back fMRI test (Cohen et al., 2016). Separate analyses were conducted for neural activity to faces with positive and negative emotion, focusing on brain regions involved in emotional processing (i.e., amygdala, insula, ventral striatum). All analyses controlled for age, race, sex, household income, and T1 adolescent health outcome.

Results from a multilevel growth curve model revealed that higher initial level of perceived neighborhood safety predicted lower T3 sleep disturbance (Î² = -.05, *p* = .001), internalizing (Î² = -.07, *p* < .001), and externalizing symptoms (Î² = -.05, *p* = .001). Greater increases in neighborhood safety from T1 to T3 predicted lower internalizing (Î² = -.08, *p* = .030) and externalizing symptoms (Î² = -.15, *p* = .008), but not sleep disturbance (Î² = -.06, *p* = .098) at T3. Moreover, adolescents' insula reactivity to positive emotion moderated the link between changes in neighborhood safety and adolescent sleep disturbance (Î² = -.04, *p* = .028) as well as internalizing symptoms (Î² = -.07, *p* = .026). Simple slope tests revealed that when adolescents showed higher levels of insula reactivity to positive emotion (i.e., 1 SD above the mean), greater increases in neighborhood safety significantly predicted less sleep disturbance (*B* = -4.55, *SE* = 1.88, *p* = .016) and internalizing symptoms (*B* = -9.36, *SE* = 3.12, *p* = .003). Yet, when adolescents showed lower levels of insula reactivity to positive emotion (i.e., 1 SD below the mean), the associations between increased neighborhood safety and adolescent sleep/internalizing symptoms were not significant (*B* = -.89, *SE* = 1.61, *p* = .582; *B* = -.72, *SE* = 2.77, *p* = .795, respectively). Additionally, ventral striatum and amygdala reactivity to positive emotion did not moderate the association between changes in neighborhood safety and adolescent health, and no moderation effect of neural reactivity to faces with negative emotion was found.

Our findings demonstrate the importance of neighborhood safety in adolescents' mental and physical health, which signify that both earlier levels and increases in neighborhood safety can improve adolescents' mental and physical health. In addition, our findings also highlight the protective role of higher insula reactivity to positive emotion within the context of changing neighborhood environment.

1-G-57 - Family environment moderates the relationship between parent psychopathology and adolescent white matter volume: Evidence from the ABCD® Study

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Details

Objective: Adolescence is a period of significant social, emotional, and neurodevelopmental growth. Increasing rates of mental health (MH) symptoms and diagnoses in adolescents have been documented in recent decades. Structural and functional abnormalities in the brain, particularly in grey and white matter volume (WMV), have been identified in adolescents with depressive symptoms. However, it is unclear to what extent these abnormalities arise from MH symptoms or other environmental factors. The associations between parent psychopathology and other parenting characteristics (e.g., monitoring, warmth, acceptance) in the subsequent development of adolescent MH disorders has been well-delineated by previous research. Similarly, parental psychopathology is thought to impact parenting behaviors and the broader family environment. Yet, little work has been done to link structural brain metrics to parenting factors. The present study aimed to examine one such risk pathway in adolescent MH symptom onset. Specifically, we examined whether family environment moderated the relationship between parent MH symptoms and adolescent brain structure.

Methods: Data from the Adolescent Brain Cognitive Development (ABCDÂ®) Study were used to examine the relationships among adolescent WMV, family environment, and parent and adolescent psychopathology. Participants were included if they had structural scans at both Baseline (ages 9-10)

and Year 2 (ages 11-12) that passed quality control measures and were completed between 18 and 30 months of one another (n=3762). Measures included parent psychopathology at Baseline via the Adult Self-Report, adolescent psychopathology at Year 3 via the Brief Problem Monitor, and whole brain WMV at Year 2. A composite Family Environment score for Baseline was calculated using the Parental Monitoring Questionnaire, Parental Warmth and Acceptance, and Family Conflict subscales (reverse scored), with higher scores reflecting a more positive Family Environment. Linear mixed-effects modeling and the PROCESS macro (model 1) for R were used for statistical analyses. Age at Year 2 scan, sex assigned at birth, ethnicity, total intracranial volume, and raked propensity scores were included as covariates.

Results: Parental psychopathology present in early adolescence predicted adolescent psychopathology at Year 3, $\hat{I}^2$=0.15, t=9.18, p<.001. Parent psychopathology was predictive of adolescent whole brain WMV at Year 2, $\hat{I}^2$=-0.03, t=-2.33, p<.05. A Parent Psychopathology*Family Environment interaction was found to moderate this relationship, such that average (z=0.00, b=-99.14, SE_b=47.62, t=-2.08, p<.05) and more negative (z=-2.20, b=-107.27, SE_b=47.44, t=-2.26, p<.05) Family Environments were associated with lower WMV, DR^2=.0028, F(1, 3664)=12.64, p<.001. Adolescent WMV in Year 2 did not predict adolescent MH symptoms at Year 3 t=0.39, p=0.69.

Conclusions: Parental psychopathology is a notable risk factor for the subsequent development of adolescent psychopathology in this subset of the ABCD sample. Parental psychopathology and parenting characteristics in late childhood differentially impact WMV in early adolescence. Parental psychopathology predicted WMV at Year 2, and Family Environment moderated this relationship. These findings warrant further investigation across subsequent data releases to examine longitudinal trends in the relationship between environmental and genetic risk pathways towards adolescent psychopathology.

1-G-59 - Timing-dependent associations between harsh and warm parenting during childhood and adolescent functional brain network organization

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Details

Background.

Environmental influences shape the developing brain in a context-specific manner, potentially in ways that are adaptive in the short-term but maladaptive in novel contexts across development. Emergent cross-species evidence suggests that adversity (e.g., harsh caregiving) exerts unique effects on brain function depending on the developmental timing of exposure. However, whether the timing of promotive experiences (e.g., warm caregiving) influences the impact on brain function remains unknown. Moreover, little is known about how both adverse and promotive experiences shape functional brain network organization.

Methods.

The present study will evaluate how harsh and warm parenting during childhood (ages 3y, 5y, and 9y) influence functional brain network organization during adolescence (age 15y). The sample includes 173 adolescents recruited from the Future of Families and Child Wellbeing Study, a population-based longitudinal study of predominantly lower-income families with marginalized ethnoracial identities. We will apply graph theoretical analyses of resting-state and task-based fMRI data that has already been processed to interrogate functional brain network organization at the whole-brain and regional levels. At the whole-brain level, we will examine network segregation (modularity), network integration (global efficiency), and their balance (small-world propensity). At the regional level, we will characterize the hubness (betweenness centrality) of brain regions underlying cognitive and socioemotional processing (amygdala, striatum, hippocampus, medial/lateral prefrontal cortex).

Analysis Plan and Hypotheses.

We will implement latent growth curve modeling to identify early childhood levels (intercept) of, and changes (slope, from ages 3-9y) in, harsh and warm parenting. Analyses linking parenting behaviors to functional brain network organization will control for demographic characteristics. We hypothesize that greater harsh parenting will be associated with lower network segregation, greater network integration, and lower small-worldness. We predict the reverse pattern of associations for warm parenting. Moreover, as no study to date has characterized timing effects of parenting with respect to whole-brain topology, we do not specify timing-related hypotheses for whole-brain associations. At the regional level, we hypothesize that greater harsh/warm parenting in early childhood will be associated with higher/lower centrality of early-developing subcortical regions, whereas greater harsh/warm parenting in later childhood will be associated with lower/higher centrality of cortical regions, whose developmental trajectories are comparably protracted. These analyses will be completed before the Flux congress.

Implications.

By delineating developmental windows when specific brain systems and topological properties are maximally sensitive to both adverse and promotive experiences, this study could inform the type and timing of prevention and intervention efforts to promote healthy brain development.

1-G-60 - Do positive childhood experiences protect brain development? Evidence from the ABCD® Study

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Details

Objectives: Adverse Childhood Experiences (ACEs) have significant long-lasting impacts on physical and mental health in adulthood. From a behavioral perspective, resilience mitigates some of these consequences, but has not yet been fully explored in neurodevelopment. Preliminary research suggests adversity attenuates volumetric growth in the hippocampus during early adolescence. The present analysis explores whether protective childhood experiences that promote resilience have an association

with hippocampal structural development during adolescence, a critical period in childhood development. Furthermore, we explore if resilience moderates the negative effect that adversity has on volumetric hippocampal growth.

Hypotheses: We predict that high adverse childhood experiences will correlate with less hippocampal growth, such that more positive experiences will promote a greater rate of volumetric growth. Furthermore, we predict that the relation between adversity and volumetric hippocampal growth is moderated by protective experiences, such that positive experiences buffer the negative effect of hippocampal growth***.*** In particular, we hypothesize that a greater number of different protective experiences at baseline will moderate the effect of adverse experiences on hippocampal growth.

Analysis Plan: We will utilize the longitudinal data collected from the Adolescent Brain Cognitive Development[SM] Study (ABCD) to investigate correlations between hippocampal volume and positive childhood experiences. Model 1 will examine hippocampal volume and adverse childhood experiences at Baseline (9-10 years). Using self-report and structural MRI data collected at Baseline and structural MRI data collected at Year 2 (11-12 years), we will examine relations between adversity, protective factors, and volumetric hippocampal growth using linear mixed-effects modeling (Model 2). Adversity items will be obtained through questions on the life events survey (i.e., if a caregiver has been to jail) and demographics measure (i.e., if they needed food, shelter, or utilities but were not able to obtain them), as has been done in previous work with ABCD. A single adversity score will be calculated as a sum of the above measures and standardized across the sample, with higher scores indicating more adverse experiences. Protective factors will be captured through the following: the Children's Report of Parental Behavioral Inventory (CRPBI) acceptance subscale; the close friend score from the Other Resilience survey; sports, hobbies, and volunteer activity from the Longitudinal Summary Scores Sports Activity; a composite family environment from items on the Longitudinal Parent Demographics and the Social Development Parent Neighborhood surveys; the School Risk and Protective Factors survey; and, the Parental Monitoring Survey. A single protective factor score will be calculated as a sum score of the above measures and standardized across the sample, with higher scores indicating greater protection. The protective score calculation is based on developmental resilience literature and previous research examining protective factors. Analysis will be complete before Flux.

Significance: Previous research has shown a slower growth in hippocampal volume during early adolescence for those who have experienced more adversity. However, research has not examined whether positive experiences in childhood protect brain development in the presence of adversity. This analysis will provide a more complete investigation into the relationship positive and negative experiences have on brain development during early adolescence, which may lay the groundwork for promoting healthy development, especially for those children who have experienced adversity. Additionally, this analysis will provide a comparable assessment to the Protective and Compensatory Experiences (PACE) score for the ABCD dataset and may serve as a foundation for future researchers to examine protective experiences.

1-G-61 - Characterizing the association between maternal stress during pregnancy and brain function via polyneuro risk scores for general cognitive ability in newborns

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Details

Maternal psychosocial distress during pregnancy has been shown to be associated with impaired cognitive development in infants and toddlers. This association is likely partially mediated by changes in brain development including resting state connectivity. Recent work has demonstrated that sample sizes in the thousands are required to detect robust and reproducible associations between complex phenotypes such as cognitive ability and brain-wide features. These sample sizes are not yet available in infant neuroimaging. The polyneuro risk score (PNRS) method has been developed to leverage large sample sizes of population-based studies like the ABCD study. This method determines the associative strength (beta-weights) of each feature in a set of brain features (for instance, brain-wide resting state connections). These beta-weights are then applied to a new test data set and summed to calculate a PNRS for each subject. Previous work in the ABCD cohort has shown that the resting state PNRS for general cognitive ability explains between 15 and 21% variance. The aim of this study is to apply PNRS for general cognitive ability from the ABCD study to infant resting state data and test whether maternal psychosocial distress during pregnancy is associated with the PNRS for general cognitive ability. The infant data will be drawn from two infant cohorts with harmonized pregnancy assessments and scanning protocols. Resting state data from 100 infants is available. The PNRS from the ABCD cohort has been generated and the resting state data from the infant cohorts has been preprocessed. The next steps are to apply the beta-values from the adolescent ABCD sample to the infant cohorts and calculate the PNRS for each infant. Maternal psychosocial distress will be composed of self-reported stress (Perceived Stress Scale), anxiety (State-Trait Anxiety Inventory), and depressive symptoms (Center for Epidemiological Studies Depression scale) averaged across multiple time points during pregnancy. To combine stress, anxiety, and depressive symptoms, a latent distress score will be calculated. We expect that higher distress levels are associated with a lower PNRS for general cognitive ability.

1-G-62 - Alterations of brain microstructure and functional connectome development associated with exposure to various sources of air pollution during the transition to adolescence

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Details

Ambient air pollution comprises chemicals with documented neurotoxic effects and poses a particular risk to child neurodevelopment and mental health. Neuroimaging studies have linked air pollution to increased mental health concerns and to differences in brain structure in children, but the impact of pollution on underlying brain microstructure and function remains largely unknown. Geographical limitations of previous studies fail to capture nuanced variability in both the compositions and sources of pollutants. Here, we will leverage the longitudinal, US-wide Adolescent Brain Cognitive

Developmentâ„ Study (ABCD StudyÂ®) to assess how parallel microstructural and functional brain changes in children ages 9-12 years are associated with exposure to different sources of ambient fine particulate matter (PM2.5). To this end, we will employ (a) multivariate cross-decomposition to uncover latent associations between sources of PM2.5 and cortical microstructure changes and (b) predictive connectomics to link functional connectivity changes with exposure to sources of PM2.5.

These analyses will include data from the forthcoming 5.0 annual data release, including air pollution, sociodemographic, and behavioral data collected at baseline (i.e., from children ages 9-10 years, Nâ‰ˆ11880), and MRI data from both initial and 2-year follow-up visits.

Air pollution data include annual concentrations of 15 measured components of PM2.5 (1): nickel, iron, bromine, vanadium, potassium, lead, zinc, copper, calcium, silicon, elemental carbon, sulfates, nitrates, ammonia, and organic carbon. We will apply positive matrix factorization to these 15 components to identify 5-7 sources of exposure. Sociodemographic and behavioral covariates include chil's sex, race/ethnicity, handedness, average daily screen time, physical activity, combined household income, perceived neighborhood safety, MRI scanner manufacturer, and head motion during scans, in addition to the population density, urbanicity, distance to major roadways, and nighttime noise at the chil's primary residential address.

Imaging data include processed diffusion-weighted MRI data to estimate cortical microstructure from intracellular diffusion via restriction spectrum imaging (2) and resting-state functional MRI data to estimate functional network connectivity (3). From these data, we have estimated annualized percent change per region or network across the two-years (4, 5).

Covariates will be regressed out from the air pollution estimates and annualized changes in intracellular diffusion and in network connectivity using multilevel modeling. Partial least squares correlation (PLSC) will be used to identify latent associations between intracellular diffusion and air pollution sources. PLSC projects two multivariate 'blocksâ€ of data (here: intracellular diffusion, air pollution) into a lower dimensional space, leveraging information across related variables to identify several multivariate patterns of association between blocks. Predictive modeling using the network-based statistic (6) will be used to identify pollution-associated changes in large-scale network connectivity. NBS-Predict leverages machine learning and network science in a cross-validation framework to identify multivariate patterns of functional connectivity related to an outcome (i.e., pollution source).

Perturbations of overlapping neurobiological processes during the heightened vulnerability to mental health issues that is characteristic of the transition to adolescence may have varied and far-reaching consequences. We expect these results to illuminate links between micro-scale neurobiological impacts of air pollution exposure and alterations of function to downstream behavioral and mental health consequences, to eventually help identify sensitive periods and biomarkers for early intervention. Further, parsing the effects of different sources of PM2.5 exposure can inform caregiver behavior and support policy and legislative recommendations.

1-G-63 - The impact of early life adversity on physiological response to acoustic cues

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Details

The developing brain is highly susceptible to stress, resulting in long lasting alterations to central nervous system (CNS) function and reactivity following experiences of early life adversity (ELA). For example, both adolescents and pregnant women with ELA exposures had larger eye-blink startle responses to loud noises within a fear potentiated startle procedure, when they were expecting unpleasant stimuli (muscle contraction or shock). Such elevated startle reactions have also been observed in posttraumatic stress disorder (PTSD) patients. Moreover, elevated physiological reactivity during threat learning in childhood is associated with later vulnerability to developing PTSD symptoms in response to subsequently experienced traumatic events. Thus, physiological reactivity to the environment is both associated with ELA and may act as a risk factor for adverse reactions to later experienced adverse events. To date, most of the studies examining elevated physiological reactivity following ELA has focused on examining reactivity when there is a direct threat to the participant (threat learning, or anticipation of an aversive stimuli). In the current study, we instead examined physiological reactivity in the context of a naturalistic procedure (viewing affectively salient video clips from scary movies), as a function of young adults ELA exposure. Such naturalistic stimuli are increasingly used in fields like imaging neuroscience as they provide a way to strongly evoke emotions while also recapitulating 'real lifeâ€ sensory processing and behavioral demands. These stimuli can also be divided across a range of dimensions to examine different components of physiological reactivity. To address this question, we will use data collected from an electrocardiogram (ECG) study of 69 undergraduate students. In this study, participants watched affectively salient videos while ECG was collected. Information about their ELA history was also collected during the lab visits through the Questionnaire of Unpredictability in Childhood (QUIC). To unpack the influence of ELA on physiological responsivity to acoustic cues, we plan to extract information about sound intensity (in units of Decibels; dB) from the video clips using Praat/PraatR and segment the clips into smaller sections based on the level of intensity (e.g., high and low). We will calculate each participant's mean cardiac interbeat-interval (IBI) from the ECG data using Python as a measure of physiological responsivity. We will then examine if differences in mean IBI between levels of sound intensity vary as a function of early life adversity. Analysis will be completed with results included by Flux. This novel analytical approach aims to further our understanding of how ELA may alter the relationship between autonomic reactivity and environmental cues. We hope to use this study as a proof of concept to later test this paradigm directly in children and adolescents of varying levels or dimensions of ELA exposure in different social (e.g., family and friend dynamics) and environmental contexts (e.g., school and neighborhoods).

1-G-64 - Prenatal stress exposure, newborn BNST, and infant temperament at 6 months

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Details

Anxiety disorders impact a significant proportion of the population and lead to functional impairment (Essau et al., 2018). Cross-species research has identified the bed nucleus of the stria

terminalis (BNST) as a critical neural substrate for anxiety phenotypes. The BNST is a small brain region with direct projections to the hypothalamus that drive the hypothalamic-pituitary-adrenal axis response to stress (Avery et al., 2016). Despite promising work on the BNST in human adults, no studies have examined this structure earlier than late childhood (Feola et al., 2022). This is particularly striking given: (1) rodent research highlighting the essential role of the BNST in infant learning (Chang & Debiec, 2016), (2) evidence that this region is susceptible to stress (Moriceau et al., 2004), including mild prenatal stress (Soares-Cunha et al., 2018), and (3) the prenatal period and early life represent a time of rapid growth of the BNST, suggesting this may be a potentially sensitive period for stress-effects on the BNST (Halladay & Herron, 2023). To address this gap in the developmental neuroscience of the BNST, we assessed perceived stress during pregnancy and at infant age ~4 weeks obtained high-resolution T1- and T2-weighted MRI, diffusion-weighted MRI, and approximate 10 minutes low-motion resting-state fMRI. The location of the BNST was traced on the University of North Carolina's infant newborn T2 atlas using the manual protocol developed by Theiss et al. (2017). The anatomically defined BNST masks allowed us to conduct analyses on BNST structural and functional connectivity. Infant temperament was evaluated at age 6 months using the Infant Behavior Questionnaire-Revised.

Our current ongoing longitudinal sample consisted of 324 families, with 294 mothers completing stress assessments and 151 completing the 6-month IBQ-R. Of the infants, useable data has been collected from 106 with both T1- and T2-weighted, 80 DWI, and 106 rsfMRI scans. We are in the process of manually editing image segmentations and will complete our analyses prior to the conference. Our analytic plans and hypotheses are three-fold. 1) Estimate variation in BNST structural and functional connectivity. While it is unclear what connections will be identified at this age in development, prior non-human primate research (Oler et al., 2017) suggests we may observe both structural and functional connectivity between the BNST and other brain regions in infancy. 2) Examine the association between prenatal stress exposure and BNST connectivity in newborns. We hypothesize that maternal stress during pregnancy would predict newborn BNST connectivity with a subcortical network of stress-responsive brain regions including the amygdala, hippocampus, and hypothalamus. 3) Examine newborn BNST connectivity as predictors of infant temperament at 6 months. We hypothesize that infant temperament at 6 months would be predicted by newborn BNST connectivity.

This multi-modal research will provide, for the first time, fundamental knowledge on human BNST development in early life. Findings will advance clinical theory on individual differences in responses to prenatal stress, and the neural basis of early emerging risk trajectories for anxiety. Furthermore, results may contribute to our mechanistic understanding of how prenatal stress rewires this brain region to confer risk for psychopathology. Broadly, this study has critical implications for prevention and interventions targeted early in life.

H – Executive functioning

1-H-65 - The maturational timing of executive function from adolescence to adulthood: Generalizability and reproducibility across datasets, measures, and levels of analysis

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Details

Contemporary and historical theories of human neurobehavioral development suggest goal-directed cognition (executive function (EF)) matures from childhood through adolescence, and deviations from normative development underlie peaks in accidental fatalities and the emergence of psychopathology during adolescence. Initial individual investigations with relatively small datasets or a narrow subset of measures suggest general adolescent EF improvements. However, no large-scale, multi-assessment, multi-dataset reproducibility investigations of adolescent executive function development have been performed. Further, common analytic approaches do not quantitatively define maturational timing and/or plateaus towards adult-levels of performance. The magnitude of executive function changes during adolescence, the precise timing of when adolescents reach adult-levels, and the potential diversity of processes assessed by varying executive function tasks, thus remains widely debated. This undermines definitions of the boundaries of the adolescent period, synthesis of research across studies, and potential long-term real-world utility of neurodevelopmental perspectives into clinical care. Integrating four large independent datasets, two longitudinal and two cross-sectional (total age range: 8-35-years-old, N=10,766, visits=13,819) that included twenty-three measures from seventeen distinct EF tasks, we provide a novel, precise quantitative charting, multi-assessment, and multi-dataset investigation and replication of EF development from adolescence to adulthood. Across assessments and datasets, EFs followed a canonical non-linear developmental trajectory, with rapid and statistically significant development in late childhood through mid-adolescence (10-15-years-old), before stabilizing to adult-levels in late adolescence (18-20-years-old). Both cross-sectional and longitudinal age effects among EFs were best captured by domain-general processes consistent with theories of unitary EF and fluid cognition. Scaled domain-general EF scores generate reproducible adolescent growth charts across datasets, tasks, and sociodemographic factors. Results provide a canonical trajectory of EF maturation from adolescence to adulthood that demarcates the boundaries of adolescence, can be practically integrated into future studies, and used to identify deviations in health and disease.

1-H-66 - Variability in the engagement of recurring brain states increased with age during adolescence and predicted executive function task performance in over 2000 participants

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Details

Objective: Flexibly responding to ongoing stimuli is required for navigating the world. Variability in brain signals (i.e., neural variability) supports this skill and other executive functions (EFs). Neural variability allows the brain to explore a collection of potential neural configurations to enable flexibility. The relationship between neural variability and EF is critical during adolescence, a period characterized by rapid environmental changes. Indeed, increased neural variability has been reported across adolescence and is associated with better task performance. Previous studies operationalize neural variability in several ways, including Blood-oxygenation-level-dependent standard deviation and multiscale entropy. Little work has studied the developmental trajectories of the variability in the engagement of recurring brain states. It remains unclear if a deviation from typical development might contribute to EF alterations. We investigated these questions using predictive analyses in two neurodevelopmental datasets.

Methods: Replicating previous work, we identified four canonical brain states by applying nonlinear manifold learning to the Human Connectome Project (HCP) task-based functional magnetic resonance imaging (fMRI) data. A recently introduced framework extended these brain states to the Philadelphia Neurodevelopmental Cohort (PNC; N=1208; 658 females; age: 14.68Â±3.32) and Healthy Brain Network (HBN; N=1275; 491 females; age: 11.69Â±3.39) resting-state data to assess state engagement variability. Specifically, representative time points from the four brain states were regressed from each PNC or HBN time point of interest using non-negative least squares regression. Output coefficients indicated state engagement at that time point. State engagement variability can be examined with the standard deviation of each state's coefficients across time. We used MANOVA to study how state engagement variability changed with age. We further tested the possibility of training a linear model to predict EF using state engagement variability before applying it to previously unseen participants from another dataset (PNC to HBN or vice versa). EF was evaluated by performing a principal component analysis on scores from the Penn Computerized Neurocognitive Battery and the NIH Toolbox for PNC and HBN, respectively. Two additional linear models were created to predict age using state engagement variabilities. Predicted age served to estimate brain age based on state engagement variability. We assessed deviation from typical development by computing the squared difference between chronological and brain age. Deviation was correlated with EF scores to investigate its behavioral implications.

Results: State engagement variability increased with age in both PNC and HBN (PNC: $F(4,1201)=20.793$, $p<0.001$; HBN: $F(4,1268)=36.482$, $p<0.001$). With external validation, it successfully predicted EF in previously unseen participants, even when EF was measured using a different tool. Predicted EF correlated positively with observed EF (tested in PNC: $r=0.160$, $p<0.001$; tested in HBN: $r=0.202$, $p<0.001$). We additionally demonstrated that developmental deviation in state engagement variability was associated with worse EF (tested in PNC: $r=-0.242$, $p<0.001$; tested in HBN: $r=-0.270$, $p<0.001$), controlling for age.

Conclusions: Our findings demonstrate that state engagement variability, a form of neural variability that has not previously been the focus of much research, supports EF during development. We assessed continuous brain state engagement at the resolution of individual time points. State engagement variability increases with age and can predict EF. On-time development is also critical, with accelerated and delayed state engagement variability development both associated with worse EF.

1-H-67 - Ignore the Tap: Neural Correlates of Children's Voluntary Tactile Attention

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Details

Study Objective:

The study objective was to examine how tactile event-related-potentials (ERPs) elicited to attend and ignore conditions in a sample of 6- to 8-year-olds relate to individual differences in children's executive functioning.

Method:

The sample included 47 children aged 6 to 8 years of age. The children were outfitted with a 32-channel EEG cap and tactile stimulators on both middle fingers that were connected to a pneumatic stimulator that inflated a membrane that created a tactile tap. The children completed a tactile attention task during EEG collection as well as various tasks from the NIH Toolbox Cognition Battery. For the tactile attention, the children were either instructed to focus on the taps to their hands for 50% of the task blocks and to focus on their breath for the other 50% of the blocks. The trials included a visual cue (either an arrow to the left or right) that was constant during the entire block and was a reminder to which hand was being stimulated and whether they were to ignore or attend to the stimuli. The task took around 15 minutes to administer. For the executive functioning measure, we focused on the Flanker task from the NIH Toolbox, which asks participants to indicate which way a middle arrow is facing amid surrounding arrows (flankers). The flanker task takes around 4 minutes and is completed via an iPad.

Results:

EEG data was analyzed through the HAPPE+ER pipeline and ERP components were identified via principal component analysis. The N80 is a neural correlate of attention that is reported in adult studies, but not in child studies. Within tactile attention research, there are few ERP studies with children, so these data are among the first to examine neural indices of tactile attention in children. Analyses focused on the N80 component. A multilevel model using restricted maximum likelihood estimation with a random slope of trial was done to understand the relationship between N80 amplitude and Flanker scores. There was no difference in N80 amplitude between the attention conditions, whereas in the adult literature one signature of the N80 is an enhancement for attended stimuli. However, the effect of Flanker score on N80 amplitude was significantly moderated by attention condition. The slope of Flanker score during the ignore condition was significant, while the slope during the attend condition was not. Further analyses will include examination of the N2cc, Nd, and pre-stimulus anticipatory components.

Conclusions:

The lack of an overall attentional effect on the child tactile N80, combined with the findings on the relations of Flanker score with N80 amplitude, shed light on the developmental nuances of attention in tasks where children are instructed to attend or ignore tactile stimuli. Using such attention tasks with a developmental population can provide insights into the neural indices of attention and the relations with executive function.

1-H-68 - Random forest analysis identifies important clinical and imaging predictors of impaired neurocognitive development in children with congenital heart disease

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Details

A majority of children born with congenital heart disease (CHD) are now surviving to adulthood due to effective medical and surgical management a population growing an estimated 5% per year. However, they are more likely to show early developmental delays and later neurocognitive deficits, including problems with executive function and higher rates of ADHD. These deficits persist through adolescent development. While the causal mechanisms of these neurocognitive concerns are not fully understood, it is imperative to identify clinical and imaging risk factors to facilitate timely intervention. Here, we implement Random Forest to predict measures of executive function in two independently acquired populations of adolescents with CHD (and matched controls) the multi-institutionally acquired Single Ventricle Reconstruction Trial (SVRIII, n=452), and a single-site population of patients with hypoplastic left heart syndrome (HLHS) (DOD/Connectome, n=241).

We trained random forest regression models to predict executive functions (EF) as measured using the NIH Toolbox, Delis-Kaplan Executive Function System (D-KEFS), and the Behavior Rating Inventory of Executive Function (BRIEF), across three subdomains of EF Mental Flexibility, Working Memory, and Inhibition. A separate RF model was trained for each outcome measure using the DOD/Connectome dataset, and independently validated on the SVRIII dataset (hold-out set). DOD/Connectome dataset was partitioned into 80% for training and 20% for testing. We estimated the best parameters for the random forest algorithm via a randomized grid search of parameters using 10-fold cross-validation on the training set only. The best parameters were then used to fit the model on the full training set and validated on the test set. Algorithm performance was measured using root-mean squared-error (RMSE). We included patient clinical variables, perioperative clinical measures, structural white matter (DTI), and structural volumes (volumetric MRI) as predictors. Structural white matter was measured using along-tract diffusivity measures of 13 inter-hemispheric and cortico-association fibers. Structural volumes were measured using FreeSurfer. Variable importance was measured by the average Gini-impurity of each feature across all decision trees in which that feature is present in the model, and rank-biased overlap (RBO) was used to measure the degree of overlap in feature importance across each EF subdomain, and across subdomains. To compare functional contributions of important features across cohorts, we developed a novel approach for feature interpretation: Functional Domain Analysis. Here, we mapped a brain function ontology onto the features used by each model, i.e., brain regions/networks thought to underlie these skills, such as limbic, language, motor, etcâ€¦, which allowed us to directly compare the domains most important to the prediction of each neurocognitive outcome.

We were able to predict EF scores within one standard deviation in the test set across EF domains. Working Memory was the best-performing subdomain, with the NIH Toolbox Flanker test achieving a RMSE of 12.15 in the test set. Feature importance analysis identified a significant over-representation of para-limbic associated features (both structural and diffusion), with each measure of EF having at least 25% para-limbic representation. This novel, surprising finding identified a set of features that may be potential targets for domain-specific biomarkers of EF deficits. Feature importance in within-subdomain measures had an average RBO of 0.162, and across-cohort EF outcomes had a mean RBO of 0.105, showing significant agreement in predictive features of EF subdomains. In conclusion, MR-derived features can accurately predict EF outcomes in adolescents with CHD, and importantly, para-limbic associated features show a strong association with EF, and may be potential targets for domain-specific biomarkers of EF deficits.

1-H-69 - Study of sleep and ADHD variables on inhibition performance in brain and behavior of youths

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Details

With later bedtimes and early school starting times, adolescents, on average, can get an insufficient amount of sleep (~7 hours), resulting in poor sleep quality. Poor sleep quality negatively influences cognitive function as measured by academic achievement, or executive function (EF). Poor sleep quality in youths can impact EF, and often results in symptoms that mimic or exacerbate attention deficit hyperactivity disorder (ADHD). EF ability and EF dysfunction are associated with â€˜core control networks' (including cingulo-opercular and fronto-parietal) across multiple control-demanding tasks. These functional networks negatively correlate with the default mode network (DMN) at rest and are positively engaged during tasks when the DMN typically displays negative activation, implying opposition between the DMN and the control networks. Poor sleep relates to less opposition between the DMN and putative control networks. Youths with ADHD have been shown to have less suppression of the DMN than those without ADHD.

In this study, we examined the impact of different aspects of sleep quality (duration, activity, and latency) and the presence or absence ADHD diagnosis or symptoms, on brain engagement of control and DMN networks during an inhibition (stop signal) task, and on behavioral assessments of EF.

The behavioral work examined data from 119 youths (47 F), ages 8-18 years (*M*=12.5). The sample included 48 typically developing youths and 71 diagnosed with ADHD (31% with comorbidities). Sleep metrics were collected using Phillips Respironics Actiwatch-2, and included those who wore the watch ~24 hours a day, for at least 3 days. Eight average variables were created to measure different aspects of sleep, and standard deviations of these mean variables were used to measure within subject variability. Principal components analysis (PCA) resulted in 3 independent sleep components (duration, activity, and latency) for average and variability measures. Inhibition was measured across two tasks.

The fMRI imaging work used a subsample of 48 youths from the behavioral analysis with sufficient performance and motion control on a stop signal task (stop vs. baseline). A control network mask comprised of the cingulo-opercular and fronto-parietal networks (cortical and subcortical regions included), along with a mask of the DMN (cortical and subcortical regions included) were analyzed for interactions with sleep and ADHD variables. An opposition score between the control and DMN mask was used as the dependent variable for analyses, along with the average parameter estimates (PEs) of the control and DMN masks separately.

The behavioral work found significant interactions between average sleep activity and ADHD diagnosis in predicting both accuracy (r^2= .43, corrected p= .004) and response time (r^2= .18, corrected p= .015) for inhibition performance. The same was seen for the interaction between sleep activity variability (SD) and ADHD in predicting both inhibition accuracy (r^2= .42, corrected p= .015) and response time (r^2= .12, corrected p= .014). In all models, the diagnosed ADHD group appear to be less impacted by increased sleep activity or increased variability in sleep activity during inhibition performance.

The imaging work found a significant relationship with age predicting Control-DMN network opposition during the stop signal stop vs. baseline contrast (r^2= .12 p= .008). When testing for interactions with the sleep variables and ADHD symptom burden to predict network opposition, average control PE, and average DMN PE, all results were null. We will next examine the PEs for the cingulo-opercular and fronto-parietal networks separately, along with 8 pre-planned ROIs of the DMN to interrogate interactions with sleep quality and ADHD symptoms. Altogether, this work examines the complexity of two variables (sleep, ADHD) that feed into controlled (EF) behavior.

1-H-70 - Inhibitory Control in First-Time Fathers: Neural Correlates and Associations With Postpartum Mental Health

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Details

Difficulty with inhibitory control, a form of self-regulation, has been linked to negative parenting outcomes and mental health challenges in mothers. However, the implications of inhibitory control for first-time fathers have not been investigated. Given the heightened risk of postpartum mental health issues in both mothers and fathers, research investigating the relationship between inhibitory control and adjustment to fatherhood is warranted. This study explored the neural underpinnings of inhibitory control and its associations with paternal mental health at six months postpartum using an adapted Go/No-Go fMRI task with infant cry, pink noise, and silent conditions. Contrary to our expectations, we did not observe any differences in fathers' inhibitory accuracy when completing a Go/No-Go task with infant cry sounds compared to silence or pink noise, although we did identify distinct patterns of neural activation across the three sound conditions. Specifically, fathers exhibited neural activation in a greater number of prefrontal brain regions when effectively inhibiting in the presence of infant cries (e.g., dlPFC, insula, IFG, aPFC, SMA). Moreover, fathers' postpartum depressive symptoms were positively associated with their activation in the aPFC during inhibition trials. In contrast, postpartum anxiety was not associated with fathers' brain activation across any task conditions. This study offers insights into the neural underpinnings of inhibitory control, responses to infant cries, and postpartum mental health in first-time fathers, providing a foundation for future research.

1-H-71 - The impact of varying dimensions of adversity on the neurofunctional associations of working memory in early childhood

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Details

Early childhood, ages 4 to 7, is a period of rapid development that facilitates the acquisition of working memory (WM) and related areas of neurocognition. WM is a central component of executive function that refers to the retrieval, recall, manipulation, and temporary storage of incoming information (Baddeley et al., 2003). The literature points to domain-general brain activation of WM in the prefrontal cortex (PFC) with distributed activation in regions specific to the domain of the task. Visuospatial tasks show activation in occipital, parietal, and frontal regions (Baddeley et al, 2010; Camos, 2017; Christophel et al., 2017). Burgeoning research suggest that WM development is influenced by experiential input. Unpredictable, depriving, and threatening experiences of adversity are shown to undermine the development of working memory and underlying neural substrates Finn et al., 2017; Rosen et al, 2020; Sheridan et al., 2017; Ucacheva et al., 2022). In early childhood, parents and caretakers play a central role in child development as they are curators of the environment, moderators of their chil's exposure to the world, and can serve as primary protective barriers or sources of risk in adverse environments (Bowlby, 1969; Masten et al., 2008). More work is needed to understand and disentangle the relative influence of different dimensions of adversity (unpredictability, deprivation, threat) and how they function differentially across proximal caregiving contexts versus distal environmental influences that may explain individual variability of neurocognition in early childhood.

In the current study, we aim to examine how adverse proximal caregiving contexts versus distal environmental circumstances within the dimensions of unpredictability, deprivation, and threat, differentially function to explain variability of the neurofunctional associations of visuospatial WM in early childhood. We hypothesize that adversities in these dimensions in the context of caregiving may explain most of the variability in altered neurofunction during a visuospatial WM task. To do this, we gathered functional near infrared spectroscopy (fNIRS) data, which measures the blood oxygen level dependency as an indirect measure of cortical brain activation~~,~~ from 84 children (41 Male), while they completed a visuospatial WM task on a computer. Children were asked to remember the tree in which the monkey hid his bananas during a randomized delay period. Child age ranged from 4-7 years old (mean= 4.76). Our fNIRS cap configuration provided 50 channels that covered frontal and parietal regions of interest from Brodmann's atlas.

For adversity measures, we have three dimensions of adversity with measures capturing proximal caregiving risk and more distal environmental risk within each dimension. For deprivation, proximal measures included Beck Depression Inventory and the Perceived Stress Scale as parent reported mental health indices, and distal measures included financial and resource measures like the Income to Needs Ratio and the Family Resource Scale. For threat, we used proximal measures such as the parent reported Traumatic Events Screening Inventory, and distal measures such as a neighborhood safety metric from the Child Opportunity Index. For unpredictability, proximal measures include parent report Family Support Scale, and distal factors such as how often the family has moved residences.

All data collection has been completed and we are in the process of preparing data for analysis. For our analyses, we plan to look for significant activation in all 50 channels. Next, we will test associations of channels with significant activation with WM performances. We will run separate models to test for main effects and interactions for all channels with each measure of child adversity. Child age, bilingual status, and gender will be included as covariates for each model. All analyses will be completed prior to Flux.

I- Language

1-I-72 - Phonological and semantic incongruity effects in typical hearing and cochlear implant-using children: electrophysiological evidence

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Details

Objective. The process of naturalistic spoken word recognition is influenced by both bottom-up acoustic-sensory information and top-down cognitive-visual information. These cues are used to process the meaningful sounds (phonology) and semantic representations of speech. Several studies have used EEG/ERPs to study children's spoken word recognition (Desroches et al., 2013; Malins et al., 2013), but less is known about the role of visual speech information (facial and lip cues) on children's neural mechanisms of this process. It is also unclear if populations with different early sensory experiences (e.g. deaf children who receive cochlear implants; CIs) show the same pattern of neural responses during audiovisual spoken word recognition. Here we investigate typical hearing (TH) and CI-using school age children's ERP components to phonological (N280, P3) and semantic (N400) incongruities during a picture-audiovisual word matching task.
Methods. Children (TH n = 15; CI n = 11; ages 7 13 years) were asked to match picture primes and AV video targets of speakers naming the pictures, under four conditions: match (picture: ROSE word: 'roseâ€), rhyme (ROSE 'noseâ€), word-initial cohort (ROSE 'roadâ€), and unrelated (ROSE 'bearâ€). ERPs were time-locked to the onset of the target's meaningful visual and auditory speech information.
Results. In conditions with initial speech sound incongruity between prime and target labels (rhyme and unrelated), we observe different patterns between groups in the processing of phonological mismatches. Specifically, we find an N280 negativity effect between match and rhymes/unrelated conditions for the CI group. In the TH group, however, we find a pattern of more positive P3 responses to rhymes/unrelated words compared to matches. All conditions that do not have semantic congruency between the prime and target evoke more negative N400 amplitudes when compared to the match condition, though semantic incongruity effects emerge at different timepoints across conditions and groups.
Conclusions. We interpret these preliminary findings in light of the unique strategies that may employed by these two groups of children based on the salience of different speech cues. These findings will better inform our understanding of attentional and perceptual speech processing in children, and can have implications for improving speech accessibility for populations with different sensory experiences.

1-I-73 - Anatomical distinction and intervention-driven changes of frontal language regions in struggling readers

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Details

Children with reading difficulties struggle to accurately recognize and decode written language. These difficulties have been correlated to structural and functional differences in the left inferior frontal cortex (IFC), an area associated with a variety of language functions including lexical access and phonological processing. Studies of this region have shown differences in activation for real words compared to pseudowords and nonwords in struggling readers (Olulade et al., 2015; Joo et al., 2021). Additional studies in typical readers have identified distinctive text-selective regions in the IFC (Fedorenko et al., 2012; Pallier et al., 2011**).** However, in struggling readers, the spatial and functional properties of these text-selective regions, as well as the changes they undergo over reading development, are not well understood.

In our current study, children with a history of reading difficulty (N=18, ages 8-13y) participated in an 8-week, intensive reading intervention program, which has been shown to improve reading ability in children with dyslexia (Donnely et al., 2019). Reading assessments as well as functional MRI scans were collected pre-intervention and 4 months post-intervention. During the scans, participants viewed stimuli from different visual categories. Text stimuli included high and low frequency real words, pseudowords, and consonant strings. Non-text stimuli included false fonts, objects, faces and limbs. Participants performed two runs of one-back task (4.3 minutes each), and two runs of a fixation task , where they responded when a fixation dot changed color. The fixation task directs attention away from the stimulus while maintaining fixation, whereas the one-back task ensures that stimuli are attended and task-relevant. Critically, the visual stimuli were equivalent across runs, allowing us to study both a) the response of frontal cortex to different categories of visual stimuli and b) how responses change as a function of the cognitive task. The data were preprocessed with fMRIprep (Esteban et al., 2017). A GLM was fit to the data using Nilearn (Abraham et al., 2014). Native space contrast maps were calculated as text > all other categories except for false fonts (combining data across all imaging sessions), at a threshold of t>2.

The resulting contrast maps revealed two spatially distinct, text-selective regions in left IFC which we defined as two separate regions of interest (ROIs) in each individual. (1) A more anterior region located in the inferior frontal sulcus (IFS) and (2) a more posterior region along the precentral gyrus which was generally larger and spread more dorsally (PrG).

We found a significant task difference in both frontal ROIs, such that the BOLD responses (percent signal change) were stronger for the one-back task compared to the fixation task, specifically for words and pseudowords. Interestingly, ROI analysis of pre- and post-intervention showed different patterns of change in the IFS and PrG regions. The PrG region showed an increase in text activation for the one-back task but no change for fixation task. The task effects in this region also became more pronounced after the intervention with text categories having the largest increase compared to other categories. In contrast, the IFS showed an overall decrease in activation for the fixation task across all categories, with

no significant changes in text-selectivity. This suggests that the intervention-driven changes in IFC are specific to attention-demanding tasks and do not reflect an automatic, bottom-up response to text. Moreover, regions in frontal cortex that are immediately adjacent yet spatially distinct have different response profiles, task effects, and magnitudes of plasticity following intervention.

1-I-74 - Associations among SES, home language input, and resting-state functional connectivity in children

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Details

Objective. Socioeconomic resources, such as family income or parental education, have been significantly associated with resting-state functional connectivity (rsFC) in children. Less is known about how variations in more proximal factors, such as the home language environment, are related to rsFC. The present study examined relations among socioeconomic resources, the naturalistic home language environment, and rsFC between the left inferior frontal gyrus (IFG) and left superior temporal gyrus (STG), two cortical regions consistently found to support language development in children. We hypothesized that greater socioeconomic resources and higher levels of language input would be associated with greater connectivity between these two regions, suggestive of more efficient language-related neural processing. **Methods.** Demographic information, naturalistic home audio recordings, and resting-state fMRI data were acquired on a socioeconomically, ethnically, and racially diverse sample of children aged 5-9 years (*n = 41 with complete SES and fMRI data; n = 37 with complete naturalistic home audio recordings and fMRI data*). Socioeconomic resources were indexed using average parental education and family income-to-needs ratio. The home language environment was operationalized as average hourly adult-child reciprocal verbal interactions (conversational turns) and average hourly adult word count. Covariates included child age and sex, as well as audio recording time and average parental education where appropriate. **Results.** Higher levels of parental education were marginally associated with greater connectivity between the left IFG and left STG (*êžμ* = .31; *p* = .055), but family income-to-needs ratio was not (*êžμ* = .22, *p* = .20). Higher average hourly conversational turns were significantly associated with greater connectivity between the left IFG and left STG (*êžμ* = .41, *p* = .04). Neither average hourly adult words (*êžμ* = .23, *p* = .23) nor average hourly child vocalizations (*êžμ* = .26, *p* = .17) were significantly associated with connectivity between the left IFG and left STG. **Implications.** Together, results suggest that adult-child conversational turns may be an important experiential factor associated with functional connectivity between key language regions in the brain.

1-I-76 - Exploring Mechanisms of Phonetic Category Learning Through Perceptual Attunement

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Details

Infants begin life able to discriminate both native and non-native speech sounds. By 10-months, infants improve at discriminating similar sounding native speech sound differences (e.g., English voiced â€˜ba' vs voiceless â€˜pa') and decline at discriminating speech sound differences that are not used to contrast meaning in the native language (e.g. Hindi retroflex â€˜É—a' vs dental â€˜É–a'; Werker & Tees, 1984). 'Acquired Distinctivenessâ€ (AD), in which two similar speech sounds are consistently paired with two different objects, is a perceptual learning mechanism that boosts discrimination (Yeung & Werker, 2009). 'Acquired Equivalenceâ€ (AE), in which two similar speech sounds are inconsistently paired with two objects, is a learning mechanism that diminishes discrimination (Honey & Hall, 1989). AD (Yeung & Werker, 2009) has been shown to be effective in changing non-native speech sound discrimination in infants aged 6-8 months. In a recent study using the same EEG discrimination paradigm employed here, we found that a passive statistical learning mechanism, distributional learning, effectively changed speech sound discrimination at 6-8 months, but not after 10-months of age (Reh et al., 2021), consistent with the possibility of a critical period that begins closing by 10-months (Werker & Hensch, 2015).

The current study was designed to test whether the efficacy of AE and AD similarly changes across the first year of life or, because AE and AD involve linking sound to meaning, they remain effective even at the older age. We are testing this by comparing English-learning 6- and 12-month-old monolingual infants. As in Reh, et al. (2021), we are using a native English, but acoustically difficult, phonetic contrast (English â€˜ra' vs â€˜'la'). At first, infants are presented with three sequential trials labelling a familiar object (e.g., " Look at the banana/dog/hand!") to signal an object labelling task (Yeung et al., 2014). Then infants are presented with either consistent or inconsistent speech sound/object pairings, following which phonetic discrimination is assessed. As in Reh, et al. (2021), discrimination is assessed by measuring the ERP (event related potential) response to change trials in an oddball task.

To date, we have tested 55 of the proposed 80 infants, with 29 at 6-months and 26 at 12-months. If AE/AD are effective learning mechanisms across all ages, then AD will boost, and AE will diminish, discrimination of â€˜ra' vs â€˜la' at both ages. If the efficacy of these learning mechanisms is delimited to a 6â€“10-month sensitive window in perceptual development (Werker & Hensch, 2015), then these mechanisms will only be effective in the younger age group. Currently, the 6-month-olds are following the expected pattern, while there is still too much variability at 12-months to be confident of the pattern. We expect to finish data collection and analysis by the end of summer 2023.

The results of this study will advance our knowledge of how infants become adept 'native language listenersâ€ and will provide insight as to whether the kind of learning opportunity infants encounter (passive listening versus word learning) impacts the timing of plasticity.

1-I-77 - Task-elicited functional connectivity of the language network

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Details

Introduction

Lateralization of language function to the left hemisphere is well-established in neurotypical individuals. Neuroimaging studies demonstrate that up to 96% of right-handed individuals and 81% of left-handed individuals have left hemisphere language lateralization (Berl et al. 2014; Greve et al., 2013; Olulade et al., 2020). However, to date, studies of language lateralization have examined only isolated brain regions. As a complex cognitive process, language engages a functionally connected neural network (Vissers et al., 2012) which may be better characterized by examining functional connectivity (FC) of this network. FC represents brain activity in two or more brain regions that shows a statistical relationship over time, and reflects communication and coordination between brain regions, capturing functionally specialized neural networks (Vissers et al., 2012).

The current study will examine lateralization of FC elicited by a language task in a large sample of adults from the Human Connectome Project (HCP; Van Essen et al., 2013). Using a seed-based approach, we will examine language-task elicited FC lateralization between language critical ROIs, such as Broca and Wernicke, that form the language network. We will also examine the relationship between FC lateralization and performance on a behavioral assessment of language. The specificity of this relationship will then be contrasted with associations between FC lateralization and behavioral assessments of nonverbal cognition and motor skills.

Methods

Data will be analyzed from the HCP Young Adult Release (Van Essen et al., 2013). This dataset includes approximately 1200 neurotypical young adults aged 22-35 with behavioral and 3T functional magnetic resonance imaging (fMRI) data. We will analyze language-task dependent brain function. The language task involved trials of brief auditorily presented narratives (5-9 sentences), and participants respond to two-alternative forced choice comprehension questions (Binder et al., 2011). Data will be the HCP minimally preprocessed data (Glasser et al., 2013). We will apply further processing to estimate functional connectivity using matlab code available at https://github.com/ColeLab/TaskFCRemoveMeanActivity/.

Connectivity seed regions are Broca and Wernicke using a parcellation framework derived from the HCP atlas (Glasser et al., 2016). Clusters of language related brain regions also will be defined as in Baker et al. (2018) and Briggs et al. (2018): Frontal inferior frontal gyrus, mesial supplemental motor area, inferior frontal sulcus and junction; Temporal superior temporal sulcus (STS) and gyrus, inferior temporal sulcus and gyrus; Global semantic 44, 45, 55b, IFJA, 8C, SFL, 8BM, STSdp, STSvp, temporal area 1p, PHT (e.g., Larson et al., 2022).

FC lateralization will be calculated using average correlation strength and the following index: [(Right - Left) / [abs (Right) + abs (Left)]. For instance, we will apply this index to the average correlation of Broca and the temporal cluster in the right and left hemisphere. We will use seed regions to examine statistically correlated activity with language network clusters and language network regions, and t-tests and correlation analyses to examine associations with behavior and demographics. Individual behavioral measures will include the Peabody Picture Vocabulary Test (receptive vocabulary), Matrix Reasoning (nonverbal cognition), and the Peg-Board Dexterity task (motor skills). We will obtain participant demographics, including age, gender, race, ethnicity, and handedness.

Anticipated Results and Conclusions

We hypothesize FC lateralization of the language network will be present for the language task. We further predict that greater FC language lateralization will be associated with relatively better behaviorally measured language skills, based on the theory that language function is increasingly specialized to the left hemisphere across neurotypical development. We also hypothesize specificity of this relationship;FC lateralization of the language network will not be significantly associated with nonverbal cognition or motor abilities. Thus, this work should convincingly establish that language-related individual differences are related to how the language network functions as a lateralized system of coordinated brain activity.

J- Learning

1-J-78 - Investigating the influence of language modality on visual statistical learning in deaf children

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Details

Statistical learning is a key, implicit strategy that infants and children employ to develop a variety of cognitive abilities, including language. Data from visual statistical learning (VSL) studies have been used to support the auditory scaffolding hypothesis (Monroy et al., 2022). This theory suggests that experience with auditory input, such as spoken language, aids in the development of statistical learning. But what about children who do not have access to auditory input, such as those experiencing deafness? Findings have shown that deaf children perform worse than hearing children on VSL tasks. However, these studies have notoriously left out deaf children exposed to American Sign Language (ASL) from birth in which ASL is a robust language that provides opportunities for exposure to statistical regularities. Additionally, many VSL tasks have failed to include a spatial-location aspect. The recognition of location patterns is important for children learning to navigate their environments. Location information might also better reflect the primarily visual world that deaf children experience as it pertains to their language experience (i.e., ASL). The neural correlates of VSL have been largely understudied in deaf populations and are necessary to provide information about the underlying mechanisms of this learning. This research will examine the neural correlates of VSL in deaf children, focusing on the P300 event-related potential (ERP) component, as prior evidence supports a role for P300s in statistical learning (Jost et al., 2014).

This work will aim to study how language, regardless of the modality, scaffolds VSL in deaf children. There are two main goals. First, to test spatiotemporal VSL ability in deaf children with and without ASL experience alongside hearing children. Second, to investigate the underlying neural mechanisms for spatiotemporal VSL through ERPs primarily the P300 component in deaf children with and without ASL experience alongside hearing children.

We will test hearing, deaf signing, and deaf non-signing 2-8-year-olds. Participants will view videos of six shape pairs moving around the screen while a continuous EEG is recorded in 12 channels via a Biosemi ActiveTwo system. The procedure is a modified version of the Kirkham et al., (2007) visual statistical learning task. The training phase will consist of randomly ordered trials in which one shape appears at a time for 1s in one of six locations. The location of the second shape in the pair is contingent on the location of the first shape, with a 500ms delay between the first and second shapes. After training, half

of the trials in the test phase will be familiar and half will be new. The novel test trials will start with the first shape in each pair being in the original location, while the second shape of each pair changes location from the pattern in the training phase. After each pair appears, participants will be asked 'Have you seen this pair before?â€ and will use a button press to make a decision. Learning will be assessed through the accuracy of predictive eye gazes toward the target locations in the novel versus familiar trials, along with the proportion of correct responses via the button press. Language measures will include the Preschool Language Scales (PLS-5) and the Clinical Evaluation of Language Fundamentals (CELF-5). ERPs will be time-locked to the onset of the predictor stimulus. A linear mixed model will analyze the ERP, eye-tracking, and language assessment data.

This work will contribute to the emerging understanding of how language experience can scaffold the development of cognitive skills that are important for both academic and social success. In addition, deaf children with ASL experience from birth have been notoriously left out of the developmental cognitive neuroscience literature. This study will focus on recruiting these children to understand more about their unique experiences.

1-J-79 - The differences in performance, anxiety and EEG activity in children with and without autism during mathematics

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Details

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and the presence of restricted and repetitive behaviors. Given the difficulties in social engagement, individuals with ASD have higher levels of anxiety compared to the general population (Vasa & Mazurek, 2015). Anxiety is evidenced by increased stress responses in the body and brain. Stress manifests in physiological symptoms such as changes in heart rate, electrodermal activity (EDA) and blood pressure (Katmah et al., 2021). Previous EEG studies have detected anxiety as high EEG power, especially in the frontal cortex (Sundaresan et al.,2021). A high degree of students with ASD experience academic difficulties, specifically with math (Jones et al., 2009). Math is an area that can be challenging and trigger anxiety due to its abstract nature, while others excel with math due to a propensity to pattern recognition. Such a two cluster trend in math ability has been identified in students with autism (Bullen et al., 2022). Little research has been done looking into how math performance in ASD and non-ASD children and how it relates to math anxiety and related physiological responses.

Objectives: The purpose of this study was to identify differences in performance, anxiety, and neural activity in kids with and without autism during a partnered math task.

Methods: A sample of children (N=28) with (n = 10) and without ASD (n = 18) performed a math flashcard task with their parents while their neural activity was recorded using electrode-level EEG signals. All children had IQs within the average range. Videos of sessions were coded for the number of

flashcards each child completed as a measure of performance. Math anxiety was assessed using a self-report questionnaire.

Results: ASD participants had significantly higher math anxiety (M = 3.30, SD = 3.199) than TD participants (M = 0.78, SD =1.1215), $t(11.854)= -2.796, p = 0.047$. EEG Max Power was also significantly higher in ASD participants (M = 727366.61911, SD = 701413.53414) than TD participants (M = 118429.1438, SD = 358648.655512), $t(13.437) = -2.534, p = 0.039$. There were no significant differences between groups in math performance.

Conclusion: Data demonstrate neurological underpinnings of brain activity indicative of anxiety during math tasks. Despite this, no differences in math performance were observed. ASD participants had significantly increased math anxiety and EEG power activity compared to their typically developing peers, suggesting greater neurological difficulties coping with the tasks, despite there being no difference between groups in performance. These findings are consistent with other interesting discrepancies between functioning and academic performance in ASD samples, such as academic performance in certain areas being higher than IQ (Bullen et al, 2022). They also support the neurological underpinnings of such discrepancies. Further analysis of academic performance as it relates to neurological biomarkers and emotional state could continue to shed light onto how to best support students with autism. Further, using comparison samples of autism to neurotypical samples is particularly useful in helping educators understand how to differentially support students with ASD in general education classrooms.

1-J-80 - Associative Learning and Adolescent vs. Adult dmPFC

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Details

The dorsomedial region of the prefrontal cortex (dmPFC) is an area of the mouse frontal neocortex encompassing the anterior cingulate cortex and motor supplementary area. This region is implicated in a variety of cognitive abilities, including working memory, decision-making, and cognitive flexibility, and is remodeled during adolescent development. As mice grow into adulthood, dendritic spinesâ€“the site of synaptic connectionsâ€“are pruned and fewer transient synapses are formed, such that a larger fraction of existing synapses are stable across days (Holtmaat et al. 2005, Boivin et al. 2018, Delevich et al. 2020). At the same time, inhibitory neurotransmission onto L2/3 PYR and a subset of L5 PYR increases during adolescence (Piekarski et al. 2017, Vandenberg et al. 2015). Furthermore, long-range axonal projections continue to grow into dmPFC, forming new synaptic boutons and enabling information integration from other brain areas (Johnson et al. 2016). In particular, dopamine-releasing axons more densely innervate the dmPFC, and the density of dopamine receptors is in flux (Tseng & O'Donnell, 2005; Naneix et al. 2012; Hoops & Flores, 2017). As of yet, how and when these microcircuit changes affect associative learning throughout adolescence and into adulthood is currently not understood. We have found that, despite their changing brains, adolescent mice perform at least as well as adult mice in a head fixed go no-go

auditory discrimination task, and may even demonstrate a behavioral advantage. We are currently using two-photon calcium imaging during this task to measure neural activity in the dmPFC of cohorts of adolescent and adult mice. We plan to present analyses comparing representation of task-related variables in dmPFC activity when performance is matched. We will also use decoding models to compare neural function in the two age groups. We hypothesize that task related variables will be represented by more neurons in the adolescent dmPFC compared to adults, and that decoding will be more more accurate from adolescent recordings compared to adult recordings. This work will enable higher resolution understanding of the function of adolescent frontal cortices and their role in supporting adolescent learning and choice.

1-J-81 - Stanford Mental Arithmetic Response Time Evaluation (SMARTE) in the ABCD Study.

Mathieu Guillaume [1], **Ethan Roy** [1], **Amandine Van Rinsveld** [1], **Bruce Mccandliss** [1]

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Details

Introduction. Sufficient mathematical knowledge is essential to function properly in our modern society. It is therefore crucial for researchers, teachers, and clinicians to be able to assess learners' mathematical abilities with validity, reliability, and speed. Here we describe a new tablet-based assessment application designed to measure mathematical fluency, the *Stanford Mental Arithmetic Response Time Evaluation (SMARTE)* tool.

Method. SMARTE consists of three 2-minute tasks (dot enumeration, single-digit arithmetic, and multi-digit arithmetic) designed to provide a rapid, valid, and reliable assessment of math fluency. We analyzed data from 3841 US youth (1788 girls, mean age: 13) who completed SMARTE in the third year of the Adolescent Brain Cognitive Development[SM] study and 2931 youth (1409 girls, mean age: 15) who completed SMARTE in the fifth year. Because of the COVID-19 crisis, some youth were tested online while others were tested in person, as per the original protocol.

Results. The SMARTE main score and subscores were highly correlated with each other at each time point. Although context had an impact on math performance - with youth tested in person performing better overall than youth tested remotely - it did not significantly interact with the performance. In addition to the cross-sectional analyses, we explored SMARTE's longitudinal reliability and sensitivity to growth and found that all three SMARTE modules were highly reliable between the time points. We also built a series of growth models and found that all three modules significantly captured growth between the two time points.

Conclusion. SMARTE is an appropriate tool to quickly assess mastery of non-symbolic and symbolic arithmetic. SMARTE was found to be reliable and stable over two years, both remotely and in-person. Widespread use of SMARTE in grades 1-12 could be useful for cross-sectional and longitudinal assessment and tracking of mathematical learning.

1-J-82 - Capturing the causal impact of the words teachers teach: learning and retention dynamics in a naturalistic classroom training study

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Details

Developmental cognitive neuroscience (DCN) research has a crucial opportunity to explore how principles of learning and memory, typically studied in controlled laboratory settings, can effectively play out in real-world environments, such as school classrooms. To this end, a team of DCN researchers collaborated with educational practitioners to conduct a classroom-based study investigating the cognitive processes involved in new word learning as part of an existing research-practice partnership. Through collaborative meetings, the researchers and educators co-created study methods and an approach that could be integrated seamlessly into the school day with minimal disruption to educational activities or the child's schedule.

In this two-week study, a team of researchers and teachers collaborated to investigate the cognitive processes involved in learning new vocabulary words. The study focused on first to fourth-grade students (n=101) who were tasked with learning 20 low-frequency, five-letter words, such as ‘chiveâ€, ‘skulkâ€, and ‘rivenâ€, (dubbed "magic" words). Word lists were counterbalanced across three classrooms such that the words being learned in other classrooms served as controls. To make the study more applicable to authentic classroom dynamics, the learning strategies and activities were co-designed with teachers to reflect their teaching practices. Throughout the study, the researchers traced the students' cognitive indicators of perceptual recognition, semantic association, and free recall, with measurements taken at various intervals ranging from the beginning of the learning sprint to one year afterwards (e.g., 50, 100, 200 days after the end of the learning sprint). Through the collection of multi-dimensional data, researchers aimed to gain a comprehensive understanding of how students learn new vocabulary words, as well as to identify the underlying cognitive mechanisms at play. Over the course of the two weeks of active teaching and learning, cognitive metrics indicated significant accuracy gains for memory recall ($p<0.001$), perceptual recognition ($p<0.001$), and semantic associations ($p<0.001$) that were specific to magic words counterbalanced across classrooms in third and fourth grade students. However, when retention was assessed days after the end of the active learning period, the measurement approach (i.e. free recall vs. semantic association) appeared to have a profound effect on inferences about what learning was retained. Similar trends were reflected in first and second grade student data. Free recall performance dropped significantly across the retention period, but in contrast, performance in the semantic association task remained unchanged after the end of the active learning phase and, in fact, showed a slight numerical increase a year later.

The findings of this study suggest that, despite some memory decay, participants were able to retain deeper-level lexical semantics after just two weeks of classroom-based learning. By analyzing a range of cognitive indicators, we can begin crafting a more complete picture of cognitive development, allowing for a more nuanced interpretation of the learning process. This investigation, which was led by teachers and conducted in a real-world classroom setting, highlights the potential for developmental cognitive neuroscience theories, methods, and approaches to shed light on the impact of authentic learning experiences. Critically, this study not only makes important contributions to enduring developmental

cognitive neuroscience questions, but makes these contributions while simultaneously honoring educators as key collaborators in the process, in a way that reflects real learning environments.The co-design of the study further underscores the value of cross-disciplinary dialogue, which must account for the complexities of rigorous scientific study as well as the dynamic nature of classroom environments.

1-J-83 - Event-Related Potential Studies of Reading in Relation to Developmental Dyslexia: A Systematic Review

Silvia Clement-Lam [1], **Oliver Lasnick** [1], **Ayan Mitra** [1], **Brianna Kinnie** [1], **Jie Luo** [1], **Cheryl Lyon** [1], **Devin Kearns** [1], **Fumiko Hoeft** [1]

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Details

Existing cognitive models of reading posit the existence of multiple 'routes' for different facets of reading ability, such as the dual-route model's lexical route for memory-based word recognition, and phonological route for the execution of grapheme-phoneme correspondence rules (Coltheart et al., 2001). Within these frameworks, models for reading disorder (developmental dyslexia) cite atypical development of the non-lexical (phonological) route as a selective impairment. However, the alternative triangle model of reading allows for an additional orthographic-semantic pathway that involves direct mapping from form to meaning (Harm & Seidenberg, 1999; Seidenberg, 2005). Event-related potential (ERP) studies are often employed to study temporal aspects of real-time linguistic processing. Given their excellent temporal resolution, ERPs are appropriate for the investigation of on-line neural processes that underlie linguistic processing deficits in dyslexia. Prior studies have suggested that ERPs have the potential to identify biomarkers for dyslexia (see Brem et al., 2013; Guttorm et al., 2010 for examples). Yet, a comprehensive and systematic review of which components selectively characterize reading deficits in dyslexia is currently lacking. We therefore undertook a systematic review of ERPs in dyslexia within the framework of the triangle model of reading. This study was pre-registered at https://osf.io/dbgc3. Using the 2020 PRISMA guidelines (Page et al., 2021), we performed title, abstract, and full-text screening of 1,286 papers identified by our initial systematic database search. Details of the database search strategies and inclusion/exclusion criteria are described in the preregistration report. After screening, 72 articles were determined to be eligible for inclusion in our review. We have recently completed the data extraction and quality assessment of these 72 papers. Currently we are synthesizing the extracted information on experimental design and qualitative/quantitative results, including both descriptive and inferential statistics. We identified several prominent ERP components studied in these papers, including the N100, N170, N200, P200, P300, and N400. We expect converging evidence to reveal that ERP components successfully differentiate typical readers and dyslexic readers with respect to the 3 levels of the triangle model: orthography, phonology, and semantics. We expect the time window from 100-200ms (commonly indexed by the N170) to be associated with the orthographic deficit in RD individuals, and the one from 250-500ms (P300, N400) to be associated with phonological deficits. For semantic processing in RD, because findings from the current literature have been less conclusive, we hypothesize that there will be mixed results in ERP components associated with semantic processing (e.g., N400). We also expect to see a wide range of variation in ERP experimental designs, with corresponding differences in the presence of specific components or time windows across studies. By elucidating the time-course of ERP components involved in phonological, orthographic, and semantic processing in individuals with and without reading disorders, this systematic review will provide valuable

insights into potential neural markers underlying reading processes in individuals with reading disorders. By further comparing experimental paradigms, we will also gain insight into the source of potential discrepancies in results between papers.

K – Mechanisms (Hormones, neurotransmitters, physiology)

1-K-84 - Developmental changes in the neural oscillatory dynamics serving selective attention are closely associated with pubertal testosterone levels

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Details

Testosterone levels increase sharply during the pubertal transition and this has previously been associated with structural and functional brain maturation. Most of the prior neuroimaging literature examining the impact of testosterone have focused on structural brain development, with only a few recent studies probing changes in brain function. In this study, we investigated the impact of pubertal testosterone levels on the neural oscillatory dynamics serving selective attention in a sample of 87 participants aged 6 - 13 years old. Participants completed a number-based Simon task while undergoing magnetoencephalography (MEG) and the resulting data were transformed into the time-frequency domain. Significant time-frequency windows, compared to baseline, were imaged using a beamforming approach, and the resulting source maps were subsequently analyzed using multiple regression models. Testosterone levels were significantly correlated with age and reaction time. Our key findings included spectrally-specific changes in alpha and gamma oscillatory power in the occipital, parietal, and frontal regions as a function of testosterone. Additionally, sex-specific effects were found in the occipital and frontal cortices, suggesting sexually divergent effects on brain development. Overall, our results provide crucial new evidence linking changes in pubertal testosterone to maturation of alpha and gamma oscillations in key attention regions, while also indexing sex differences that possibly emerge due to the increasingly different testosterone levels between boys and girls.

1-K-85 - Aperiodic EEG and 7T MRSI evidence for maturation of E/I balance supporting the development of working memory through adolescence

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Details

During adolescence, the prefrontal cortex (PFC) undergoes protracted structural and functional development, supporting the maturation of cognitive control and executive functions. Recent studies in rodent models, postmortem human tissue, and *in vivo* studies in humans, have shown PFC increases in inhibitory, GABAergic parvalbumin (PV) interneurons and decreases in excitatory, glutamatergic processes, consistent with critical period plasticity during adolescence. Recent EEG work has demonstrated that the broadband background aperiodic activity is associated with the excitatory/inhibitory (E/I) balance and

neuronal population spiking. The Fitting Oscillations and 1/f (FOOOF) protocol derives the 1/f spectral slope (referred to as the aperiodic exponent) and an offset. The steepness of the slope (i.e., the exponent) has been previously linked to shifts in the E/I balance. However, there has been little validation of this approach in humans to date, nor direct demonstration of how individual variability in FOOOF measures relates to underlying differences in neurobiology and neurodevelopment. In this study, we collected a large, longitudinal dataset including rest EEG as well as PFC GABA and glutamate measures using 7T Magnetic Resonance Spectroscopic Imaging (MRSI). We hypothesized that aperiodic activity in PFC would decrease through adolescence in parallel with increases in Glu/GABA balance through adolescence, reflecting greater E/I balance through adolescence.

EEG and MRSI data (separate sessions) were collected on 164 participants (87 assigned female at birth), between 10-32 years of age (mean age 19 +/- 5.8) with to 3 visits per person at approximately 18mo intervals, for a total of 286 sessions. EEG was collected during 8min resting state comprised of randomly alternating 1min eyes closed and eyes open fixation. MRSI was obtained on an oblique 24x24 voxels slice (1.0x0.9x0.9mm) including dorsolateral PFC (DLPFC) using a J-refocused spectroscopic sequence (TE/TR=35/1500ms). MRS analysis was done in accordance with our previous work (Perica et al., 2022). The FOOOF python toolbox was used to characterize the PSD as a combination of an aperiodic component with overlying period components, or oscillations. The aperiodic component was fit as a function across the entire spectrum (1-50Hz). A combination of generalized additive mixed models and linear mixed effect models were used to assess relations between all EEG and MRS measures.

Results showed that the aperiodic EEG exponent ($F = 63.16$, $p < 0.0001$) and offset ($F = 240.07$, $p < 0.0001$) significantly decrease across adolescence. The Glu-GABA imbalance measure, derived from regressions of the two metabolites, was found to significantly decrease with age ($F = 11.04$, $p = 0.001$). The glutamate-GABA imbalance significantly increased with aperiodic exponent ($\hat{I}^2 = 0.15$, $t = 2.01$, $p = 0.04$) but not offset ($\hat{I}^2 = 0.04$, $t = 0.56$, $p = 0.58$). Finally, the Glu-GABA imbalance was a significant mediator of age-related changes in exponent (ACME: -0.00067, 95% CI [-0.0015, 0.00], $p = 0.032$).

Using novel EEG and MRSI methodology in a large, longitudinal, developmental dataset through adolescence, this study demonstrates an association between developmental changes in DLPFC glutamate and GABA and changes in DLPFC EEG markers of neural excitatory and inhibitory activity. Shifts in these excitatory inhibitory circuits may reflect cortical maturation including refinement of cortical networks, synaptic pruning, myelination, and alterations in the E/I balance. Our results showing reductions in aperiodic offset may reflect maturational decreases in overall spike rate of cortical neurons, while our results showing decreases in exponent suggest maturational dominance of excitatory over inhibitory function through adolescence. Together, these findings provide novel *in vivo* evidence reflective of critical period plasticity in DLPFC through the adolescent period that may underlie known improvements in cognition.

1-K-86 - Longitudinal Changes in Pubertal Development, Hormones, and Neural Reward Response in the HCP-D Study

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Details

INTRODUCTION:

A wide body of research has identified adolescence as a critical period for the development of brain systems associated with reward processing. Far fewer studies, and especially fewer longitudinal studies, have focused on the role of pubertal development and gonadal hormones in shaping the function of reward processing brain areas during adolescence. The present study aims to fill this gap by examining the role of pubertal development and hormones (i.e., testosterone, DHEA, estradiol, and progesterone) on longitudinal changes in neural reward activation during adolescence, using large-scale data from the Human Connectome Project in Development (HCP-D).

HYPOTHESES:

We will test competing hypotheses as to whether neural reward response rises and plateaus with age, or rises and peaks during mid-adolescence, followed by a decline in late-adolescence. We hypothesize the strongest effects in striatal reward regions including the nucleus accumbens, and will conduct exploratory whole-brain analyses. We additionally hypothesize that pubertal development and hormones will predict longitudinal changes in neural reward activation, above and beyond the effects of age and sex. Lastly, we hypothesize that pubertal timing (i.e., pubertal stage relative to one's peers) will predict neural reward response above and beyond the effects of puberty and hormones. We hypothesize that testosterone levels and accelerated pubertal timing will be associated with heightened neural reward activation across development. All other hypotheses concerning puberty and hormones are exploratory with regard to directionality.

METHOD:

Our study population is a cross-sectional sample of 1,304 youths (ages 5-22, 50.0% male) from HCP-D. 254 of these (ages 9-18, 49.1% male) participated in two longitudinal follow-up visits, each 1-2 years apart. This subsample follows a mixed longitudinal design with two cohorts beginning at ages 9-10 and 13-14, followed to ages 13-14 and 17-18, respectively. At each visit, all participants completed two self-report measures of pubertal development. Testosterone, DHEA, estradiol, and progesterone levels were collected via hair and saliva samples. All participants underwent 3T MRI scanning and completed a reward processing task during fMRI acquisition. BOLD activity was measured both during an anticipation phase, and upon the receipt of random monetary reward or punishment.

PLANNED ANALYSES:

Our primary contrast of interest is (Reward - Loss). Data will be analyzed using general additive mixed-effects models to allow for non-linear effects of age, puberty, and hormones on neural reward response. All analyses will include sex interaction effects to account for sex differences in pubertal timing and tempo, pubertal hormone concentrations, and possible sex differences in the effects of puberty and hormones on neural reward response across development. In addition to estimating effects of each predictor variable, we will conduct efficient approximate leave-one-out cross-validation model comparison, which provides an expected log pointwise predictive density difference (ð›¥ELPD) between models as well as standard errors of that difference. Model comparison will be conducted for each ROI to determine whether and for which brain regions pubertal development adds to predictive power beyond age and sex, and hormones add to predictive power beyond age, sex, and puberty.

SIGNIFICANCE:

The proposed research, which is grounded in neurodevelopmental theory and leverages access to a uniquely large and comprehensive dataset, is poised to establish the foundational neuroendocrine mechanisms by which pubertal development influences reward processing. Understanding the neurodevelopmental trajectories of reward processing as uniquely characterized by age, pubertal stage, and sex represents a crucial first step toward building a comprehensive theory of adolescent brain development, motivated behavior, and risk-taking.

L- Memory

1-L-87 - Assessing the reactivation of motor learning-related patterns of activity in the developing hippocampus and putamen

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[1] University of Utah

Details

Background and Objectives: Previous research in young adults has demonstrated that the "offline" (i.e., in the absence of active task practice) periods following learning offer a privileged window for a recently-acquired memory trace to be consolidated into a stable, long-term form. This process is supported, in part, by the spontaneous reactivation of learning-related brain activity patterns during these offline epochs. Interestingly, recent research from our group demonstrated that 7-12-year-old children exhibit superior – relative to young adults – consolidation of a new motor memory trace over a post-learning interval of wakefulness. This raises the intriguing possibility that children exhibit an enhanced reactivation of learning-related patterns of neural activity. Accordingly, the goal of this project is to assess whether the developmental advantage in motor memory consolidation is supported by greater reactivation in task-relevant regions of interest (i.e., hippocampus [HC] and putamen [PUT]).

Methods: Seven- to 12-year-old children and 18-30-year-old young adults (eventual sample=74) will perform two sessions, separated by 5 hours, of a motor sequence learning task. The two sessions allow us to assess initial learning of the motor sequence and its offline consolidation. For both sessions, participants will be positioned in an MRI scanner and whole-brain BOLD signals are recorded with a T2*gradient echo-planar sequence (MB factor=5; TR/TE=797/31ms; FA=59°; 55 transverse slices; 2.5mm thickness; voxel size=2.5mm^3) during task performance as well as during pre- and post-task resting state [RS] scans. The post-task RS scan affords the assessment of learning-related neural reactivation in the subsequent offline epoch. A structural T1-weighted 3D MPRAGE image will also be acquired (TR/TE/TI=2500/2.98ms/1070ms; FA=8°, 176 slices, voxel size=1.0mm^3). Of note, data collection is currently in progress (4 datasets acquired to date) and we expect 30 datasets to be acquired and analyzed by the time of Flux 2023.

Analysis plans: To assess consolidation, offline changes in motor performance between the end of initial training and the 5hr retest will be computed and compared between age groups. Consistent with our recent research, we expect children to exhibit greater offline changes, reflecting enhanced consolidation. Multivoxel correlational structure (MVCS) analyses will be employed to assess the reactivation of learning-related brain activity patterns. Specifically, for each epoch (task and post-task RS), the correlation between each of the *n* voxel time courses within each region (i.e., HC and PUT) will be computed, yielding an *n*-by-

n MVCS matrix that reflects the pattern of brain activity. The similarity between the task and post-task RS matrices will then be computed, with higher similarity indicating greater reactivation of learning-related activity patterns. We hypothesize children to show a higher similarity as compared to adults for both the HC and PUT. In addition to the age group comparisons highlighted above, we will assess age-related changes in consolidation and reactivation *within* the group of children (i.e., from 7 to 12 years) via regression analyses. Age-related decreases in both metrics are expected, indicating that the developmental advantages in offline consolidation and reactivation are greatest in younger children.

Implications: This research will provide novel insights into the neural processes supporting motor learning and memory processes in children, including potentially revealing a mechanism underlying the childhood advantage in offline consolidation. Moreover, this project will lay the foundation for future research examining the modulation of offline processing in children via targeted memory reactivation. This approach offers an avenue for boosting memory in children with and without motor learning-related impairments, ultimately providing a framework for pediatric clinical practices.

1-L-88 - Differences in Concept Uses Associated with Early Life Adversity

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Details

Concepts are mental representations used to categorize events or objects for a functional purpose (e.g., selecting actions that best fit the current situation). Our brain compresses highly detailed and variable sensory information to form abstract concepts to efficiently navigate the world. Such mental representations are acquired throughout development via experience. Thus, we would expect early life experiences, to influence which concepts are learned and how they are used later in development. To assess this, we measured the impact that experiences of early-life adversity had on the use of concepts using novel measures of memory performance designed to probe recognition, associative, and spatial memory. In a sample of 27 children ages 6 16 years old (M_{age} = 9.64, SD = 3.30; 15 female, 12 male), we found both age-related and adversity-related differences in concept use. During the recognition memory portion of our task, we found that reporting more negative events was associated with greater context insensitivity (B = -0.089, $p < 0.001$), while older age was associated with greater context sensitivity (B = 0.040, $p < 0.01$). During the associative memory portion of our memory task, we found participants reporting more negative events utilized a context-anchored strategy (i.e., selecting the correct location for the category of item in a given context; B = 0.022, $p < 0.004$), while older age was associated with greater use of an item-anchored strategy (i.e., selecting the correct location for a specific item regardless of context; B = 0.017, $p < 0.024$). However, we did not detect any differences with measures of overall accuracy or sensitivity of memory performance. Our results suggest that a greater number of exposures to early life adversity is associated with altered context-dependent use of concepts, which in turn results in nuanced differences in what is learned and remembered. We propose that alterations in information compression within the brain may underlie these behavioral differences. Given the role of concepts in enabling efficient energy expenditure (by anticipating metabolic needs specific to the unique features of an individual's environment) these findings suggest the need for future research to directly test the hypothesis that childhood adversity may alter metabolic efficiency via differences in the acquisition of concepts and information compression. Additionally, this work highlights the need to

carefully consider context as a relevant feature of task design and analyses when assessing how environmental exposures may impact the use of concepts in the service of memory.

1-L-89 - Home Sweet Home: Relations between episodic and semantic memory in childhood

Sabrina Karjack [1], **Nora Newcombe** [2], **Chi Ngo** [3], **Kara Storjohann** [2]

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Details

Semantic knowledge guides adaptive behaviors through generalization; episodic memories preserve individual experiences. Some models propose that generalization occurs via linking individual yet related episodes (Kumaran et al. 2012). If so, generalization should be contingent on memory for specific instances, as observed in adults (Banino et al. 2016). However, in development, semantic memory surfaces years before episodic memory, and Ngo et al. (2021) showed generalization did not depend on episodic memory in young children. This study aims to further characterize the contingency. Children of 3-8 years (*n* = 128) watched cartoon animals find homes in distinctive environments. These events had a coarse-level regularity (e.g., mammals-town 1; birds-town 2), a more specific regularity (e.g., horses-castle in town 1), and an episodic component (e.g., horse 1-location within castle). We tested children's inferences about unstudied animal-place associations as well as episodic memory of the animal-place associations on continuous and categorical scales. As a control variable, we tested children's category knowledge of mammals and birds. Preliminary results show age is a significant predictor of generalization accuracy at all levels. Episodic memory specificity shows a similar significant age-related change. Generalization for new animals, new places, and baby animals is contingent on episodic specificity, with a greater linkage for older children (6-8) than younger children (3-5). This design reveals age patterns in generalization and episodic memory, and helps to characterize generalization-episodic memory interdependence in childhood.

1-L-90 - Attention to category versus item-specific information impacts neural engagement and subsequent memory quality in children and adults

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Details

The way learners engage with new materialâ€”such as which particular task they perform during an initial experienceâ€”has been shown to influence later memory in both children and adults. Yet, the neural underpinnings of this attention-related memory effect are not well understood. Potentially, developmental changes in how attention is directed toward the item-specific over category-level features at the neural level may contribute to age-related improvements in memory precision. Here, we used fMRI to ask how alternately attending to category versus item dimensions of experience impacts neural engagement and subsequent memory quality in children and adults. Adults (N=42; 24-35 years) and children (N=42; 7-9 years) viewed blocks of consecutively presented scene photographs and were

instructed to attend to either the category (type of place) or item-specific (picture details) level of information. Questions screens presented after blocks then asked participants to indicate which of two pictures matched those from the preceding block at either the item-specific (did you see this grocery store, or that one?) or category (did you see a grocery store, or a bowling alley?) level. Outside the scanner, we then surprised participants with a memory test for the scene photographs from the attention task, which allowed us to examine how orienting to category over item-specific details impacted later memory. The memory test included studied scenes along with highly similar new scenes (lures) yoked to each studied photograph. We computed participants' ability to discriminate between studied scenes and lures as a behavioural measure of memory precision, and examined how this precision varied by attention task. With respect to ongoing performance during the attention task itself, we found that responses to end-of-block questions were well above chance, suggesting children and adults successfully modulated their attention to focus on either the item-specific or general category-level of the scenes as instructed. Moreover, there was distinct neural engagement associated with each task: category attention recruited parietal and frontal regions, while item attention engaged ventral visual and medial temporal lobe cortex. With respect to how these tasks impacted memory, both children and adults showed greater memory precision for pictures initially presented during the item than the category attention task. We reasoned that attentional modulation of memory behaviour might be related to evidence for distinct item and category states in the brain. We used a pattern classifier to measure the discriminability of whole-brain category versus item-specific neural states. We found that while the two tasks could be discriminated on the basis of fMRI patterns in both children and adults, they were significantly less distinguishable in children. Interestingly, we also found that the degree to which these brain states were distinguishable was positively associated with individual differences in item attention-related increases in memory precision. These results suggest although item-specific over category attention supports memory precision across age groups, the ability to selectively orient to these dimensions shows refinement beyond childhood that can have consequences for memory quality. Age-related refinements in orientation may provide a mechanism by which attention supports developmental improvements in the encoding of high-fidelity memories.

1-L-91 - Changes in Episodic Memory Performance and Hippocampal Functional Connectivity as Predictors of Internalizing Symptom Trajectories in Youth

Jordan Foster [1], **Lucinda Sisk** [1], **Taylor Keding** [1], **Dylan Gee** [1]

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Details

Introduction: Episodic memory, the capacity to form and retrieve conscious memories of specific past events, is central to healthy human development. Altered episodic memory processes have been shown to play key roles in the development and maintenance of internalizing symptoms, including symptoms of stress, anxiety, and depression. Though structural differences in the hippocampus, a region heavily implicated in episodic memory processes, have been observed in individuals with internalizing symptoms, associations between changes in functional connectivity between hippocampal and other brain regions in youth with unique internalizing symptom trajectories has remained largely unexplored. In addition, it is currently unknown how early-life stress (ELS) might moderate associations between changes in hippocampal functional connectivity and changes in episodic memory across time. The present study has 3 aims: (1) to identify latent groups of youth that differ in their trajectories in

internalizing symptoms across 5 timepoints; (2) to examine changes in hippocampal resting-state functional connectivity (rsFC) as a predictor of changes in episodic memory performance and latent group membership; and (3) to examine the moderating role of ELS exposure in associations between changes in hippocampal rsFC and changes in episodic memory performance.

Methods: The current sample will include children aged 9-13 years (N = 4,203) who took part in the baseline (T1), 6-month (T2), 1-year (T3), 18-month (T4), and 2-year (T5) follow-up assessments of the Adolescent Brain Cognitive Development (ABCD) Study, and had complete resting-state data at T1 and T5. Data from the NIH Toolbox Picture Sequence Memory Task at the T1 and T5 will be used to assess episodic memory performance. Hypothesis-driven ROI-based analyses will be used to examine hippocampal rsFC with the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), and amygdala at T1 and T5. Youth self-reported scores from the Brief Problem Monitor Scale at T2, T3, T4, and T5 will be used to assess internalizing symptoms. Responses to the Life Events Scale at T3 will be used to assess early-life stress.

Hypotheses: We predict that (1) latent groups of youth that differ in terms of internalizing symptom trajectories will be identified; (2) changes in rsFC between the hippocampus and mPFC, PCC, and amygdala will be positively associated with change in episodic memory performance, which will in turn be associated with latent group membership; and (3) ELS will moderate the association between change in hippocampal rsFC and change in episodic memory performance, such that the effect of changes in hippocampal rsFC will be stronger for youth with greater ELS exposure.

Planned Analyses: A latent class growth analysis will be conducted to explore different non-linear trajectories of internalizing symptoms across 4 timepoints. Differences in episodic memory scores between T1 and T5 will serve as mediator variables in multinomial logistic regression analyses, in which differences in hippocampal rsFC scores between T1 and T5 will serve as predictor variables and internalizing symptom class membership will serve as the dependent variable. Moderation analyses will then examine interactions between changes in hippocampal rsFC and ELS exposure as predictors of change in episodic memory performance. Participant age, household income, and scanner site will be included as covariates in all models.

General Implications: Delineating the longitudinal associations between episodic memory and hippocampal connectivity in youth with internalizing symptoms is expected to provide novel insights into the mechanisms driving risk for psychopathology, which may provide greater clarity as to when and how episodic memory processes can be targeted in psychotherapeutic interventions for youth.

1-L-92 - Childhood maltreatment and memory bias for social and non-social events: exploring neural mechanisms that promote risk for mental health problems

Thais Costa Macedo De Arruda [1], **Camille Johnston** [1], **David Smith** [1], **Johanna Jarcho** [1], **James B. Wyngaarden** [1], **Iliana Todorovski** [1]

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Details

Childhood maltreatment often results in cognitive and affective impairments that increase risk for mental health problems. Memory deficits and corresponding alterations in hippocampal function may contribute to this risk. Positivity and negativity biases in recall are well-documented facets of memory deficits. Because abuse often involves adverse interpersonal experiences, it is plausible that memory bias may be more pronounced for social relative to non-social events. Therefore, survivors may remember social interactions as more negative than they actually were. Given that prior research has demonstrated that negative recall bias is associated with increased risk for mental health problems, it is critical to test the extent to which childhood maltreatment and memory bias for social versus non-social experiences relate to risk for internalizing and externalizing symptoms (e.g., depression, aggression, etc.). Shortcomings in traditional experimental paradigms have prevented these critical relations from being tested. To overcome these shortcomings, we conducted a study in which young adults (N=41) with a range of childhood maltreatment exposure completed a novel, ecologically valid paradigm where they received positive or negative peer (social) and monetary (non-social) feedback while undergoing fMRI. They were then unexpectedly asked to recall feedback. Forthcoming analyses will test the extent to which childhood maltreatment is associated with greater negativity bias for social versus non-social feedback, and whether the strength of this association relates to internalizing and externalizing symptoms. We will also test the extent to which hippocampal activation during encoding of feedback influences associations between childhood maltreatment, memory bias, and mental health issues. Findings will provide novel targets for interventions that mitigate risk for mental health problems in individuals who experienced childhood trauma.

M- Methods

1-M-93 - Neural Mechanisms of Reward Processing in Preadolescent Irritability: A Novel 3D CNN Application on fMRI Data

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Details

Objectives: The application of deep learning methods, specifically convolutional neural networks (CNNs), to fMRI data has recently emerged as a promising tool in psychiatry research. Compared to traditional fMRI analyses, CNNs assume minimal assumptions of training data and can capture higher-level patterns and complex, nonlinear relationships within the data. Additionally, CNNs can automatically learn and extract meaningful features from raw fMRI data, adapt to large datasets, and handle high-dimensional and noisy data, making them advantageous for identifying neurobiological mechanisms underlying mental illnesses and developing personalized treatment plans. Provided a large, diverse dataset, such as the Adolescent Brain Cognitive Development (ABCD) Study, the application of CNNs could uncover key underlying neurobiological markers of psychopathology during development. Irritability, defined as a lowered threshold for anger or expression of frustrative non-reward, is a valuable candidate behavioral vulnerability due to the robust, transdiagnostic predictive power of pediatric irritability. Here, we used a novel application of a 3D CNN to a reward processing fMRI task from the ABCD Study to predict the dimensional outcome of preadolescent irritability to extract brain regions most predictive of irritability severity during anticipation of reward.

Methods: 6,065 preadolescents (3,065 male, 9.96Â±0.63 years old) completed the Monetary Incentive Delay (MID) reward processing fMRI task and parent-reported Child Behavioral Checklist (CBCL). Three irritability-related items from the CBCL were summed (totals ranging from 0-6) to represent irritability severity. Roughly 85% of each potential score was reserved for model training (4,866 subjects) and the rest was reserved to evaluate the model (1,199 subjects). Synthetic Minority Oversampling Technique (SMOTE) was used to address the imbalanced irritability dataset by synthetic generating fMRI data for scores to match the majority score of 0 (2,751 each, totaling 19,257 samples). A 3D CNN (consisting of 4 convolutional layers and 1 fully connected layer) was applied to a contrast of the reward and neutral cue conditions during anticipation of reward and trained to predict irritability severity scores. Feature maps following the last convolutional layer for each subject were extracted and multiplied by the predicted irritability value. These feature maps were averaged, masked, and normalized to produce a single 3d brain image where each voxel's value represents the model weight reflecting how predictive it is of irritability severity.

Results: The model had excellent accuracy with a mean squared error of 2.66 and predicted irritability severity scores within an absolute value average of 0.48 Â± 1.54 SD. Thresholding the feature map for above average predictive model weights (>.55) resulted in bilateral representation of the caudate nucleus, amygdala, parahippocampal gyrus, hippocampus, and cerebellum. In other words, altered activation in these regions were most significant in predicting irritability severity in preadolescents during anticipation of reward.

Conclusions: This study demonstrates the potential of applying 3D CNNs to fMRI data to predict significant, dimensional clinical outcomes such as irritability severity in preadolescents during anticipation of reward. The results highlight key brain regions involved in emotional response and reward processing, including the caudate nucleus, amygdala, and hippocampus, which are most predictive of irritability severity. The novel application of a 3D CNN to the reward processing fMRI task from the ABCD Study provides a promising tool for future studies investigating the neurobiological mechanisms underlying mental illnesses.

1-M-94 - Missing MRI data in the ABCD study: Associations with study variables and the impact of rs-fMRI Quality Control Stringency

Matthew Peverill [1], **Justin Russell** [2], **Max A. Halvorson** [3], **Kevin M. King** [3], **Rasmus M. Birn** [4], **Ryan Herringa** [1]

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Details

Resting state functional magnetic imaging (rs-fMRI) is an important tool for exploring the human brain. Spurious findings related to head-motion substantially complicate analysis. Consequently, researchers have adopted increasingly stringent thresholds of acceptable motion below which frames are excluded from analysis, or scrubbed (Power et al., 2012, 2015). While these quality control techniques have allowed for important advances in our knowledge of human brain connectivity, data scrubbing introduces a new source of missingness when participants with insufficient low-motion frames are excluded from analysis. This missingness is often related to other variables of interest and, therefore,

may threaten the generalizability of findings (e.g., Cosgrove et al., 2022). However, little is known about how different quality control decisions (e.g., motion scrubbing threshold) affect sample representativeness. We used logistic regression models to examine attrition from the Adolescent Brain and Cognitive Development (ABCD) study resulting from increasingly stringent rs-fMRI quality control processes (operator exclusion at scanner, exclusion during preprocessing, and post-preprocessing motion scrubbing at .5, .4, .3, .2, and .1mm). Using a series of cross-controlled logistic regression models, we found that participants were disproportionately scrubbed from the sample on the basis of sex-assigned-at-birth (male), parent education (no college or graduate education), race/ethnicity (non-white), neighborhood disadvantage, lower cognitive performance, higher psychopathology, and younger age. While some variables were biased by any amount of QC-related exclusion (e.g., race/ethnicity, neighborhood factors, and age), other biases emerged only following motion scrubbing (e.g., sex-assigned-at-birth, cognitive performance, and psychopathology). In parallel, we generated QC-FC plots (Ciric et al., 2017) describing the likely degree of motion-related artifact in the rs-fMRI data at each scrubbing threshold. Our results highlight the need to balance internal validity (e.g., presence of motion artifact) against generalizability when designing quality control pipelines in rs-fMRI analysis and provide field-specific guidance to researchers making such decisions while analyzing the ABCD dataset. Our results additionally highlight the need for neuroimaging analysis tools which are more robust to variations in data quality. Finally, these findings highlight a need for further research on the nature and degree of neural variation between participants who produce high-quality neuroimaging data and those who do not. Such research would describe biases which could result from motion scrubbing and suggest methodological improvements allowing for more inclusive research designs.

1-M-95 - Sleep disturbances are associated with disrupted functional connectivity in children.

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Details

Introduction

Sleep disturbances and disorders among children are seen as a global concern as it is thought to be present along with other comorbidities of childhood psychopathology and behavioral problems and structural and functional changes in the brain (Reeve and Bell 2022, Rimvall et al. 2020, Steenhuis et al. 2020, Yang et al. 2022, Isaiah et al. 2021; Hernandez et al. 2023). Specifically, prior research suggests that sleep disturbances are associated with a reduction in whole brain volume and total surface area (Hernandez et al. 2023) and reduced average connectivity within the default mode (DMN) and dorsal attention (DAN) networks (Yang et al. 2022). However, limited prior research has examined the connectome-wide associations with childhood sleep disturbances.

Methods

We used resting state fMRI data and the Sleep Disturbance Scale for Children (SDSC) (Bruni et al. 1996) from the Adolescent Brain Cognitive Development (ABCD) study. We extracted 10 minutes of low motion (FD<0.2mm) rs-fMRI data from 6264 subjects (age 9-10 years) and constructed functional connectivity (FC) matrices by calculating Pearson correlation between each pair of 394 regions of interest

(ROI) including 333 cortical and 61 subcortical ROI (Gordon et al 2016; Seitzman et al. 2020)**.** We calculated the SDSC total score by summing each chil's score on the 26 items Likert scale denoting the individual scores on the 26 different sleep disturbance factors (viz. hours of nightly sleep, night waking, jerking, sleep-talking, daytime tiredness etc.). We then calculated the Pearson correlation coefficient between the total SDSC scores and FC matrices. We then applied a Network Level Analysis (NLA) (Eggebrecht et al. 2017; Wheelock et al. 2021) on all edges in the entire connectome to determine network-pairs enriched for associations with sleep disturbances. We established network-level significance using Permutation testing in which we shuffled the SDSC total score labels for each participant 10k times.

Results

SDSC total scores ranged from 26 to 126 [MW1] (Mean = 36.2). Upon applying NLA to examine network-level enrichment in ABCD data, we found that FC within motor and DMN, and FC between motor, DMN, DAN, cingulo opercular (CO), and ventral attention networks (VAN) was associated with sleep disturbances. Moreover, we found that sleep disturbances were also associated with FC within the default mode network, visual network.

Conclusions

Our preliminary results suggest that sleep disturbances are associated with variance within and between functional brain networks across primary sensory and higher-order association cortex. This is consistent with prior work implicating the DMN and DAN in childhood sleep disturbances (Yang et al. 2022). In our future work we will further explore the subscales of the SDSC to determine whether specific types of sleep disturbances are driving changes in functional connectivity. We further plan to split the ABCD sample using the ARMS to establish the reproducibility of these associations.

1-M-96 - "YOU have one chance to get it right": Perspectives on biological research in Black and Latinx communities

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Details

Research involving the collection and analysis of biological data (e.g., neuroimaging, physiological function, genetics) has been enormously effective in elucidating how environments shape human development (McEwen, 2012). Yet disparities in representation within Black, Indigenous, People of Color (BIPOC) communities threatens population generalizability of this research (Gard et al., 2023).

Inclusive research practices that feature community perspectives in study design, implementation, and dissemination may be the key to increasing BIPOC representation in biological research. Community-based participatory research (CBPR) wrests joint decision-making power with community members and researchers. By empowering community members and organizations (i.e., 'cultural insidersâ€) to advocate for local needs, CBPR has been shown to increase civic participation, scientific literacy, and

research engagement among the most marginalized populations (Collins et al., 2018; Ozer et al., 2017). The *Representation And Research Ethics (RARE) Project* at the University of Maryland leverages CBPR to build a data consortium of BIPOC families interested in participating in biological research studies. A power-holding community advisory board guides the selection of studies, refinement of protocols, cultural humility training for researchers, and dissemination efforts.

Here we describe the results of the first phase of RARE, which had the following **objectives**: (1) understand BIPOC perspectives on biospecimen data collection (i.e., blood, saliva, neuroimaging); (2) learn about community members perceptions of university research and researchers; and (3) elicit community feedback on the basic structure of the RARE data consortium. **Methods** included conducting 50 semi-structured qualitative interviews and three focus groups ($N_{participants}$ = 15) with community members and community leaders in Prince George's County, Maryland, USA. Participants self-identified as Black or African American (n = 39, 60%) or Latino/a/x/e (n = 26, 40%). 72% of participants identified as female and participants ranged in age from 24 67 years. Interviews were transcribed, open-coded to identify eight major themes and 37 subcategories, and then closed-coded by two independent raters to establish case-level and code-level reliability.

Results revealed that five major barriers to participating in research: concerns for confidentiality, time commitment, no transportation, few social benefits outlined by the researchers, and a lack of tangible incentives (i.e., beyond monetary compensation). Participants also expressed a preference for participating in some types of biological data collection over others. Participating in MRI studies was seen as less invasive than studies that collected saliva, blood, or hair. Concerns for genetic analyses permeated nearly every interview. Lastly, in generating a structure for the RARE data consortium, participants emphasized the need for ongoing relationships with community members characterized by mutual respect, demonstration of a long-term commitment to community empowerment, and the importance of disseminating research findings.

Collectively, our interviews and focus groups with community members revealed immense interest in applying CBPR methods to biological research studies. And yet, as one participant noted 'You have one chance to get it rightâ€.

1-M-97 - Using the "puberty-age-gap" to assess the impact of pubertal timing on emotion in the ABCD Study

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Details

Adolescence is marked by significant change and is often considered a window of opportunity to increase positive developmental outcomes. Most individuals will go through puberty during adolescence, accompanied by hormonal, physical, and emotional development. A critical developmental task in adolescence is cultivating skills to promote emotional well-being; some suggest that adolescence may be a particularly sensitive period for emotional development[1,2]. Researchers have found that earlier pubertal timing, or the onset of puberty occurring before peers, is a risk factor for developing different

dimensions of psychopathology[3]. Pubertal timing variation has also been linked to altered brain function in regions involved in emotional processing[4].

In a recent paper, Dehestani and colleagues tested a novel way of measuring pubertal timing, the 'puberty-age-gap.â€ They found that a machine learning model including parental reports of puberty in their model provided the best predictions of internalizing symptoms over a model including both hormones and physical characteristics. My proposed work will build on Dehestani's work by using a similar modeling approach with two key changes: (1) I will use how adolescents *themselves* describe their pubertal status as a predictor, and (2) I will test whether the puberty-age-gap is associated with *both* brain function in emotion circuits and emotional well-being. This *preregistered* project will examine the following research questions:

1. How does pubertal timing relate to functional activations during emotional processing?
    1. What is the best model for assessing this question (i.e., physical pubertal characteristics only or hormonal and physical characteristics)?
2. How does pubertal timing, derived from adolescent reports, relate to emotional well-being?

We predict pubertal timing, particularly earlier timing, will be associated with differences in brain function during an emotional processing task and will predict variations decreased emotional well-being later. After completing the present analyses, we will examine more complex interactions between puberty, brain, and emotional well-being.

Methods. We will use the publicly available Adolescent Brain Cognitive Development (ABCD) study to examine the above research questions. First conceptualized in 2015, the ABCD study recruited 11,800 children to follow across their adolescence (9-10 at baseline). For the present proposal, we will use puberty measures (e.g., self-report and hormones), age, Child Behavior Checklist Internalizing Symptoms subscale[7], sociodemographic information (e.g., socioeconomic status), body mass index, and functional neuroimaging data from the emotional processing task.

Analyses. We will use generalized additive mixed models to predict (1) activation in regions of the brain associated with emotional processing (e.g., amygdala, prefrontal cortex) and (2) emotional well-being. We will use model comparisons to report the best-fitting models.

Research Significance. To mitigate adverse developmental outcomes, the present proposal aims to leverage the adolescent period as an opportune window for intervention. *Puberty* is a complex developmental process that needs further examination concerning brain function during adolescence and emotional well-being later on.

1. Crone, E. A. & Dahl (2012) R. E. *Nat. Rev. Neurosci.* 2. Silvers, J. A. (2022). *Curr. Opin. Psychol.* 3.Dehestani, N. *et al.* (2022). Preprint. 4. Vijayakumar et al., (2019). *Cortex*. 5.Herting, M. M. *et al.* (2020) *Front. Endocrinol.* 6. Peel, A. J. *et al.* (2022) *Br. J. Psychiatry.* 7. Achenbach, T. M. (1994). *Lawrence Erlbaum Associates, Inc*. 8. Crone, E. A. & Elzinga, B. M. (2015). *WIREs Cogn. Sci.*

N- Networks

1-N-98 - Developmental trajectories of EEG aperiodic and periodic power from 2 to 44 months

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Details

Introduction: The infant brain undergoes dramatic structural and physiological change over the first 1000 days. In addition to rapid increases in brain volume, developmental changes during this period include myelination, migration and maturation of interneurons, and the establishment of thalamocortical connections. While structural changes in the developing brain have been characterized, less is known about the developmental trajectory of brain oscillations over this period. Analysis of resting-state EEG across early development can provide insight into the timing of physiological changes. In addition, establishing growth trajectories of resting state EEG power measures can provide a foundation for evaluating alterations in brain development across neurodevelopmental disorders.

Methods: Longitudinal resting-state EEGs from 592 healthy infants aged 2 to 40 months old (1335 EEGs) were collected from four different longitudinal studies within the same lab. The majority of research participants from these lab-based studies were white and with incomes at least double the federal poverty line. Individual power spectra were parametrized into aperiodic and periodic power spectra. Generalized additive mixed models were used to characterize age-dependent changes in the following EEG measures: aperiodic offset, aperiodic slope, as well as periodic peak frequency and amplitude across theta/alpha (4-12hz), low beta(13-30Hz), and high beta (20-30Hz) bands. Age-based changes in resting-state EEGs from toddlers with Down syndrome (n = 33) at 18, 24, and 36 months were also qualitatively compared to the large sample described above.

Results: Rapid increases in aperiodic power were observed in the first year, with minimal change between 1 to 3 years. In contrast, periodic peak frequency and peak amplitude in the theta/alpha range steadily increases with age, whereas periodic power in the beta range (13-30Hz) exhibited nonlinear changes. Specifically, a low beta peak begins to emerge in some infants as early as 6 months, increasing in prevalence and amplitude across the 3 years. Whereas a prominent high beta peak is transiently observed between 4-18 months, peaking in amplitude at 7.5 months. In contrast, in toddlers with Down syndrome we observe continued increases in aperiodic power between 18 and 36 months, and minimal change in periodic alpha and beta peaks.

Conclusion: We observe dynamic age-dependent nonlinear changes in EEG power across the first 3 years after birth that likely reflect sensitive periods of developmental brain maturation. Preliminary data suggest that toddlers with Down syndrome have altered trajectories in both aperiodic and periodic power. Future work is needed to understand how alterations in expected trajectories impact developmental outcomes.

1-N-99 - Linking functional connectivity to symptoms of borderline personality disorder in youth

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Details

Introduction | Borderline personality disorder (BPD) is associated with debilitating symptoms that considerably influence patients' social and vocational status (Leichsenring et al., 2023). Although most BPD diagnoses are made in early adulthood, recognizable symptoms often manifest earlier in adolescence. However, the underlying developmental neurobiology of BPD symptoms is not fully understood. Previous reports have linked functional brain network organization to behavioral phenotypes in the general population (Smith et al., 2013). There is growing evidence suggesting that high-quality data with large sample sizes are required for reliable and reproducible studies of brain-behavior associations (Marek et al., 2022). Here we aimed to leverage publicly available, large datasets to investigate how multivariate patterns of functional connectivity relate to symptoms of BPD in young adults and adolescents.

Methods | We used functional Magnetic Resonance Imaging (fMRI) data from young adults from the Human Connectome Project (HCP-YA; *N* = 870, ages 22-37, 457 female; van Essen et al., 2013) and youth from the Human Connectome Project: Development (HCP-D; *N* = 223, age range 16-21, 121 female; Somerville et al., 2018). A validated proxy of BPD liability score was estimated using the NEO Five Factor Inventory (NEO-FFI) for each participant (Few et al., 2016). Functional MRI data were preprocessed using fMRIPrep and the eXtensible Connectivity Pipelines-DCAN (XCP-D). High-quality data with low mean framewise displacement (mean [FD]<0.2mm) were retained for the subsequent analyses. A ridge regression model with 10-fold cross-validation and nested hyperparameter tuning was trained and tested in HCP-YA to predict BPD scores from regional functional connectivity on held-out test data, while controlling for in-scanner motion, age, and sex. The trained model was further tested on the developmental dataset (HCP-D) that was unseen to the model. Model performance was assessed as the Pearson correlation coefficient *r* between the empirical and predicted BPD scores at the region- and group-level. Statistical significance was assessed using permutation tests and bootstrapped confidence intervals.

Results | We found that multivariate functional connectivity patterns significantly predicted out-of-sample BPD liability scores in unseen data in both young adults (HCP-YA: $r = 0.14$, 95% CI = [0.08 0.21]; $p_{perm} = 0.001$) and older adolescents (HCP-D: $r = 0.24$, 95% CI = [0.12 0.36]; $p_{perm} = 0.001$). Predictive capacity of regions was heterogeneous across the cortex, with highest contributions from functional systems related to emotion regulation and executive function, such as the ventral attention network. Finally, regional predictive capacity was associated with developmental changes in functional connectivity, such that regions with higher predictive capacity are the ones that undergo the most functional development in youth. To ensure that the reported findings were consistent across alternative processing choices, we performed sensitivity analyses using functional networks defined at a lower parcellation resolution, resting-state fMRI data-only rather than concatenated task and rest fMRI scans used in the original analysis, and functional projections from subcortical regions. Findings were consistent across the analyses.

Conclusion | Altogether, the present study demonstrates that multivariate functional connectivity patterns predict BPD liability scores in adolescents and young adults. Findings suggest that

developmental abnormalities in functional connectivity are associated with symptoms of BPD, providing important insight into understanding BPD as a neurodevelopmental disorder.

1-N-100 - Stability of metrics of functional brain organization in infants – a precision imaging case study

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Details

Functional brain organization derived from resting state (rs) fMRI data can be used as an indicator for healthy brain functioning and development and is highly individual specific, which can be demonstrated given sufficient amounts of data. For infant neuroimaging, this need for large amounts of data for individual precision functional mapping poses a challenge. Recent work has investigated the usability of Template Matching (TM) in infant populations, which is a network mapping technique, that has been shown to stably detect individual networks in adolescents and adults with less than 20 minutes of data. TM creates highly individual specific networks in an infant sample, however given the amounts of available data, normalized mutual information (NMI) of networks within individuals did not reach a stable plateau of reliability. The present work follows up on these investigations, with the aim to determine the duration of data needed for a stable characterization of individual functional brain organization in infants which can hopefully be used to guide precision functional imaging in this age group.

This examination revisited the original work by Laumann et al and the My Connectome Project by utilizing one neonate (instead of an adult) from whom rs-fMRI data was acquired over five consecutive days. This infant showed very low motion across days and retained 98% of their data at a framewise displacement threshold of 0.3mm (210 minutes of high quality data), making it an ideal example case to study stability of metrics. We investigated the stability of networks by comparing various intervals of a split-half of the data to each other and to the half treated as ground truth (100 minutes from 16 runs). In addition, we took a more direct look at network topology by correlating parcellated functional connectivity matrices for the same intervals of data.

TM allowed us to detect all major adult networks in both split-halves of the data. The split half NMI for 100 minutes of data was 0.66 which is comparable to what has been published for adult precision imaging subjects. Unlike in adults where a plateau of NMI values for TM was reported for 20 minutes of data, the NMI plateaued at around 60 minutes of the available 100 minutes. Similarly, correlation of parcellated functional connectivity matrices stably estimated network topology with ~1h of low motion data. Even though NMI values did not plateau at 20 minutes, it is worth mentioning that the steepest increase happened from 1 (0.31) to 20 minutes (0.56) with a more shallow increase to the plateau. Comparing different non-overlapping 20 minute intervals with the ground truth, NMI values ranged from 0.49-0.59 (M=0.54, STD=0.04) and from 0.40-0.53 when comparing intervals towards each other (M=0.48, STD=0.04). Which is considerably more stable than 10 minutes intervals of data - 0.36-0.51 (M=0.43, STD=0.05) compared to the ground truth and 0.25-0.44 (M=0.34, STD=0.05) compared to each other - which in prior work already showed to be sufficient to detect networks that are highly individual specific. These results demonstrate that even though topographic variability appears greater in infants than adults,

it stabilizes at a feasible amount of time (60 minutes) and is already fairly high at 20 minutes, which is a commonly collected amount of data. This difference might be due to the lower signal-to-noise ratio caused by the smaller head size that is further away from the coil and the voxel size relative to the brain size increasing the partial volume effect. Furthermore, as infants are measured during natural sleep, transitions between sleep stages could induce additional natural variability. Moving forward, we can use this case example to investigate the stability of other metrics (e.g. network detection without priors using Infomap) that are known to require large amounts of data.

1-N-101 - The convergence of brain network architectures of working memory and psychopathology in late childhood

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Details

It has been proposed that working memory is a transdiagnostic predictor of psychopathology. Functional brain network organization of the fronto-parietal (FP) and cingulo-opercular (CO) networks have been identified as important for both working memory and psychopathology. However, the literatures linking these brain networks to each construct have thus far largely proceeded separately, which precludes an understanding of the brain network mechanisms linking the two. This information is particularly important during late childhood and early adolescence, during which there is an increasing risk for psychopathology. Thus, this study leveraged the ABCD Study dataset to assess the common functional brain network features underlying working memory and psychopathology in a large sample of children aged 9-10 years (*n* = 4,170).

Parents reported child psychopathology in the Child Behavior Checklist (CBCL). Children completed an Emotional N-back (EN-back) task probing working memory and a resting-state fMRI scan. We constructed a resting-state functional connectivity matrix for each subject and calculated system segregation, a graph metric indexing connectivity between networks relative to connectivity within networks. Higher values denote greater segregation between the networks. We calculated system segregation between the FP and CO networks and the 10 other brain networks specified in a functional brain atlas (Gordon et al., 2016), resulting in 21 brain metrics. Then, we separately tested for relationships between each measure of system segregation with working memory accuracy and total CBCL score. Lastly, we compared the significant system segregation predictors to identify common brain network features between working memory and psychopathology.

System segregation of the FP and default mode networks was related to both greater performance on the EN-back task and lower total CBCL score, indicating a common architecture. Performance on the EN-back task and total CBCL score also exhibited unique relationships with system segregation of the FP and CO networks. For example, EN-back performance was related to system segregation of the FP and cingulo-parietal networks, while total CBCL score was related to system segregation of the CO and cingulo-parietal networks. The common FP-default mode network link aligns with work showing the relevance of reduced connectivity across the FP and default mode networks for working memory performance and neurodevelopmental disorders, which are prevalent in this age range. These results underscore the relevance of FP and CO networks for both working memory and psychopathology and

set a framework for probing the common network architecture across the transition to adolescence, during which the qualitative profile of psychopathologies begins to shift.

1-N-103 - Adult functional network models impede reproducible outcome prediction in pediatric populations

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Details

Introduction

Adult resting state networks (RSN) have been reliably indexed using various analysis methods. However, using adult RSN in pediatric functional connectivity (FC) datasets may result in poor model fit between network pairs which might harm the generalization of the results. Pediatric research studies have chosen either to report FC results using adult networks (Rudolph et al. 2018; Nielsen et al. 2022) or pediatric networks (Eggebrecht et al. 2017; Kardan et al. 2022). No studies to date have quantified the difference in age prediction accuracy and reliability of pediatric FC when using adult vs pediatric network models.

Methods

Data Inclusion. We used rs-fMRI and age data from both Human Connectome Project (HCP) and Baby Connectome Project (BCP) in our study. In HCP data, we extracted 10 minutes of low motion data from 965 subjects (age 22-35 years) collected on two separate days (Seitzman et al. 2020). In BCP data, we utilized 7.2 minutes of low motion data from 170 sessions composed of 112 unique subjects (age 8 to 26 months)(Kardan et al. 2022). In both HCP and BCP, we constructed FC matrices by calculating Pearson correlation between each pair of 333 regions of interest (ROI), 333 ROIs in total(Gordon et al. 2016). An adult (Gordon et al. 2016) and a baby set of communities (Kardan et al. 2022) were applied to organize rs-fMRI connectomes into functional brain networks.

Age Prediction. We combined cross-validation with linear support vector regression (LSVR) model to predict age. To control shared variance, correlated samples (i.e., multiple sessions or siblings) were always kept in either training or test set. For each round, we calculated the Pearson correlation (r) between the predicted and actual ages as the measure of prediction accuracy. In BCP data, we employed a split-half analysis to evaluate the reproducibility while in HCP data, we adopted a test re-test analysis by measuring prediction consistency using Pearson correlation across days to evaluate the reliability.

Network Level Reliability. To provide a biological interpretation of the results from the ML model, we applied two methods. 1) Network Level Analysis (NLA) (Eggebrecht et al. 2017; Wheelock et al. 2021) on all edges in the entire connectome, where we quantified network-level reliability and reproducibility using Matthew's Correlation Coefficient (MCC) for HCP and BCP respectively. 2) Predicting age with edges from

selected networks (Rudolph et al. 2018; Nielsen et al. 2019; Kardan et al. 2022). We evaluated prediction accuracy when only including edges within network pairs.

Results

When applying NLA to examine network-level enrichment in HCP data, enriched network pairs generated by adult networks (Gordon et al. 2016) were more consistent across days (or split halves) than those generated by infant/toddler networks (Kardan et al. 2022) as indexed by MCC. Similarly, in BCP data, infant/toddler networks produced more consistent network-level age associations across split halves than adult networks. We further benchmarked prediction accuracy for models including edges within network pairs. Given the magnitude of age-related changes in FC in the first two years of life, the overall prediction accuracy of network pairs was greater for BCP than that of HCP. Consistent with prior research (Nielsen et al. 2019), higher FC feature count in the LSVR model resulted in higher prediction accuracy. However, HCP FC organized using adult networks resulted in higher prediction accuracy than those organized using BCP networks across increasing number of edges. Importantly, BCP FC organized by BCP networks led to higher prediction accuracy than FC edges organized by adult networks.

Conclusions

Age-specific network models are crucial for producing biologically interpretable, accurate, reliable, and reproducible predictions. This work has important implications for the prediction of clinical outcomes in developing populations and highlights the need for standardized systems level atlases in pediatric populations.

1-N-104 - Network analysis of limbic resting state connectivity in abstinent cannabis-using adolescents and young adults

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Details

Objective: Cannabis use is one of the most commonly used substances in the U.S., with the prevalence of use increasing during adolescence and young adulthood. This developmental period is also associated with ongoing neurodevelopment, particularly in brain regions related to affective processing. As such, cannabis useâ€"specifically in adolescenceâ€"has been associated with aberrant affective processing when examining task-based fMRI studies. While a few studies have demonstrated increased network connectivity within cannabis users within frontal, parietal, and temporal regionsâ€"areas that are rich in cannabinoid type-1 receptorsâ€"minimal studies have investigated limbic resting state network connectivity in these populations. Here, we aim to investigate limbic network resting state connectivity outcomes between cannabis-using and non-using adolescents and young adults after a period of monitored abstinence. We hypothesize that cannabis-using individuals will demonstrate increased measures of network connectivity; even after a period of monitored abstinence. Within the cannabis-using group, we hypothesize that there will be associations between limbic network connectivity and various cannabis severity measures.

Methods: Sixty adolescent and young adult participants between the ages of 16-26 (51.7% Female) underwent at least two weeks of monitored abstinence from all substance use (excluding nicotine) prior to MRI. Cannabis users were defined as weekly users (>40 past-year use and > 100 lifetime uses; n=27) compared to non-using controls (0 past-year use and <20 lifetime uses; n=33). Participants underwent an 8-minute resting state scan with participants laying with eyes open staring at a fixation cross. Resting state imaging data was preprocessed using fMRIPrep. Network data was derived using Schaefer et al. (2018) and Tian et al. (2020) atlases; limbic network included subcortical parcellations and temporal pole and orbitofrontal cortical network parcellations. Network outcomes were calculated across timeseries data and compared in linear regressions examining cannabis group status while controlling for past-year alcohol use and cotinine levels.

Results: For measures of limbic network connectivity, cannabis-using groups displayed increased clustering coefficient and transitivity relative to their non-using counterparts. Within cannabis group, past-year cannabis use was negatively correlated with node participationâ€"a measure of network centrality that captures diversity of node interconnectionsâ€"such that more past-year cannabis use was associated with lower network participation scores. Moreover, total cannabis withdrawal scores were positively correlated with a variety of network connectivity measures (strength, clustering coefficient, path length, transitivity, global efficiency, and density). However, total cannabis use dependence symptom count and lifetime cannabis use were not correlated with network outcomes.

Conclusions: Network connectivity analyses in limbic regions revealed that cannabis-using groups tended to demonstrate increased node clustering. Interestingly, density of past-year cannabis was associated with less diversity of node connectivity. Moreover, severity of withdrawal symptomatology was associated with several measures of network connectivity strength; implicating recent withdrawal severity as a potential marker of cannabinoid receptor recovery, particularly in limbic regions. These results, along with previous findings, demonstrate increased network â€˜efficiency' for cannabis-using individuals or could be posited as the need for increased network support while at rest. This is true for the present analyses even following a period of confirmed negative toxicology. Future studies should characterize limbic connectivity prior to cannabis use and investigate network connectivity measures between limbic and other cortical regions, specifically in samples of adolescents and young adults.

1-N-105 - The development of structure-function coupling in neonates: Associations with cognition

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Details

Introduction: How structure relates to function is a critical open question in neuroscience. While previous research has focused on specific tracts and ROIs, advances in neuroscience have allowed us to take a network approach to the question, enabling the simultaneous examination of whole-brain patterns of connectivity. Here, we examine regional variation in structure-function coupling, capturing the degree to which a cortical region's structural connections support patterns of coordinated neural activity. In adults and adolescents, structure-function coupling varies across the cortex, and is associated

with age and cognition, but to our knowledge no work has examined regional variation in structure-function coupling in neonates.

Methods: We capitalize on multimodal data collected from healthy term-born neonates ages 38-45 weeks postmenstrual age (*n*=234; age at scan *M*=41.4 wks, *SD*=1.3 wks; gestational age *M*=38.9 wks, *SD*=1 wk). Each neonate had a high-quality diffusion imaging scan and > 10 minutes of high-quality resting-state fMRI data after motion censoring. We applied probabilistic diffusion tractography and estimated functional connectivity between cortical regions, constructing two 333 x 333 weighted adjacency matrices using the same cortical parcellation, representing respectively the structural and functional connectomes. As previously (Baum et al., 2020; Gu et al., 2021), we operationalize structure-function coupling as the rank correlation coefficient between the structural and functional connectivity profiles of each region. All analyses control for child sex, in-scanner motion in both scans, and fMRI frames retained post-censoring. Composite scores from the Bayley Scales of Infant and Toddler Development at age 2 were used to assess language and cognition (*n*=121, age *M*=2.1 yrs, *SD*=0.13 yrs).

Results: In neonates, average structure-function coupling is almost entirely positive (*M*=0.36, *SD*=0.03), and varies across the cortex, with higher coupling in auditory cortex, lateral prefrontal cortex, and inferior parietal cortex . During the first month of life, average structure-function coupling is negatively associated with age ($\hat{I}^2$=-0.41, $p< 1 \times 10^{-11}$). Age-associated decreases in structure-function coupling occur broadly across the cortex: in V1, auditory cortex, precentral and postcentral gyrii and the paracentral lobule, lateral prefrontal cortices, and in the left posterior cingulate (p_{FDR}<0.05), but age-associated decreases are disproportionately enriched in primary sensory networks, specifically in auditory and somatomotor-hand networks (permutation-based *p*<0.05). This age-associated 'decouplingâ€ of structure and function reflects increasingly segregated patterns of functional connectivity (participation coefficient: age $\hat{I}^2$=-0.11, *p*=0.001; modularity quality index: age $\hat{I}^2$=0.13, *p*=0.025) and increasingly integrated patterns of white-matter connectivity with age (participation coefficient: age $\hat{I}^2$=0.59, $p< 1 \times 10^{-14}$; modularity quality index: age $\hat{I}^2$=-0.62, $p< 1 \times 10^{-16}$). Finally, we sought to understand the implications of structure-function coupling at birth for later behavior. Higher structure-function coupling in the frontoparietal network, controlling for age, is associated with better cognitive ($\hat{I}^2$=0.24, *p*=0.012, p_{FDR}=0.035) and language ($\hat{I}^2$=0.25, *p*=0.008, p_{FDR}=0.025) abilities at two years.

Conclusions: Coupling between patterns of white matter connectivity and spontaneous functional activity varies across the cortex in neonates, with age-associated decreases in coupling occurring most strongly in sensory areas. Increasingly integrated white-matter connectivity might directly sculpt segregated patterns of functional activity, if white-matter connections not only promote synchrony between regions, but also synapse onto networks of inhibitory interneurons and facilitate sparse, regionally specialized neural activity. Our results provide valuable insight into the relationship between structure and function across the cortex, and how interregional variation in structure-function coupling during the first month of life might shape later cognition.

1-N-106 - Examining individual variability in functional brain network topography over development

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Details

Objective: A longstanding objective in neurocognitive research has been to subdivide the human brain into a mosaic of anatomically and functionally distinct areas to understand how the brain segregates and integrates information. The discovery of resting state functional MRI (rs-fMRI) has led to the characterization of human brain organization based on the co-activation patterns of brain areas. However, such network organization is created by spatially co-registering data across multiple individuals which assumes homogeneity in brain organization and obscures meaningful subject-specific features. Recent work using Precision Functional Mapping (PFM) techniques have rendered unique insights into individual functional brain network architecture, revealing idiosyncratic network topography such as individual variation in functional network size (i.e., how much cortical real estate is taken by each network). Such variation in individual topography has been shown to relate to individual differences in behavior such as cognition and motor skills. However, it is not known when individual variation emerges over development.

Methods: In this study, we aim to examine whether the surface area of functional networks differs between three different age groups: neonates, adolescents, and adults. We utilized functional neuroimaging data from the Adolescent Brain and Cognitive Development study (n=6000) and the Midnight Scan Club precision imaging study (n=10) to derive adolescent and adults individual network maps using Template Matching. For neonates, we derived individual network maps from extended acquisitions of neonatal resting state fMRI data (n=8, duration: 80-200 minutes).

Analysis: In our analyses, we will calculate the mean total surface area for each group. As neonates have less gyrification than the other two groups, we hypothesize that the mean total surface area will be smaller for neonates compared to adolescents and adults. We will also calculate the proportional surface area for each individualized network in each age group. Using the large sample from ABCD, we will create a distribution of proportional surface area for each network and examine potential age effects based on where the network size for neonates and adults fall within this distribution. We hypothesize that the relative proportion of the cortex devoted to each network at different age points will vary.

Implications: Taken together, our study will provide important insights into age-related changes in individual-level functional network topography, and open opportunities to investigate how such changes in functional network topography relate to emergence of various behaviors in health and disease.

P – Rewards/Motivation

1-P-107 - Examining the relationship between anhedonia and learning the value of mental effort in adolescents

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Details

Anhedonia is common in individuals with depression and is associated with weaker affective responses to enjoyable experiences, blunted enthusiasm for prospective rewards, and reduced drive to obtain positive outcomes. Because of these motivational deficits, decision-making is often impacted in individuals high in anhedonia. However, decision-making is crucial for adaptive behavior, including for choices about whether cognitive control - experienced as the exertion of mental effort - should be exercised. In novel environments, individuals must learn about the value of their cognitive control through experience, but there is little evidence informing how anhedonia influences this learning process, including in adolescents. Adolescence is a critical developmental stage for understanding the correspondence between anhedonia and the efficient deployment of mental effort due to the maturation of motivational processing during this period. To investigate whether learning the value of cognitive control varies according to anhedonia in adolescents, the current study is actively recruiting 60 participants ages 13-17 years old (evenly distributed across parent-reported gender identity) for an online testing session. Data collection is ongoing and preliminary analyses will be conducted prior to this presentation. To connect learning about mental effort to anhedonia, this study leverages an incentivized task-switching paradigm and the Anhedonia Scale for Adolescents (ASA; Watson et al., 2021), a self-report survey that quantifies several dimensions of anhedonia in this age group. Higher ASA sum-scores indicate elevated levels of anhedonia. The motivated task-switching paradigm - which requires participants to respond to the color or pattern of an adolescent-friendly stimulus - measures how individuals titrate their mental effort according to two sources of information: difficulty and reward. The paradigm manipulates the difficulty of engaging cognitive control by varying the frequency of task-switching (i.e., color- or pattern-report trials). It also manipulates the reward received for engaging cognitive control by varying the incentives for correct and rapid task-switching performance. The difficulty and reward manipulations are signaled to participants with cues presented prior to blocks of task-switching trials. As the experiment progresses, participants can learn to integrate and leverage the prospective difficulty and reward cues to guide the economical allocation of their mental effort. To elucidate how anhedonia shapes learning about mental effort during adolescence, we will use linear mixed effect models that examine the effects of difficulty, reward, time, and ASA sum-scores on the accuracy and speed of task-switching performance, controlling for age. Given that previous research couples anhedonia with motivational deficits, but adolescence is considered to be a period of motivational sensitivity, we predict that, with accumulating task-switching experience, lesser anhedonia scores will be associated with the modulation of mental effort according to how challenging task-switching is, but not according to the incentives for performing task-switching well. Meanwhile, greater anhedonia scores will be associated with the selective engagement of mental effort in task-switching trials that are both less challenging and more incentivized. In all, this study will help clarify the relationship between individual differences in anhedonia, motivated cognitive control, and learning about mental effort during adolescence.

1-P-108 - Neurocognitive and computational correlates of action-control in children with attention-deficit/hyperactivity disorder

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Details

Objective

Children with attention-deficit/hyperactivity disorder (ADHD) display reinforcement learning (RL) impairments, which have been proposed to have a key role in ADHD symptoms. Further, RL principles are employed in behavioral ADHD treatment. Yet, there is a lack of mechanistic understanding of RL processes in ADHD. We conducted 3 studies aiming to characterize cognitive and brain function patterns of action-control (an RL mechanism guided by habitual and goal-directed behaviors) in children with ADHD. The ventromedial prefrontal cortex (vmPFC) and striatum are implicated in action-control. In particular, the anterior caudate mediates goal-directed behavior, and the posterior putamen mediates habitual behavior. Research notes alterations in structure and function of corticostriatal circuits in ADHD. We predicted that children with ADHD would have deficits in action-control with distinct cortical and striatal activation patterns.

Methods

To examine action-control in Studies #1 and #2, we developed and validated a child-friendly cognitive analogue of the outcome-*devaluation* paradigm with 3 phases: (1) acquisition: learning action-outcome associations, (2) devaluation: one outcome is devalued and, (3) choice test between valued and devalued outcomes. In Study #1, we tested 21 healthy children (HC) and 19 off-medication (off-med) ADHD children (6-10 years). We applied a trial-by-trial Q-learning computational model on acquisition and choice trials to fit cognitive data and examine individual response mechanisms. In Study #2, we tested 9 HC and 9 off-med ADHD children (6-10 years) using the same outcome-*devaluation* task during functional magnetic resonance imaging (fMRI) to examine event-related brain activation. The acquisition phase was completed inside the scanner, the devaluation phase outside, and the choice test inside to avoid contextual differences. In Study #3, we tested 14 HC and 19 off-med ADHD children (6-10 years) using an outcome-*overvaluation* computer-based task, also with 3 phases: (1) acquisition: learning action-outcome associations, (2) overvaluation: one outcome is overvalued and, (3) extinction: 2 stimuli (associated with valued or overvalued outcome) presented; asked to choose 1 in extinction.

Results

Study #1 analysis showed that HC and ADHD groups employed the goal-directed more than the habitual system to control actions. Yet, the ADHD group exhibited a predominance of habitual responding. In acquisition, the ADHD group showed greater perseveration in selecting inaccurate responses despite feedback. In choice test, the ADHD group showed higher rates of learning noise: a tendency to explore choices rather than sticking to feedback-based correct answers. Study #2 analysis showed overall increased activation in goal-directed behavior regions (vmPFC and anterior caudate nucleus) in HC

during stimulus presentation. Late vs. early acquisition phase analysis revealed a group difference in vmPFC activity: in late acquisition, the ADHD group exhibited higher vmPFC inhibition, while HC had higher vmPFC activation. Study #3 showed that both groups acquired action-outcome associations during phases 1 and 2. During extinction, HC responded at a higher rate on overvalued-associated stimuli than the ADHD group, indicating higher tendency toward goal-directed behavior.

Conclusion

Our results indicate that compared to HC, children with ADHD exhibit a tendency toward habitual response rather than goal-directed behavior. Further, we found evidence of a distinct neural signature underlying action-control in children with ADHD. Characterizing ADHD with action-control as an endophenotype provides a novel, mechanistic understanding of ADHD. Our research will broaden understanding of neural circuits underlying cognitive symptoms of ADHD and elucidate treatment approaches to create a balance between ADHD symptom relief and cognitive deficit remediation.

1-P-109 - Early Life Deprivation Moderates the Relation Between Inflammation and Nucleus Accumbens Gray Matter Volume in Adolescents

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Details

Introduction

Early life stress (ELS) is associated with increased risk for psychopathology, including depression and anxiety, in late adolescence and early adulthood. To gain a better understanding of the complex relation between ELS and increased risk for psychopathology, it is important that researchers examine the mechanisms that link stress exposure to disorder. Deprivation, a form of ELS, is related to altered reward processing. Further, exposure to ELS predicts elevated levels of inflammation in adolescence which, in turn, are associated with altered reward reactivity. The neuroimmune network hypothesis offers a framework to model the relations among ELS, inflammation, and the brain, positing that exposure to stress alters communication between the immune system and reward-related brain regions. This framework predicts that ELS moderates the neuroimmune relation, meaning that the association of inflammation with the brain differs as a function of exposure to ELS. In this study, we investigated how early life deprivation affects the relation between the inflammation marker C-Reactive Protein (CRP) and gray matter volume (GMV) of the nucleus accumbens (NAcc), a brain region associated with reward.

Methods

Our sample included 110 (63F/47M) individuals (15.76 Â± 1.27 years) who were participating in a longitudinal study of outcomes of ELS. ELS deprivation scores included income-to-needs ratio, neighborhood-level socioeconomic metrics from the CalEnviroScreen (a neighborhood level database of socioeconomic factors representing access to resources), and self-reported data from the Multidimensional Neglectful Behavior Scale. The total deprivation score represents resource availability / access to care for participants during childhood. Peripheral inflammation was indexed by CRP, a key

marker associated with elevated inflammation, measured using a dried blood spot protocol. Using voxel-based morphometry, we calculated GMV of the bilateral NAcc from T1w structural brain images obtained with a 3T MRI scanner. We conducted regression analyses to model the interaction term of ELS deprivation and CRP to predict NAcc GMV, controlling for age, sex, assay batch, BMI, and a scanner upgrade.

Results

ELS deprivation moderated the relation between CRP and NAcc GMV ($\hat{\beta}$[95%CI]= -0.303, t=-2.40, p=0.0183): whereas the high-ELS group had a negative linear relation between CRP levels and NAcc GMV, the low-ELS group had the inverse relation.

Discussion

In this study we tested, and found support for, the prediction that ELS moderates the neuroimmune relation. Whereas adolescents raised in non-deprived conditions have a positive neuroimmune relation in which greater inflammation predicts higher NAcc GMV, adolescents who experienced high deprivation exhibited the opposite pattern in which elevated CRP predicts lower NAcc GMV. Thus, the experience of deprivation appears to attenuate the positive association between CRP and NAcc GMV. Importantly, low GMV in reward brain regions has been found to be associated with maladaptive outcomes, implicating immune-related alterations in NAcc GMV as a mechanism that might link ELS to psychopathology.

Our finding of ELS deprivation as a moderator of the relation between immune function and brain structure contributes to a growing body of research supporting the neuroimmune network hypothesis. Elucidating precisely how early life deprivation adversely affects reward processing years later is an important task for future research that will advance our understanding of the development of maladaptive reward processing. Our structural findings add a critical dimension to previous research, that have largely studied the relation between immune levels and brain *function*. Going forward, longitudinal studies investigating how deprivation affects this neuroimmune association over time will increase our knowledge of mechanisms underlying the development of disorders, like depression, that involve alterations in reward circuitry.

1-P-110 - Paternal involvement and children's reward processing in the monetary incentive delay task: the possible role of children's sleep health

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Details

Adolescence is characterized by increased risky decision-making, which can be exacerbated by poor sleep. Many factors can affect the proper sleep of an adolescent, and parents' involvement in their life is one of them. Maternal involvement has received significant attention, yet the few studies that have examined paternal involvement support that greater paternal involvement is associated with better sleep health in infancy. To our knowledge, no studies have examined the role of paternal involvement in adolescents'

sleep health nor subsequent effects on performance and brain activity during a monetary incentive delay (MID) task.
To this end, we leveraged the ABCD data set (release 4; 2-year follow-up ancillary study; N=613; 325 males; 288 females, age = 142.20 months) and examined associations between paternal involvement, children's sleep health, performance, and neural activity during the monetary incentive delay (MID) task. Paternal involvement was measured via the Alabama Parenting Questionnaire. To investigate children's sleep health, we leveraged Fitbit data, including the following indices: (1) sleep latency (the time it takes to fall asleep), (2) sleep midpoint (midpoint between sleep and awake time), 3) total minutes 'lightâ€ sleep, 4) total minutes in 'deepâ€ sleep, 5) total minutes in 'remâ€ sleep and 6) total time sleep duration. We examined fMRI average beta weights in the bilateral accumbens and insula during the MID task in trials indexing the anticipation of reward (activity in reward versus neutral trials) and losses (activity in reward versus neutral trials).
Using linear mixed effect models implemented via the lme4 R package, we found a significant negative relationship between father involvement and adolescents' light sleep duration. We also found a significant interaction between the father's involvement and the chil's sex in predicting total and light sleep duration, sleep midpoint, and latency. Stratified the models based on the child sex (assigned at birth) showed that the father's involvement was not significantly related to sleep indices for female offspring. However, for male offspring, greater paternal involvement was associated with longer sleep latency and later midpoint. We then examined the relationship between sleep health and MID performance. There was a significant association between light sleep duration and average reaction time for both reward and loss anticipation trials, such that less light sleep duration was associated with longer reaction times. Moreover, for females, longer sleep latency, and later midpoint predicted less activation during both loss and reward anticipation conditions in the accumbens. Examining the relationship between neural activity and MID performance also revealed a significant negative correlation between brain activity in the left accumbense and average reaction time during reward anticipation trials.
Our results suggest that the father's involvement may significantly impact sleep health in adolescents, suggesting that the father's involvement may be associated with less time spent in light sleep and, for males, longer latency and sleep midpoint. While longer sleep latency, and later midpoint were associated with less accumbens activity during reward and loss anticipation for female offspring, a pattern that has been associated with cognitive-control deficits and risky choice selection previously. We did not document significant associations between sleep indices and MID activation for male offspring. However, our study found support for the role of paternal involvement on MID performance via children's sleep health. Future studies should examine interactions between maternal involvement and household composition.

1-P-111 - Youth Irritability and Reward-Related Brain Functioning in the ABCD Sample

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Details

Objective: Irritability is conceptualized as low threshold for frustration and anger (Brotman et al., 2017). Irritability frequently cooccurs with a number of psychiatric problems and uniquely predicts future mental health problems in adolescents and adults (Sorcher et al., 2022; Brotman et al., 2006). The pathophysiological model of youth irritability proposes that severe irritability is due to aberrations in reward related brain function (Brotman et al., 2017). However, prior work has largely focused on reward

in the context of frustration only. Nevertheless, irritable youth may also exhibit deficits across other components of reward processing. Previous studies examining non-frustrative reward processing have observed neural differences related to irritability, specifically increased striatal activation, and altered nucleus acccumbens (NAcc) and amygdala (AMY) connectivity with prefrontal cortex (PFC) areas during reward tasks (Dougherty et al., 2018; Kryza-Lacombe et al., 2020). More research is needed to delineate reward-related brain function in irritability using large, diverse samples to inform its pathophysiology.

Methods: Functional MRI data from 6,065 participants in the Adolescent Brain and Cognitive Development (ABCD) baseline sample were analyzed. Participants were excluded for poor fMRI or behavioral data quality, or a history of brain trauma or seizures. Brain activation and connectivity (generalized **psychophysiological interactions; gPPI**) were measured during the Monetary Incentive Delay task. Data were analyzed during the anticipation period, in which they were informed that they could win money (reward), lose money (loss), or no money was at stake (neutral), and the feedback period, in which they were informed whether they hit or missed the target. Linear Mixed Effects models in R were used to examine the effects of irritability and task condition on region of interest (ROI) activation and ROI connectivity with the right and left AMY and NAcc. ROIs included the right/left AMY, striatal areas, and PFC areas. All analyses covaried for race/ethnicity, SES, sex, pubertal development, and age, nested by family and MRI scanner, and were corrected for multiple comparisons with the False Discovery Rate.

Results: During anticipation, higher irritability was associated with *greater* activation differences between loss and reward trials in the left middle frontal gyrus (MFG), and *smaller* activation differences between loss and neutral trials in the left inferior frontal gyrus (IFG), left NAcc, left caudate, and right MFG. In addition, during anticipation, higher irritability was associated with less connectivity between the AMY and striatal regions. Furthermore, right AMY connectivity varied based on irritability level: in the right dorsal lateral PFC higher irritability was associated with *opposite pattern* of connectivity between neutral and reward trials, while for the left MFG and right NAcc higher irritability was associated with *greater* differences between neutral and loss trials and neutral and reward trials, respectively. During feedback, higher irritability was associated with different activation for misses than hits in the right and left AMY. The effect of irritability on activation and connectivity remained significant even after accounting for youth anxiety, ADHD, and depressive symptoms as additional covariates.

Conclusions: Youth with higher levels of irritability compared to youth with lower levels of irritability demonstrate aberrant reward-related brain activation and connectivity in the striatum, AMY, and PFC regions, which are key regions involved in reward, emotion, and cognitive control. Importantly these effects remained even after accounting for other forms of psychopathology, demonstrating that irritability shows a specificity in its aberrant reward processing. Future work will investigate how the co-occurrence of problems may show unique patterns of neural function in reward processing.

1-P-112 - Characterizing age-related change in learning the value of cognitive effort

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Details

OBJECTIVES

In order to efficiently navigate their environments, individuals of all ages must decide what tasks are deserving of their cognitive control; phenomenologically, the exertion of their cognitive effort. Making these decisions involves weighing the benefits of deploying cognitive effort (e.g., obtaining reward for performing a task well) against its costs (e.g., ceding mental energy to one task instead of another). When individuals encounter novel environments, they must learn about the benefits and costs of their cognitive control through experience. Prior research demonstrates that adults learn in this way; this study characterizes if and how children and adolescents detect, integrate, and leverage information about the benefits and costs of their cognitive control to govern their cognitive effort expenditure.

METHODS

Participants (*N* = 150) ages 10 to 20 years old, evenly distributed across continuous age and self-reported gender identity, are being recruited to complete a pre-registered online experiment that investigates how the value of cognitive effort is updated through experiential learning. To do so, the study uses a motivated task-switching paradigm that manipulates the difficulty of, and the reward received for, successfully engaging cognitive control. Participants are asked to respond to 240 trials probing different features of a stimulus (i.e., the color or pattern of an alien cartoon). Before seeing a 20-trial block of these color and pattern probes, participants are told which galaxy they are in (i.e., the planet or moon galaxy), and they can learn through experience which galaxy is associated with more or less cognitive demand (high or low task-switch rate). They are also told how much monetary reward they can earn for performing task-switching correctly and quickly (1 or 10 cents). Greater performance accuracy and faster performance speed serve as indices of elevated cognitive effort exertion. Over time, participants can detect the prospective difficulty cues, integrate them with the prospective reward cues, and leverage their composite to economically allocate cognitive effort. Past work has established that learning and decision-making strategies, and estimating the benefits and costs of cognitive effort, mature into, during, and out of adolescence. Therefore, we predict that learning to titrate cognitive effort according to reward and difficulty cues will improve from late childhood to early adulthood. To evaluate this hypothesis, we employ linear mixed effects models that examine the interacting influences of age, reward, difficulty, and time on the dependent variables describing task-switching performance: accuracy and speed.

RESULTS

Preliminary results (*N* = 103) indicate that, throughout the experiment, performance accuracy shallowly improves across age for the 1 cent galaxies, while performance accuracy steeply improves from childhood to adulthood in the 10 cent galaxies. The 1 and 10 cent slopes increasingly diverge after mid-adolescence, suggesting that reward information guides performance accuracy in older adolescents and adults more than in children and young adolescents. Meanwhile, in both the high and low task-switch rate contexts, performance speed is modulated by the reward cues in each difficulty context for younger and older participants, but performance speed is not affected by differential reward for adolescents.

CONCLUSIONS

Taken together, these results align with previous findings that adolescents, unlike adults, do not regulate the degree of their cognitive effort according to reward information. Elucidating age-related

refinements in learning to adjust cognitive effort in relation to multiple cues about its value is important for understanding how children through adults reason about, and act on, information about the benefits and costs of their cognitive control.

1-P-113 - Measuring Cognitive and Motivational Processes: A Large-Scale Validation Study of Iowa Gambling Task Computational Parameters

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Details

The Iowa Gambling Task (IGT) is a widely used behavioral task that assesses adolescent and adult decision-making, with links to externalizing and substance use outcomes. Recent advancements in computational models have afforded new insights into the cognitive processes associated with IGT performance. However, it remains unknown whether such computational parameters demonstrate comparable measurement validity to traditionally-used task accuracy indices. The present study evaluates the validity and retest stability of the reward sensitivity and learning components derived from an IGT computational model. With data analysis currently underway, we leverage data from three large cohorts of adolescent and adult twins (N = 1,628). We will examine associations between the reward sensitivity component and self-reports on reward sensitivity measures, and between the learning component and working memory assessed using span tasks and learning assessed using the Rey Auditory Verbal Learning Test. We will also assess retest stability over one year during adolescence and over three years in young adulthood. Because prior work implicitly makes the assumption about these parameters being unique components, we expect to demonstrate convergent and discriminant validity in the form of a double dissociation in the pattern of correlations: stronger correlations between the reward sensitivity component and self-reported reward sensitivity measures than with measures of working memory and learning, combined with stronger correlations between the learning component and measures of working memory and learning than with self-reported reward sensitivity measures. We also expect to demonstrate low to moderate 1-year and 3-year retest stability. The findings from this study will provide valuable information about the validity and retest stability of IGT computational model parameters, which will inform future research on the development of cognitive and motivational processes, particularly during adolescence and young adulthood.

1-P-114 - Exploring the functional network connectivity during reward anticipation across early adolescence

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Details

Pre-Registration Poster

Adolescence is characterized by the continued structural and functional development of frontostriatal circuitry implicated in behavioral regulation. Anticipation of rewards and decision-making in ambiguity are cognitive constructs that are significantly maturing during this critical period. Though studies have established different brain regions responsible for reward anticipation, examining the dynamic connections between brain regions during reward processing is required. Thus this current study focuses on understanding the changes in functional network connectivity in the frontostriatal networks during reward anticipation across adolescence. The study will use the data collected as part of the Neuroventure Study (Bourque,2016), a longitudinal fMRI study where 150 adolescents (mean age of 12 during baseline) performed the fMRI paradigm of the Monetary Incentive Delay task at baseline (T1), after 24 months (T2) and after 48 months (T3). The current study plans to understand the functional connectivity of anticipation to rewards by using the general psychophysiological interaction (gPPI) approach where seed-to-voxel functional network connectivity would be studied with the ventral striatum as the seed region. Network connectivity at each time point would be computed and the change in functional network strength across three time points would be determined. Results of the first time point network connectivity will be shared at the conference. Based on previous studies, we are expecting to see reduced response during reward anticipation in subcortical regions like the ventral striatum with increased functional network connectivity in the ventral striatum at T3 compared to baseline.

Key words : adolescent, reward anticipation, functional network connectivity.

Q – Socioemotional Processing

1-Q-115 - Dissecting neural correlates of affective and cognitive empathy in preschoolers: an fNIRS study

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Details

Introduction

Empathy is fundamental for bonds and social interactions (Bernhardt & Singer, 2012). As failure of empathy might evolve into antisocial behaviour (Frick & Viding, 2009), understanding the mechanisms behind its development is fundamental for efficient early interventions. There is an extensive literature on empathy in adults, highlighting two main components of empathy, an affective one (i.e. sharing others' feeling) and a cognitive one (i.e. understanding others' feeling) (Shamay-Tsoory, 2011), supported by different brain networks (Decety & Jackson, 2006). However, how and when these two components mature is still not well understood, and investigating their neural correlates while this skill is still developing might clarify how the developing brain processes these two components.

Toddlerhood is the appropriate age to study the development of empathy, as from 2 years, preschoolers differentiate emotions originated from themselves and others (Amsterdam, 1972), which is a fundamental ability for empathy (Lamm et al., 2016). Tasks used so far to assess the development of empathy might not be appropriate to dissect which empathic component matures first. Most of the previous works assessed empathy towards adults or a doll, but investigating empathic reactions towards other children

would more realistically resemble preschoolers social interactions. Moreover, the assessment of cognitive empathy has often been confused with the one of perspective-taking - which are two different skills (Stietz, 2019) - and relied only on children's verbal skills, but this might confound assessments of developmental ordering. Instead, investigating the neural underpinnings of the development of empathy towards other children can show changes in the brain that underpin social behaviours, and show markers of empathy regardless its verbal or behavioural manifestation.

Methods

We designed a new block-design task in which 50 3-to-5-year-olds were presented with 8 emotionally salient and 8 neutral scenarios, with situations taken from naturalistic observations of children in a nursery (Bulgarelli and Jones, 2023). Contrary to other previous tasks, both empathic components were tested in each emotionally salient scenario. Each scenario showed an emotionally salient or emotionally neutral event (affective empathy vs. neutral fact). After each scenario, the participant was asked to reflect on the character's feeling or reason for action (cognitive empathy vs. cognitive reasoning). During this task, we recorded neural activations from frontal and temporoparietal regions, known to be engaged in empathy in adults (Decety & Jackson, 2006), using functional near-infrared spectroscopy (fNIRS).

Expected results and conclusions

Data analysis is ongoing. We expect to dissect different neural networks for affective and cognitive empathy, possibly mapping the adult ones. Finding stronger neural correlates for one component of empathy over the other, might elucidate which empathic component develops first. While gender differences in empathy have been documented in adults (Christov-Moore, 2014), whether they root in childhood in unclear, therefore we will explore neural differences between male and female preschoolers.

This works provides the first systematic investigation of neural correlates of empathy in preschoolers, proposing a new task that can be used by other researchers in the field and opening up new avenues to further explore the development of empathy.

1-Q-116 - The EmpaToM-Y-Eng: validation of an functional magnetic resonance imaging measure of social processing in adolescents

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Details

Background: Empathy and theory of mind (ToM) are vital for building social competency in young people. Impairments in these processes have been found in different mental health and neurodevelopmental disorders. Magnetic resonance imaging (MRI) studies have demonstrated dissociation of brain networks in adults that underpin empathy versus those that underpin ToM.

Adolescence is a period vital for the development of these social-affective and -cognitive abilities, due to significant development of the underlying brain networks, and social relationships taking on increased

importance as adolescents become more independent from their family unit. Adolescence is also a time where we see an increase in the onset of mental health disorders. As such, it is important to understand empathy and ToM, and their underlying brain bases, within this developmental period. However, much of the field continues to use unidimensional self-report questionnaires or tasks with low ecological validity.

Objective: The EmpaToM-Y (Breil et al. 2021) is a German-language functional (f)MRI task designed to independently manipulate and measure the dissociable processes of empathy and ToM. It has high ecologically validity due to its use of realistic complex video content and has been modified for use in adolescents. Our study aims to translate and validate this task for use in a sample of 60 English-speaking adolescents, aged 14-18.

We hope to demonstrate that the â€˜EmpaToM-Y-Eng' captures individual variability and dissociation between empathy and ToM (through behavioural, fMRI, and psychophysiological data) and has strong psychometric properties equivalent to the existing German EmpaToM-Y. We also hope to investigate in what way the EmpaToM-Y-Engl relates to other commonly used measures, namely self-report measures.

Methods and analysis plans: By the Flux conference, we expect to have finalised the creation of the task and completed the behavioural validation stage, but we do not expect to have completed the neuroimaging stage. We will present the task in detail, the results of the behavioural validation stage, and our plan for the MRI validation stage. It will be an invaluable opportunity to receive feedback from the developmental neuroscience community before we proceed with the neuroimaging component of the study.

The EmpaToM-Y-Eng will contain short video sequences depicting a person narrating an autobiographical episode with varying emotional valence. Participants rate their own emotions after watching each video, allowing measurement related to empathy, and answer questions regarding the mental state of the person depicted in the video to measure ToM capacity. Non-ToM related questions will be asked to provide a control condition.

Behavioural validation stage analysis plan: Performance on the EmpaToM-Y-Eng will be compared to the original EmpaToM-Y measure. Internal consistency (Cronbach Î±), the item total correlation, as well as item-specific difficulty and reliability values will be compared. EmpaToM-Y-Eng ratings (affect) and performance (reaction times and error rates for ToM) will be analysed by means of a repeated measures analysis of variance (ANOVA). A 2 Ã— 2 factorial design will be applied with the within-subject factors emotionally negative videos versus neutral videos and ToM versus non-ToM. We will compare the strength of our effects with the results from the previous EmpaToM-Y study. We will provide information on convergent/divergent validity through reporting associations with self-report questionnaires.

This research will result in an English version of an fMRI task for neuroscientists to investigate social processes during adolescence. We hope this will be valuable to many members of the Flux community and will facilitate future investigations about how these processes are impacted in clinical populations or used to evaluate treatments aimed to improve social processes.

1-Q-117 - Relationships between math-related attitudes and performance among children and neural and epigenetic markers of their social processing capacity

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Details

Background. Children's math performance may be influenced by a myriad of factors, many of which cannot be fully characterized through observation alone. Physiological measures may thus enhance the degree to which we understand variations in learning among children developing in diverse contexts (e.g., based on cultural background, access to resources, neurodivergence, etc.). Interpersonal neural synchrony (INS; the alignment of neural activity between interacting individuals over time) can be quantified using time-locked electroencephalography (EEG) and is thought to reflect social partners' degree of interpersonal attunement during an exchange. Receptor gene methylation of oxytocin (*OXTRm*) is an epigenetic change shown to modulate endogenous oxytocin activity, and is thought to correspond with an individual's capacity for processing social cues.

Objectives: This study examined the relationships between these neurobiological measures reflective of social functioning among child-parent dyads, observational ratings of parent-child behavioral attunement, and children's performance and self-reported math nervousness during joint math problem solving.

Method: Child-parent dyads (N=27) performed a math flashcard task together while their neural activity was recorded using EEG. On a separate date, children completed a guided interview of math-related anxiety. Task videos were coded for: (1) the number of flashcards each child completed (a proxy for performance), and (2) behavioral attunement (e.g., shared gaze, mutual responsiveness, etc.). INS was calculated using a windowed cross-lagged correlation analysis of electrode-level EEG signals, and child and caregiver salivary *OXTRm* was quantified via DNA sequencing. Using forward stepwise hierarchical linear regression, we identified the best-fitting models for predicting behavioral performance and math anxiety based on our collection of individual vs. dyadic and biological vs. behavioral social metrics.

Results: Children's math anxiety ($F(4,13) = 4.02$, $p<.05$) was negatively predicted by their *OXTRm* ($B= -.79$, $p=.002$). Children's *OXTRm* ($F(4,13) = 5.82$, $p<.05$) was further negatively predicted by both math anxiety (B= -.58, $p<.05$) and child-parent INS (B= -.39, $p<.05$). No significant models emerged predicting math performance or with observed child-parent attunement as a significant predictor.

Conclusions: These results align with research suggesting that state-anxiety responses may partially be explained by one's bias towards negative interpretation of social cues.[1] Further, physiological symptoms of math anxiety are shown to mainly emerge during anticipatory periods prior to problem solving, suggesting that interpretations of extraneous cues are important predictors of affective experience.[2] Higher *OXTRm*, linked to reduced oxytocin binding, may limit one's capacity to attend to and interpret social information, and thereby reduce anxiety.[3] Conversely, those with lower *OXTRm* may negatively interpret social cues and experience anxiety more frequently, including during math problem-solving. The negative relationship between child *OXTRm* and child-parent INS, a measure of their interaction

quality, further supports the specific social implications of oxytocin function among children in this sample.

This study illustrates the added value of neurobiological measures for studies of complex phenomena like children's subjective emotional experiences. Using transdisciplinary measures enables the characterization of behaviors in real-life contexts, facilitating the translation of developmental cognitive neuroscience research findings to broader populations and disciplines.

1. Chen, J., Milne, K., Dayman, J., & Kemps, E. (2019). Interpretation bias and social anxiety: Does interpretation bias mediate the relationship between trait social anxiety and state anxiety responses? *Cognition and Emotion*, *33*(4), 630â€“645.
2. Lyons, I. M., & Beilock, S. L. (2012). When Math Hurts: Math Anxiety Predicts Pain Network Activation in Anticipation of Doing Math. *PLOS ONE*, *7*(10), e48076.
3. Neumann, I. D., & Slattery, D. A. (2016). Oxytocin in General Anxiety and Social Fear: A Translational Approach. *Biological Psychiatry*, *79*(3), 213â€“221.

1-Q-118 - Examining associations between suicidal ideation and cognitive reappraisal among adolescent females

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Details

Suicide is one of the leading causes of death for youth worldwide and an urgent public health concern. Importantly, rates of suicidal ideation and suicide attempts increase dramatically during adolescence. According to the National Alliance of Mental Illness, nearly 20% of high school students report having thoughts of suicide (suicidal ideation), with 9% of students reporting a past suicide attempt. Given this prevalence, it is imperative that researchers work towards identifying predictors of suicidal ideation to help shape intervention for those at risk. Despite growing research in this area, identifying predictors of suicide has proven to be challenging. Examining the neural correlates of suicidal ideation among adolescents is a promising area of research, and may allow researchers to better identify the mechanisms underlying these behaviors. In this analysis, we examine whether change in suicidal ideation (SI) across early adolescence is associated with neural responses during cognitive reappraisal before and after a peer rejection event.

Participants included 92 females ages 9 to 17 years old (*M*= 12.84 , *SD* = 1.91). Participants completed the Suicidal Ideation Questionnaire at baseline and 8 months later. Change in suicidal ideation was operationalized as the difference between these scores. Participants also completed a neuroimaging session where they underwent an experimental fMRI task designed to elicit emotion reactivity and regulation. In the scanner, participants viewed positive, negative, and neutral images. Trials varied between 'Lookâ€ trials and 'Decreaseâ€ trials. During 'Lookâ€ trials, participants were instructed to react naturally and experience whatever feelings were elicited by the image. During 'Decreaseâ€ trials, participants were instructed to use cognitive reappraisal strategies to decrease the emotion elicited by

the picture. Multiple reappraisal strategies were taught prior to the scan (e.*g. imaging the situation doesn't involve you, distancing*). This task occurred twice; before and after a peer rejection task involving deception. During the peer rejection task, participants were told another peer did not want to chat with them after reading their personal biography and seeing them while they were lying in the scanner.

We then examined differences in brain activation as a function of change in SI during the (1) look negative > look neutral and (2) decrease negative > look negative trials across runs prior to rejection and post rejection. Analyses were conducted in FSL, controlled for age at scan, and employed a cluster-level correction (z>2.3, p<.05). Prior to rejection, there were no areas of brain activation associated with SI change for either contrast. After rejection, decreased SI across time was associated with greater activation in the precuneus cortex when participants passively viewed negative relative to neutral pictures. In the decrease negative > look negative trials, decreased SI across time was associated with less activation in regions of the executive control network (e.g., Middle Frontal Gyrus, Anterior Cingulate Gyrus).

It is possible that these results show that individuals who employ more cognitive resources during the reappraisal task are at greater risk for maintaining or increasing their SI across early adolescence. In contrast, they may suggest that using strategies which rely heavily on the executive control network during cognitive reappraisal may not be effectively reducing ideation across early adolescence. Further, because we only observed results in trials following rejection, it may be that the processes that support the future development of SI only emerge in the context of social rejection. Follow up analyses will be able to begin to adjudicate among these possible interpretations.

1-Q-119 - Auditory distraction by vocal anger in children and adolescents with inattention and hyperactivity

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Details

Children and adolescents with inattention and hyperactivity, present difficulties to recognise anger from other people's voices. However, previous research has not examined the involuntary auditory processing of anger in children and adolescents with these traits. In this study we tested 198 participants. These were 51 adolescents (12-13 years), 97 children (7-9 years) and 50 adults. All participants took part in a novel odd-ball auditory distraction task with vocal emotional stimuli. Participants were asked to respond to a target preceded by emotional voices (angry and happy as oddballs and neutral as standard). Reaction times and errors were recorded. The Strengths and Difficulties Questionnaire (parent, teacher, and self-rated) was used to measure inattention and hyperactivity in children and adolescents. The Current Behaviour Scale was used to measure inattention and hyperactivity/impulsivity in adults. Results showed that overall adults were faster followed by adolescents and children at the oddball task. These developmental effects were more pronounced following emotional voices, especially anger. Overall, we found slower reaction times to targets following happy compared to neutral voices in adolescents. In addition, we found slower reaction times to targets following anger compared to neutral voices in children. Reaction times across conditions were strongly significantly associated with symptoms of inattention and hyperactivity in children and

adolescents, and inattention in adults. Participants with higher levels of inattention presented slower reaction times to vocal anger. We discuss implications of the results for theories of auditory distraction in developmental populations with symptoms inattention and hyperactivity. Future research should examine the neural correlates of vocal anger (work in progress in our lab) in adolescents with symptoms of ADHD.

1-Q-120 - Using OPM-MEG technology to determine emotional face responses in very young children with and without autism

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Details

Background: It is well established that adolescents and adults with autism spectrum disorder (ASD) show atypical brain oscillatory activity underpinning critical aspects of cognition and social functioning. While magnetoencephalography (MEG) is the ideal method for neurophysiological recordings due to its excellent spatial and temporal resolution, it shows poor reliability in children under 5 years. Recent advances in MEG technology, however, have led to the development of optically pumped magnetometers (OPMs). OPM-MEG sensors can be mounted in a 3D-printed helmet based on the head size of the participant, unlike the fixed sensor positions in classic cryogenic MEG systems. This results in reduced sensor-to-brain distance compared to MEG, increasing signal strength. OPM-MEG sensors are also uniquely tolerant of head movement, which is a significant advantage when scanning young children.

Objectives: Thus, the current study uses the novel OPM-MEG system to investigate the evoked responses and oscillatory power during an emotional face processing task in young children (3-4-year-olds) with and without ASD. We are the first to scan very young children using OPMs, advancing our understanding of the development of the early neural mechanisms of emotion processing in autism.

Methods: Data were recorded using a Cerca OPM system (Cerca Magnetics Ltd., Kent, UK) in 9 typically developing (TD) children (4 males; *M*age [SD]= 4.1 [0.8] years) and 2 children with ASD (2 males; *M*age [SD]=4.8 [0.1] years). Data were recorded using a whole-head, 40-dual axis zero-field magnetometers (QuSpin Inc., Colorado, USA) during the presentation of emotional faces (Happy and Angry; 80 total trials). Data were band-pass filtered between 2-40 Hz and epoched from -500 to 1000 ms relative to stimulus onset. The coordinates of a 2mm grid in MNI space were transformed to the participants' head position using EinScan (Shining 3D, Hangzhou, China) and an LCMV beamformer was used to estimate source activity. Evoked fields were plotted for regions of interest (fusiform gyri) and a control region (precentral gyrus) to characterize the M170 response. The percentage change in power was computed between the M170 time window (150-230 ms) and baseline (-70 to 0 ms) for TD and ASD participants.

Results: Our preliminary findings show a clear M170 response to emotional faces in the fusiform gyri with a peak amplitude of 13.8 (Â±8.2) nAm and 34.7 (Â±23.6) nAM in TD and ASD participants, respectively. The mean (SD) peak latency for the M170 response was 179.7 (1.7)ms in TD children and

197.5 (0.8)ms in ASD participants. The children with ASD showed evoked responses to faces with greater amplitude and a longer latency compared to the TD group. There was no significant increase in power during the M170 time window compared to baseline, however, visual inspection showed an increase in power from baseline to faces in the left fusiform gyrus for both the TD and ASD participants. Within the TD group, we also found enhanced recruitment of other important face processing brain regions (e.g., frontal areas).

Conclusion: This is the first OPM-MEG study to be performed in young children at the age of diagnosis, who could otherwise not be reliably scanned using conventional cryogenic MEG systems. In this proof-of-principle work, we replicate the well-established face-sensitive M170 response in the fusiform gyri to emotional faces in 3-4-year-old children with and without ASD. Despite our small sample size, our findings support the use of the novel OPM-MEG system to investigate early face neural processes in children with and without ASD. Our data collection is ongoing in children 1-4 years of age (testing 3-4 children/week), and we expect to extend these results in a larger cohort of children, including equal numbers with and without ASD.

1-Q-121 - Investigating the Relationship Between Facial Expressions, Emotion Regulation, and ADHD Symptoms during Positive Emotional Situations in Early Childhood

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Details

ADHD is one of the most prevalent developmental disorders in children. While emotion regulation difficulties are a key characteristic of ADHD, most research has primarily focused on the regulation of negative emotions. While it is known that the difficulties regulating positive emotion is an important characteristic of ADHD and may contribute to later psychopathology, its relationship to ADHD symptoms in early childhood has not been fully established. To our knowledge, the present study is the first to examine regulation of positive emotions in early childhood, test its links to early ADHD symptoms, and identify its underlying neural mechanisms.

Preschoolers (N = 26, *M*age = 5.2 years, *SD* = 0.95) completed a novel positive affect inhibition task called 'Silly Sentencesâ€ during which they need to control the urge to laugh when asked to repeat back funny sentences compared to boring sentences. Children completed 6 trials of the Silly Sentences game consisting of three boring and three funny blocks. This task was video recorded to code the chil's facial expressions, and prefrontal cortex activation was also recorded during the task via functional near-infrared spectroscopy (fNIRS). The Facial Action Coding System (FACS; Ekman & Friesen, 1977) was used to examine positive facial expressions utilizing action units (AUs). The present study uses the total number of times AU 12 and AU 6 occurred across the funny blocks for each participant, as well as a combination of the lip corner puller and cheek raiser (AU 6+12) to analyze more intense facial expressions. Parents completed questionnaires regarding their chil's emotion regulation abilities and early ADHD symptoms.

Correlations and regressions were conducted to examine the connection between facial expressions, PFC activation, and ADHD symptoms. Positive correlations were found between intense positive facial

expressions and inattentive ADHD symptoms (p = 0.058), as well as hyperactive ADHD symptoms (p = 0.061) such that participants that displayed more intense positive facial expressions had greater ADHD symptoms. Left PFC activation was significantly negatively correlated with more intense positive facial expressions across both funny and boring blocks (p = 0.016), such that children that displayed more intense positive facial expressions showed lower left PFC activation. The regression model for intense positive facial expressions and soothability scores was significant, indicating that more intense positive facial expressions predicted low soothability scores and thus poorer emotion regulation. Marginal significance(?) was also found between more intense positive facial expressions and hyperactive ADHD symptoms. This indicates that more intense positive facial expressions may have the potential to predict ADHD symptoms.

Findings from our study indicate that decreased abilities to regulate positive facial expressions are important behavioral indicators of emotion regulation in early childhood which may have potential clinical implications to aid in better diagnostic tools and interventions in early childhood.

1-Q-122 - Brain state characteristics during movie-watching are related to generalized anxiety symptoms in children

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Details

Background: Anxiety is associated with lack of neural habituation to controlled negative and ambiguous stimuli. Less is known about how anxiety alters complex, naturalistic emotion processing. Recent work has demonstrated that brain states during movie-watching represent a combination of exogenous (i.e., movie content) and endogenous (i.e., feeling states) factors. Characterizing how brain state characteristics differ in high anxiety children could therefore lend insight to their day-to-day experiences, linking laboratory observations to real-world emotional functioning.

Objective: The aim of this study is to examine: 1) how brain states shift during emotionally evocative videos; 2) how individual differences in anxiety are related to brain state maintenance and shifting; and 3) if there are developmental differences in these associations across childhood and early adolescence.

Method: We characterized brain states in a large sample of 740 5-to-15-year-old children while they watched two emotionally-evocative videos. Data were split into discovery and replication datasets for both model fitting and follow-up univariate analyses. We trained a Hidden Markov Model on the temporally concatenated and network-averaged discovery dataset for 2-15 states. Model fit was assessed on the replication dataset, and scree plots of fit indices were inspected to determine the optimal number of states. The final model was next applied to each individual's dataset for state classification. Time spent in each state and moment-to-moment probability of being in each state was extracted for further analysis. Videos were annotated for emotion-specific and emotion non-specific information using the EmoCodes system. Group level state probabilities were compared against the emotion-specific content using correlations. Self-reported anxiety symptoms were assessed using the screen for anxiety related disorders (SCARED). Percent time spent in each state across the video, during

peaks in negative content, and right before and after negative content peaks was correlated with the generalized anxiety and social anxiety subscales.

Results: We identified 3 brain states across the sample which were each characterized by unique cognitive network activation patterns. Brain state 1 had increased ventral attention (VAN), visual (VIS), auditory (AUD), and default mode (DMN) activation and decreased dorsal attention (DAN), cingulo-opercular (CON) and frontoparietal (FPN) activation. State 2 was characterized by increased AUD and CON activation and decreased DAN and VAN activation. State 3 was characterized by increased DAN and decreased AUD and DMN. Across the sample, mean percent likelihood of being state 1 was associated with increased negative content in the videos ($r(749)=0.42$, $p<0.001$). Self-reported generalized anxiety scores were positively associated with the percent of time that each individual spent in state 1 ($r(639)=0.14$, $p=0.002$) and negatively with percent of time spent in state 2 ($r(639)=-0.14$, $p=0.004$). This association was driven by negative content, not scenes immediately preceding or following negative emotion peaks. No associations were found for social anxiety symptoms.

Discussion: Our findings replicate and extend previous work that found sustained activation to negative stimuli in individuals with anxiety symptoms. Specifically, we found that increased generalized anxiety was associated with spending more time in a brain state with increased sensory, DMN, and VAN activation, which are associated with bottom-up, stimulus-driven processing. Based on the activation profiles of state 1 versus state 2, it is possible that children high in generalized anxiety are more immersed in negative emotions when they are presented, making it more difficult to self-regulate in the moment. Further work is needed to link concurrent affect to emotion processing in children with anxiety.

1-Q-123 - Neural responses and socio-emotional learning during naturalistic social stimuli

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Details

Caregiving experiences are one major factor that shapes children's social and affective skills. We previously showed that parenting behaviors are associated with children's neural processing of positive emotional events during a film (Park et al. *Dev Cog Neuro*, 2022). However, our previous work did not include measures of individual differences in how children comprehend and remember film events. In this study, we evaluate how normative variation in caregiver experiences and neural processing of socio-emotional stimuli relate to children's memory. We collected fMRI data on 4- to 7-year-olds while they watched a short animated film with parent-child interactions, 'Piper'' by Pixar (n = 40). Following the scan, participants answered nine multiple-choice questions to assess comprehension and memory of the film: five questions focused on character emotions and four on factual events. Parents completed the Alabama Parenting Questionnaire Short Form, which includes scales of positive parenting and inconsistent discipline. We focused on three regions of interest (ROI) due to previously identified associations with parenting: amygdala, hippocampus, and temporal pole. Activation in these regions was extracted during film events coded as parent-child interactions. All analyses controlled for age, sex, and motion in the scanner. Positive parenting was not associated with memory for emotional or factual events (ps > 0.1), but this measure had a ceiling effect. Inconsistent discipline was negatively associated

with performance on the emotion questions (b = -2.73, p = 0.04) but not with their memory of events (b = -0.06, p = 0.30). Inconsistent discipline was negatively associated with temporal pole activation during parent-child interaction events in the film (b = -4.37, p < 0.01). Amygdala and hippocampal activation were not related to children's memory or to parenting measures. Our findings are consistent with literature that identifies an association between adults' temporal pole activation to emotion-inducing stimuli and understanding of others' mental states. Neural responses to social stimuli should be further explored as a potential mediator between early experiences and socio-emotional development.

1-Q-124 - Empathy in Adolescence: An fMRI Investigation Using Implicit Empathic Stimuli

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Details

Objective: Empathy is the ability to recognize, understand, and share the thoughts, feelings, and experiences of another person. It is a vital component of forming and maintaining close interpersonal connections, and previous research shows that empathy develops significantly in the adolescent years. Affective (feeling another's emotional state), mentalizing (understanding another's emotional state of mind), and emotion regulation processes (maintaining a distinction between self and other to reduce personal distress) together have been shown to produce an empathic response to another's suffering. Studies examining the neural correlates of empathy during adolescence have remained comparatively sparse, thus the goal of the current study was to investigate the neural correlates of empathy among adolescents using an implicit empathy task.

Method & Hypotheses: A sample of 92 adolescents aged 11 to 17 (xì„ = 14.10, SD = 1.82); 48.31% female) years underwent an fMRI brain scan while viewing images of human limbs in physically painful (e.g., finger about to get cut by a knife) and non-painful (e.g., finger near a knife) situations. These images were presented to participants in a block design task (6 painful blocks, 6 non-painful blocks). After the fMRI scan, youth completed a rating task where they saw the same images presented in the scanner and rated their 1) empathic concern, 2) perspective-taking, and 3) personal distress on a continuous scale. The following a priori bilateral anatomical ROIs were assessed based on evidence from prior studies: anterior insula (AI), dorsal anterior cingulate cortex (dACC), dorsomedial prefrontal cortex (dmPFC), temporal parietal junction (TPJ), dorsolateral prefrontal cortex (dlPFC), ventrolateral prefrontal cortex (vlPFC), and orbitofrontal cortex (OFC). It was hypothesized that all aforementioned ROIs would show positive activation during painful > nonpainful blocks. Furthermore, it was hypothesized that activation in the AI and dACC would be associated with higher ratings of empathic concern; activation in the dmPFC and TPJ would be associated with higher ratings of perspective-taking; and activation in the dlPFC, vlPFC, and OFC would be associated with lower personal distress. Neuroimaging data were preprocessed and analyzed in SPM 12. Parameter estimates of mean BOLD activation in the a priori ROIs during painful > nonpainful blocks were extracted and analyzed to assess activation (t-tests) and associations with empathic concern, perspective-taking, and personal distress ratings (regressions).

Results: Results revealed that the AI (p = .005), dACC (p = .017), dmPFC (p < .001), and vlPFC (p = .014) showed significant positive activation during painful > non-painful blocks. Although the TPJ, dlPFC, and OFC showed positive activation during painful > non-painful blocks, this activation was not statistically

significant (p's > .05). When examining associations between empathy ratings and activation, there was no significant association between empathic concern and activation in the ROIs (p's > .05). Results demonstrated a positive association between perspective-taking and bilateral AI activation (p = .035), but this result did not pass multiple comparisons correction (p < .025). Personal distress was negatively associated with bilateral dlPFC activation (p = .001), bilateral vlPFC activation (p = .007), and bilateral OFC activation (p = .013), though the bilateral OFC activation finding did not pass multiple comparisons correction (p < .013).

Conclusions: Findings indicate that neural regions implicated in pain processing, mentalizing, and emotion regulation are involved in empathy during adolescence. Furthermore, higher personal distress to empathy was linked with less activation in emotion regulation-related regions, highlighting an important avenue through which to support empathy in adolescence.

1-Q-125 - Understanding the Development of Self-Processing and Depression in Adolescence: Is Brain Function Where It Starts?

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Details

Background:

Adolescence is characterized by neural and cognitive changes in self-development and vulnerability to depression--particularly among girls. Self-evaluation is altered in girls with depression. Yet, the *directional* associations between self-evaluation and depressive symptoms across adolescence has not been robustly delineated. Does increased negative self-evaluation predict elevated depressive symptoms or is it the other way around?

In addition to a current lack of clarity regarding these longitudinal trajectories, clinical scientists have struggled with early detection of depression prior to disorder onset. Brain function, such as vmPFC activity which has been robustly associated with *both* self-evaluative processing *and* depression, may increase our chances of early detection and offers a potential avenue for prediction of *prospective* depression.

Aim:

We will assess longitudinal associations between neural and behavioral indices of self-evaluation and depressive symptoms, allowing us to parse directional associations. Through a mediation model, we will test our hypothesis that brain function during self-evaluative processing predicts future behavioral indices of self-evaluation which then predict depressive symptoms.

Method:

A unique opportunity to advance this essential research is provided by the Transitions in Adolescent Girls (TAG) study, which has now at least four waves of neural indices of self-evaluation and depressive

symptoms (N=174, initial ages 10.0-13.0, 18 months between waves). Depressive symptoms will be assessed via the Center for Epidemiological Studies Depression Scale for Children (CES-DC) and disorders via clinician-administered interviews following the Kiddie Schedule for Affectives Disorders and Schizophrenia (KSADS). Participants complete a self-evaluation fMRI task where they decide whether traits from three domains (prosocial, antisocial, and social status) describe them. The behavioral metric of self-evaluation will be the proportion of self-evaluations that are negative (negative adjective endorsed and positive adjectives rejected). Univariate analyses of vmPFC activity during the self-evaluative condition (contrasted against a high-level control during which participants describe whether the same traits are malleable for people in general) will serve as the neural marker.

Preliminary Findings:

In order to control for trait-like variability, I conducted a four-wave Random Intercept Cross-Lagged Panel Model (RI-CLPM) in the TAG study which revealed transactional associations between the behavioral index of self-evaluation and depressive symptoms across adolescence (age range: 9 - 16 years old). In addition, linear regression models have shown that vmPFC activity at wave 1 predicts *future* depressive symptoms at wave 2 *above and beyond* depressive symptoms at wave 1. Moreover, brain function and depressive symptoms were not cross-sectionally associated. Combined with existing research, these preliminary findings suggest the possibility, reflected in our hypothesis, that aberrant brain function may predict future behavioral indices of self-evaluation which, in turn, predict depressive diagnoses during adolescence.

Proposed Analyses:

To test this theory, we will conduct a multilevel mediation model whereby self-evaluative behavior mediates the relationship between brain function during self-evaluation and subsequent depressive diagnoses. We will use a minimum of four waves of data, which have already been collected, for this multilevel mediation model. To minimize researcher degrees of freedom and follow rigorous open and reproducible science practices, we have not yet run these analyses but will present them at the 2023 Flux conference.

1-Q-126 - Associations Between Emotion Neural Response and Behavioral Outcomes in Toddlers Born Preterm

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Details

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Introduction. Literature on emotional processing has primarily focused on still facial emotional expressions in children. Less is known about how dynamic information would modulate neural response in young children, especially at higher risks. To further our understanding, this study examined event-related potentials (ERPs) to dynamic facial expressions in toddlers born preterm. **Methods.** The sample consisted of 35 toddlers born preterm (18 male children, *M* = 1.89 years, *SD* = 0.45 years, range = 1.30 2.81 years, 20 severely premature and 15 moderately premature). These children and their families were recruited for a parenting intervention program. As part of the longitudinal study, children were instructed to engage in a dynamic face task when their neural activity was measured using an electroencephalogram (EEG) during pre-and post-intervention visits. Only data from pre-intervention visits (N=35) was included in the analysis. The dynamic face task consisted of 1000-ms videos with happy, angry, and neutral facial expressions. The first 500 ms of the video shows the transition from neutral to peak expression, while the peak expression is sustained on the screen for another 500 ms. Child neural activity was recorded with a 64â€electrode Brainvision ActiCHamp EEG system with a sampling rate of 1000 Hz. One data was excluded due to not meeting the data quality criteria (e.g., at least 10 trials per condition and impedance â‰¤ 20 KÎ©). The rest 34 EEG data were processed using HAPPE software for preprocessing and ERPs analyses (Lopez et al., 2022). Fz and Cz were averaged for frontocentral electrodes. Negative component (Nc) was extracted using a time window of 330-530 ms. Repeated ANOVA models were used to examine the effects of prematurity level and task condition respectively on Nc peak and mean amplitude (Î¼V), and peak latency (ms), controlling for age. Child behavioral outcomes were assessed using behavioral tasks and parent report. During problem-solving tasks, the caregiver was instructed that they could offer support to their child. The child's noncompliance, defined as the degree to which the child is willing to listen to and heed their caregiver's advice, was scored on a scale of 1 to 6, ranging from collaborative and compliant to resistant and contradictory. We hypothesized that there would be an association between child neural response and behavioral outcomes. **Results**. Analysis performed on the Nc latency revealed a marginally significant effect of task condition (F (2, 66)= 2.60, p = 0.08, $\hat{I}\cdot^2_p$= 0.015). Post-hoc analyses showed that the happy condition had a longer Nc latency than the neutral condition (t (34)= 1.95, p =0.057). Child age was also noted to have a significant effect on Nc latency (F (1, 32)= 5.04, p = 0.03, $\hat{I}\cdot^2_p$= 0.110). Nc latency in the angry (t =2.19, p =0.04) and neutral (t =2.05, p =0.05) conditions was also positively associated with child behavioral outcomes indicated by non-compliance. **Conclusions.** Our results indicate that child neural responses vary given the expressions of different emotions. More importantly, their neural response is associated with their socioemotional and behavioral outcomes. **Discussions.** Our findings support the validity of using EEG to measure socioemotional neural processing in toddlers born preterm. This study also has clinical implications that link child neural responses to their socioemotional and behavioral outcomes. For future directions, we plan to expand the examination of associations with child functioning using parent report and behavioral observation of child emotion regulation.

References

Lopez, K. L., Monachino, A. D., Morales, S., Leach, S. C., Bowers, M. E., & Gabard-Durnam, L. J. (2022). HAPPILEE: HAPPE In Low Electrode Electroencephalography, a standardized pre-processing software for lower density recordings. *NeuroImage*, *260*, 119390.

1-Q-127 - Exploring age related differences in predicting and accommodating risk preferences of peers

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Details

Adolescence is a developmental period associated with heightened rates of risk taking, and adolescents' risky decisions often impact not only themselves but also those around them. The potential motives behind these decisions, such as reputational concerns and prosocial tendencies, are likely rooted in considerations that take these impacted peers into account, as well as their relationship, given the importance of social evaluation by peers during this time in life. In these considerations, a natural step is to weigh their chosen outcome against what one assumes the peer would have preferred. However, few studies have explicitly tested the assumptions that adolescents and adults make about risk preferences of their peers and whether the accuracy of these assumptions changes with respect to age. Furthermore, it is unknown that when explicitly given peers' risk preferences that conflict with one's own preferences, how people manage the expectations from peers and accommodate them at different ages. To answer these two questions, in a cohort of typically developing adolescent and young adult friend dyads (*N* = 128, 11.98-22.82 years), we collected peers' preferences in an economic risky decision making task with safe (certain) and risky (more variable outcomes) options that vary in their expected values. Participants first completed the task absent of any information about peer preference and were then given this information in a later condition when asked to choose between the safe and risky options again. Analysis utilized a Generalized Additive Models framework which is exploratory in nature and allowed us to detect age-related changes with precision, rather than using discrete age bins. We found that people in general estimated their friend to be more risk seeking than the friend actually was but there were no age-related differences. As age increases to 20 22 years old, people were more likely to accommodate if it entailed giving up the safe option and receiving friends' undesired risky option. Since risky options were on average more advantageous than safe options in our choice set for the purpose of encouraging participants to take risks, we looked at a subset of trials where frien's desired option was in conflict with participant's but the cost of accommodating was zero. Among these trials which were evenly distributed in age, we found a significant age-related difference from 20 to around 22 years old, where people were also more likely to give up their originally preferred safe option and take the risky option to accommodate their friends. This behavior is likely driven by prosocial motives since there is no monetary incentive. Together, these results showed that although in general people's assumptions about their peer's risk preference is slightly inaccurate, older participants tended to shield their friends from undesired risky options when there was no monetary incentive at stake.

1-Q-128 - Do Neural Representations of Parents and Peers Shape Adolescent Social Decision-Making?

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Details

While all individuals make decisions that affect others on a daily basis, the social importance of such decisions is perhaps most salient during adolescence. Characterized by a time of re-organization in sociocultural and neurobiological domains, adolescents must navigate novel contexts that require them to negotiate the formation or deepening of peer relationships against the demands of simultaneously honoring parental relationships and familial obligations. Much of the existing developmental neuroscience literature focused on understanding adolescent social decision-making has done so by trying to understand what brain regions are recruited during social decision-making. Here we pursue an alternative approach by examining how neural representations of parents and peers, in relation to the self, may sway social decision behavior. In this ongoing study, we are collecting fMRI data on 60 late adolescents (current N = 40) while they make social preference judgments about themselves, a parent, and a peer (close friend), as well as complete a social decision-making task involving conflicting rewards for both aforementioned others. Specifically, in the first task, participants are shown a series of social preferences (e.g., â€˜would live in a big city', â€˜enjoys spending time in art museums') and are asked to rate how well those preferences describe a given agent (self, parent, friend) on each trial. Next, teens complete a social decision-making task where they allocate monetary and social resources between their parent and friend. Imaging data from the social judgment task will be used to extract neural representations of the three agents and compute similarities between participants' neural representations of their friends and parents to those of themselves. These similarity scores will be entered into a hierarchical Bayesian model to predict social decision preferences between the participants' parents and friends. Finally, an exploratory analysis uses text data from participants' descriptions of their parents and friends to determine whether thematic content about obligation and social support moderate links between neural representations and social decision preferences, with the aim of elucidating the psychological processes through which neural representations shape behavior. Preliminary analyses suggest behavioral indicators of mental representations influence social decision behavior; preliminary analyses of text data hint that linguistic data also encode information about social decision preferences. Planned ROI- and searchlight-based imaging analyses will compare neural representations of different familiar others, assess how neural representational overlap shapes social decisions, and probe the representational content that drives social decisions preferences about parents and peers in adolescence.

1-Q-129 - Neonatal Neural Organization and The Development of Internalizing Problems as a Function of Maternal Factors in Children Born Very Premature

Berenice Anaya [1], **Caleb Gardner** [1], **Jeanette Kenley** [1], **Rachel Lean** [2], **Christopher Smyser** [1], **Cynthia Rogers** [1]

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Details

The United States has one of the highest rates of preterm birth among high-resource countries (Blencowe et al., 2012). Infants born very preterm (VPT; <30 weeks gestation) show the highest rates of internalizing problems during early childhood and are 2-4 times more likely than Term Control (TC) children to report psychiatric problems as adolescents and adults (Rogers et al., 2012). Mapping trajectories of internalizing symptoms during childhood will help improve classification of low- and high-risk children and chart sensitive windows in the development of internalizing problems when clinical interventions may be most effective for high-risk children. Moreover, recent findings indicate that 25% of VPT children show typical emotional outcomes through age 5 years (Lean et al., 2020), suggesting that trajectories of internalizing symptoms in VPT children may be heterogeneous and that early resilience mechanisms (e.g., neural development, caregiver support) may buffer risk for psychiatric disorders. Current evidence indicates that the link between VPT and internalizing risk may be explained by alterations in resting-state functional connectivity MRI (Rogers et al., 2017), and that stressors related to premature birth (e.g., caregiver psychopathology) may disrupt caregiver-child bonding (Pennestri et al., 2015), which is foundational to children's emotional development. Prior studies have only focused on age-specific developmental outcomes, rather than investigating how functional brain organization and caregiver factors may predict change over time in VPT internalizing trajectories. In the present study, we aim to model the development of internalizing symptoms between ages 2 and 10 and examine how functional brain organization and maternal factors may contribute to risk trajectories in VPT and TC groups.

Participants were members of a large prospective cohort of 124 VPT (born at <30 weeks gestation) and 103 TC children matched for age and sex and followed from birth to age 9-10. Child internalizing symptoms were measured via parent report on the Infant-Toddler Social and Emotional Assessment (ITSEA) at age 2 and the Child Behavioral Checklist (CBCL) at ages 5 and 10. Maternal distress was assessed multidimensionally via composite scores using maternal self-reports on the Beck Depression Inventory (BDI), State Trait Anxiety Inventory (STAI), Social Support Questionnaire (SSQ), and Drug History Questionnaire (DHQ) at age 2. Resting state functional MRI (rsfMRI) data were collected at term (or equivalent in VPT infants).

Preliminary analyses using a conditional multilevel model suggest large heterogeneity in trajectories of internalizing symptoms within the VPT group and indicated that internalizing symptoms were more likely to increase over time in VPT children compared to TC children, $g_{40} = 3.19$, $p = \hat{A}.06$. Across the sample, higher maternal distress significantly interacted with age to predict internalizing symptoms, $g_{50} = 1.17$, $p = \hat{A}.05$. Regions of significance analysis indicated that child internalizing symptoms decreased over time when mothers reported lower distress but remained stable when mothers reported higher distress (> 2.06).

Given heterogeneity in internalizing trajectories, we plan to use Repeated Measures Latent Class Analysis (RM-LCA) to examine person-centered underlying classes of internalizing trajectories. Further, processing of neonatal rsfMRI data to extract whole-brain metrics of network organization (clustering coefficient, path length, and modularity) is currently underway. These network metrics will be added to the RM-LCA model, in addition to maternal distress, to examine potential links with trajectory class membership. We expect that reduced integration and segregation (as reflected by network metrics) will predict at-risk internalizing trajectories in VPT children, and that higher maternal distress may exacerbate these links.

1-Q-130 - Does prefrontal cortical thinning during adolescence mediate the relationship between childhood adversity and emotion regulation?

Courtney Cooper [1], **Florence Breslin** [1], **Zsofia Cohen** [1], **Gabriella I. Atencio** [1], **Jennifer Watrous** [1], **Amanda Morris** [1], **Kara Kerr** [1]

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Details

Objective: Difficulties in emotion regulation are associated with various mental health problems, such as depression and anxiety (Weiss et al., 2020). Thus, understanding the underlying mechanisms related to emotion regulation is key to prevention and treatment. Researchers have identified several structures in the brain that are critical in processing emotions including the prefrontal cortex (PFC). Cortical thinning in the prefrontal regions has been found to be significantly correlated with better emotion regulation in adolescent girls. Furthermore, animal and human studies have found that early adverse events impact both the volume of the PFC and its activity in response to specific stimuli (Bick & Nelson, 2016). Childhood adversity has also been linked to deficits in emotion regulation (Espeleta et al., 2018). Despite these findings, there is little research studying the potential role of the PFC development in the relationship between childhood adversity and emotion regulation over time. The current study seeks to determine whether cortical thinning in the PFC mediates the relationship between childhood adversity and emotion regulation.

Hypotheses: Based on previous literature, we have the following hypotheses: 1) childhood adversity will predict poorer emotion regulation, 2) childhood adversity will predict less prefrontal cortical thinning during early adolescence, 3) less prefrontal cortical thinning will predict poorer emotion regulation, and 4) prefrontal cortical thinning will mediate the relationship between childhood adversity and emotion regulation during early adolescence.

Analysis Plan: Using the latest data release from the Adolescent Brain Cognitive Development^{SM} Study (ABCD), we plan to conduct several analyses in a stepwise manner. First, we will calculate the percent change in cortical thickness in each region of the PFC using the Destrieux Atlas from Baseline (youth ages 9-10) to Year 2 (youth ages 11-12). Only participants who have completed both the Baseline and Year 2 scans and have passed quality control at both time points will be included. Next, we will run a series of linear mixed-effects models to determine if the number of adverse experiences in childhood impacts cortical thinning in each region of the prefrontal cortex. For all regions of the PFC that are significantly predicted by childhood adversity, another set of analyses will be used to determine which of these regions predict emotion regulation using the cognitive reappraisal items from the Emotion Regulation Questionnaire at Year 3 (youth ages 12-13). Finally, a set of mediation analyses will be conducted based on any regions of the PFC that remain. The mediation analyses will determine whether the relationship between childhood adversity and emotion regulation is mediated by cortical thinning from ages 9-10 to 11-12 in specific regions in the PFC. An adverse childhood experiences score will be calculated at Baseline (youth ages 9-10) based on Karcher et al. (2020), including parent self-reported measures of trauma from Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) and parent-reported financial adversities (not having sufficient funds for rent/mortgage, utilities, food or medical care).

Significance: While the literature has investigated the role of emotion regulation as a mediator between childhood adversity and various outcome variables, the neurological basis for the relationship between

adversity and emotion regulation is unknown. This study presents an opportunity to understand the consequences of childhood adversity on emotional processing in the brain during adolescence, a critical period for socioemotional development and mental health.

1-Q-131 - Preregistration: Amygdala Reactivity as a Mechanism Linking Structural Stigma with Emotion Dysregulation in Youth

Rachel Martino [1], **Katie McLaughlin** [1], **Mark Hatzenbuehler** [1]

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Details

Background: Stressors such as rejection and victimization are often experienced by youth with stigmatized identities, and are associated with adverse academic, health and psychosocial outcomes. Stigma-related stressors may also result in difficulties with emotion processing. There is robust evidence linking general life stressors to heightened emotion reactivity and emotion dysregulation. Children who have experienced trauma show heightened emotional reactivity as reflected in increased activation of the amygdala, a brain region associated with threat and emotional salience (McLaughlin et al., 2020). However, no study has examined amygdala activation in response to stigma-related stressors in youth. Moreover, most studies of stigma in youth have focused on either the individual (e.g., self-stigma) or situational (e.g., interpersonal discrimination) level. Recent work highlights the need to better understand how contextual factors such as structural stigmaâ€"which refers to societal-level conditions, norms and policies that constrain the opportunities, resources, and well-being of stigmatized populations (Hatzenbuehler & Link, 2014)â€"influence emotional and neural development. This project uses a multimodal approach to address these gaps.

Aims: The study aims to investigate: 1) the association of perceived discrimination and structural stigma with emotion regulation; 2) the association of perceived discrimination and structural stigma with amygdala reactivity to threat cues; and 3) whether amygdala reactivity mediates the association between stigma and emotion regulation difficulties. We will examine these associations in four stigmatized groups: girls, sexual minority youth; Black youth; and Latinx youth. We propose that children exposed to more stigma (both perceived and structural) will show greater emotion dysregulation and increased amygdala reactivity. We also propose that amygdala reactivity will mediate the relationship between stigma exposure and difficulties with emotion regulation.

Method: For this preregistered project, the study will use data from the ABCD Data Release (Data Release 5.0) that will be available for analysis in late spring. The sample consists of over 11,000 children aged 10-14 years. Emotion dysregulation will be measured using the Difficulty in Emotion Regulation Scale (parent-report) and Emotion Regulation Questionnaire (child-report) administered at Year 3 follow-up. Amygdala reactivity to threat will be measured by using the contrast of amygdala activation to fearful faces relative to neutral faces during an emotional n-back working memory task (measured at Year 2 follow-up). The study will integrate data from the ABCD study with a validated index of state-level structural stigma. The structural stigma index includes aggregate measures (e.g., social attitudes, laws, and policies) used in prior research (e.g., Hatzenbuehler et al., 2022) compiled from validated sources and modeled as indicators in a factor analysis.

Analysis: For aims 1 & 2, we will examine the association of stigma (perceived discrimination, structural stigma) with emotion dysregulation and amygdala reactivity by fitting generalized mixed effect models including random effects for study site and family. For aim 3, we will conduct a mediation analysis to test whether the covariance between stigma and emotion dysregulation can be explained by amygdala reactivity. All analyses will control for age, parental education, sex, race, and ethnicity (if not focused on these factors). Additionally, we will take a negative control approach and examine associations in non-stigmatized groups, where we expect no associations.

Implications: This project will elucidate how individual- and structural-level stigma impact emotion processing during development. By identifying the affective and neural impacts of stigma on youth, this project could inform interventions and policies targeting systemic inequities that contribute to stigma-related stress.

1-Q-132 - Impact of early adversity on adolescent neural processes and reactive aggression in the Social Network of Aggression Task

Sarah Lempres [1], **Megan Davis** [2], **Amy Carolus** [2], **Sophia Martin** [2], **Margaret Redic** [2], **Kimberly Carpenter** [1], **William Copeland** [3], **Helen Egger** [4], **Michelle Achterberg** [5], **Margaret Sheridan** [2]

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Details

Motivation: Adolescence is a critical developmental period characterized by significant physical and psychological changes, including increased impulsivity and emotional volatility (Rapee et al., 2019). It also marks a definitive social change, where social acceptance and rejection become increasingly important (Crone & Dahl, 2012). Existing literature suggests that the processing of negative peer feedback is associated with changes in activation in several brain regions, including increased amygdala activation (Achterberg et al., 2017). Furthermore, research indicates that increased activation in control regions such as dorsolateral prefrontal cortex (DLPFC) is associated with reduced aggressive behavior following negative feedback (Achterberg et al., 2020). Early environmental experiences of adversity are linked to adolescent neural and behavioral outcomes. However, little is known about how different dimensions of adversity, such as threat and deprivation, may be associated with neural activation and reactive aggression in response to social rejection. Outside of social feedback literature, dimensional approaches to understanding adversity (McLaughlin & Sheridan, 2016) have linked threat exposure to increased amygdala activation (McLaughlin et al., 2014; Sheridan & McLaughlin, 2014) and deprivation exposure to decreased DLPFC activation (McLaughlin et al., 2014). Despite these findings, few studies have explored the impact of adversity in social contexts, and those that have tend to overlook how different domains of adversity may affect social processing. In this study, we aim to investigate how threat and deprivation exposure in early childhood predict neural activation and behavioral reactivity (i.e., reactive aggression) in response to negative (vs. neutral) social feedback.

Methods: Our study consists of two timepoints, collected during preschool-age (n=917, ages=2-6) and adolescence (current N = 47; ages=14-21). Collection during adolescence is still ongoing. During preschool, parents reported chil's adversity exposure on a series of self-report measures and a semi-structured clinical interview to provide a composite score for their child's experiences of early threat

and deprivation. In our current sub-sample (n=47), 55% of our sample experienced early adversity, with 13% experiencing early neglect and 47% experiencing early threat. During adolescence, participants completed the Social Network of Aggression Task (SNAT) fMRI paradigm (Achterberg et al., 2018). Prior to the MRI, participants created a profile that they believed was rated by other peers in the study. In the scanner, participants were presented with a mixture of negative, positive, and neutral ratings, and were instructed to "blast" the peer with hypothetical noise in response to their feedback by holding down a button. Intensity ranged from 1-10, which was depicted by sequential soundbars appearing. On average, endorsed aggression was highest after negative feedback (5.09), as compared to neutral (3.26) or positive (2.63) feedback.

Hypotheses: We hypothesize that following negative (vs. neutral) feedback, participants who have experienced early deprivation will exhibit different patterns of activation compared to those who have experienced early threat. Specifically, we anticipate that threat will predict increased activity in the amygdala while deprivation will predict decreased activity in the dorsolateral prefrontal cortex (DLPFC). In line with previous work (Achterberg et al., 2020), we expect that higher DLPFC activation will predict lower levels of aggression in response to negative feedback. Expanding on previous research, we hypothesize that both deprivation and threat will be linked to adolescents' endorsed aggression in response to rejection, but that each of these pathways may be mediated by different brain regions.

1-Q-133 - The role of pubertal development on the relationship between early life adversity and resting-state functional connectivity of the nucleus accumbens

Gabriella Atencio [1], **Florence Breslin** [1], **Kara Kerr** [1], **Zsofia Cohen** [1], **Courtney Cooper** [1]

[1] Oklahoma State University

Details

The role of pubertal development on the relationship between early life adversity and resting-state functional connectivity of the nucleus accumbens

Gabriella I. Atencio, Florence J. Breslin, Zsofia P. Cohen, Courtney J. Cooper, and Kara L. Kerr

Objectives: Puberty is a critical time for the development of emotion processing and reward sensitivity. Pubertal development has been associated with emotionally reactive behaviors and changes in functional activity within the nucleus accumbens (nACC). Research suggests that stages of puberty (i.e., Tanner staging) affect resting-state functional connectivity between the nACC and areas in the medial frontal cortex and anterior cingulate. Additionally, previous research indicates that early life adversity (ELA; e.g., experiencing abuse or neglect, history of parental mental health problems, incarceration, substance use, etc.) influences the timing and onset of pubertal staging, such that earlier timing is associated with specific types of ELA. ELA has also been linked to increased functional connectivity between the ventral striatum and regions of the prefrontal cortex in both human and animal models. Some evidence suggesting these network alterations may mediate effects of ELA on internalizing symptoms. Thus, past research indicates that 1) ELA is associated with pubertal timing and nACC functional connectivity, and 2) pubertal timing is associated with nACC functional connectivity. It has yet

to be examined, however, whether pubertal development may be a mediator of the relationship between ELA and resting-state nACC connectivity with prefrontal regions. The present study aims to address this gap in the literature.

Hypotheses: We hypothesize that ELA will predict resting-state functional connectivity from the nACC and the frontoparietal and default mode networks. Additionally, we hypothesize that the relationship between ELA and nACC functional connectivity is mediated by pubertal development.

Analysis Plan: Utilizing the Adolescent Brain Cognitive Development^{SM} Study (ABCD) dataset (Data Release 4.0; 5.0 pending availability), we will examine ELA at Baseline (youth ages 9-10 years) according to the adverse childhood experiences model presented in Karcher et al. (2020), where early life adversity is reported through parent-reported items on the Kiddie Schedule for Affective Disorders and Schizophrenia for traumatic experiences and parent-reported financial adversity (*i.e.*, not having enough funds for housing, food, or medical care). We will calculate pubertal staging at Year 2 (youth ages 11-12) via the self-reported Pubertal Development Scale. Linear mixed-effects modeling and will be used to predict nACC connectivity to the frontoparietal and default mode networks at Year 2 from ELA at Baseline. Covariates will include age, sex assigned at birth, race/ethnicity, and household income, with random effects for family and scanner ID. The PROCESS macro for R will be used to assess the indirect effects of pubertal staging on the relationship between ELA and nACC connectivity.

Significance: Given the role of the nACC in reward-seeking and emotional reactivity across adolescence, it is critical to investigate the relationships among ELA, pubertal development, and nACC connectivity. A better understanding of these associations may help inform interventions and policies to build resilience in children and adolescents exposed to ELA.

Poster Session 2

Friday, September 8, 2023

A- Attention

2-A-1 - ADHD symptoms predict eyes-closed versus -open differences in spontaneous alpha activity in frontal cortices in older adolescent girls

Nathan Petro [1], **Giorgia Picci** [1], **Ilenia Salsano** [2], **Maggie Rempe** [2], **Christine Embury** [1], **Christine Embury** [1], **Lauren Ott** [2], **Samantha Penhale** [2], **Yu-Ping Wang** [3], **Julia Stephen** [4], **Vince Calhoun** [5], **Brittany Taylor** [1], **Tony Wilson**

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Details

Attention-deficit hyperactivity disorder (ADHD) is characterized by difficulties in sustaining concentration and/or hyperactivity and impulsivity. The debilitating symptoms of ADHD affect 5-7% of children and adolescents globally and confer increased risk for additional disorders. Previous work has demonstrated altered structure and resting activation patterns in frontoparietal and visual cortex, among other regions, in individuals with ADHD. Limited work has examined the role of alpha rhythms in ADHD, which have long been implicated in attention and cognitive processes. Interestingly, EEG studies have shown that alpha power differences between the eyes-open and eyes-closed resting conditions predict ADHD symptoms, suggesting that the presence or absence of external visual stimuli, even during periods of rest, may be indicative of individual differences in attention systems. However, this has not been studied using MEG techniques, which have the spatial precision to localize alpha rhythms to cortical sources. In the current study, we examined spontaneous cortical activity using MEG from 105 typically developing youth (9-15 years-old; 54 female) during separate eyes-closed and eyes-open resting conditions. In addition, the Conners 3-Parent Short Form assessment was administered to measure symptoms of ADHD among the adolescents. The MEG signals were processed using advanced source reconstruction methods and the oscillatory power was estimated in the canonical delta, theta, alpha, beta, and gamma frequency bands. Power spectral density cortical maps for eyes-open were subtracted from eyes-closed rest, and then submitted to separate regression models to test if eyes-closed versus -open power spectral density was related to symptoms of ADHD, and if this relationship differed by age and sex. Our results indicated that higher symptoms of hyperactivity/impulsivity were related to greater eyes-closed relative to -open alpha power in the bilateral occipital cortices and premotor cortex. Second, this relationship was observed only for older (but not younger) girls and not boys in bilateral inferior frontal gyri. These findings implicate sensory and attention networks in the symptoms of ADHD, consistent with prior work. In addition, the current results suggest that these networks may be sensitive to the differences in resting conditions, based on the presence (eyes-open) or absence (eyes-closed) of external visual sensory information.

2-A-2 - Patterns of motor-locked neural oscillations reveal developmental shifts when subject to top-down attention inhibition

Oghenetejiri Smith [1], **Haley Pulliam** [1], **Danielle Rice** [1], **Anna Coutant** [1], **Hannah Okelberry** [1], **Elizabeth Heinrichs-Graham** [1], **Tony Wilson** [1], **Brittany Taylor** [1]

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Details

Background: There is a clear link between the accuracy of attentional reorienting and completion of movement which is central to daily functioning. The ability to inhibit extraneous sensory input directly impacts subsequent motor planning and execution. In practice, individuals reliably respond slower to a target when given a prior invalid cue (i.e., incorrect location) than when given a valid cue (i.e., correct location). Neural oscillatory patterns in the beta band (i.e., 16-24 Hz) are known to serve discrete motor actions, and recent work in adults have shown concurrent activity in the alpha band (i.e., 9-12 Hz) when tasked with conditional inhibition. When motor processes and top-down control are considered separately, their trajectories in childhood are well understood. However, the extent to which the underlying oscillatory processes interact remains nebulous in developing samples. As such, this study sought to examine developmentally-sensitive oscillatory patterns in regions which serve attention-modulated motor performance of youths. Methods: A total of 95 participants (ages 6-14 years) completed a classic Posner attentional reorienting task during MEG, along with a T1 MRI scan. Motor-locked, time-frequency spectrograms indicated significant theta (4-6 Hz, -150-150ms), alpha (9-12 Hz, -300-0ms, 0-300ms), beta (16-24Hz, -300-0ms, 0-300ms), and gamma (72-86Hz, -50-100ms) activity prior to and during the motor response. Source reconstruction of each significant time-frequency window was performed separately for each task condition (invalid vs. valid) using a beamformer, and maps of the differences between task conditions (invalid valid) were computed. These whole-brain difference maps (i.e., the neural validity effect) were then correlated with age. Results: Children exhibited significant frequency-specific, age-related changes in neural validity effects across a distributed network spanning predominantly frontal, parietal, and temporal regions (all *p*s < .005). During the motor planning phase (i.e., -300-0ms) peaks in the right DLPFC and right superior parietal cortex were observed in alpha, whereas in beta, peaks were seen in regions of the anterior and middle cingulate. During motor execution (i.e., 0-300ms) there were alpha peaks in the left DLPFC and right superior parietal cortex, alongside peaks in beta in the left parahippocampal gyrus. Finally, peaks in theta (i.e., -150-150ms) were observed in the left superior temporal cortex. We further probed the functional relevance of activity in these regions as they related to developmental improvements in behavioral validity effects (i.e., conditional differences in reaction time) using mediation analyses. The neural validity effect during motor planning in the alpha band within the right DLPFC mediated the relationship between age and the behavioral validity effect ($\hat{I}^2$ = -.107, 95% CI[-.264, -.016]). Specifically, older participants had a stronger neural validity effect ($\hat{I}^2$ = .394, p=.001), which was associated with a decreased behavioral validity effect (i.e., better behavioral performance; $\hat{I}^2$ = -.272, p = .024). The same pattern was observed for the neural validity effect in the theta band within the left superior temporal gyrus ($\hat{I}^2$ = -.111, 95% CI[-.268, -.003]). Conclusion: We have shown that the influence of top-down attentional processes impacts motor performance in a developmentally-sensitive manner. Additionally, these cognitive-motor relationships are supported by spectrally-specific oscillations across a dispersed network of frontal, parietal, and temporal regions. Importantly, conditional differences in activity within key regions were directly related to developmental improvements in behavioral performance, underscoring the functional relevance of these age-related changes in neural oscillatory activity.

B – Brain connectivity

2-B-3 - Growth in early infancy drives optimal brain functional connectivity which predicts cognitive flexibility in later childhood

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Details

Introduction

Early undernutrition is known to have detrimental effects on cognitive skills (Kesari, 2010), with long-lasting effects until adulthood (Victora, 2008). Despite numerous attempts of interventions, global rates of undernutrition remain high (Moore, 2020), with infants in low- and middle-income countries (LMICs) at greatest risk (Nabwera, 2017). One-third of infants in LMICs are also at risk of not meeting standard developmental milestones pre-school age (McCoy, 2016; Prado, 2014), which can lead to lifelong consequences (Hoddinott, 2008). This highlights the importance of studying early neurodevelopment in regions with high rates of undernutrition to optimize early interventions.

Functional brain network organization, measured by resting-state functional connectivity (FC), has been linked to key neurodevelopmental processes required for healthy development (Dubois, 2014). It has been hypothesised that early exposure to adversity, such as undernutrition, affects early neurodevelopment, as reflected in disrupted FC, leading to poorer life outcomes (Xie, 2019). However, empirical investigations of these associations are still limited.

The overall goal of this study was to investigate the developmental trajectory of FC between 5 and 24 months in a longitudinal cohort of infants from rural Gambia, a context with high rates of undernutrition. Moreover, we explored whether differences in growth early in life are related to FC at 24 months and if early FC impacts cognitive outcome at pre-school age.

Methods

To assess FC, we used functional near-infrared spectroscopy (fNIRS) at 5, 8, 12, 18, 24 months (N=204), from the frontal, inferior-frontal and temporal regions bilaterally.

To investigate the impact of undernutrition on FC, we used delta WLZ (z-score at the later age z-score at the previous age) as independent variables in regression analyses on FC at 24 months. Using delta WLZ allowed to assess the impact of positive or negative deviation from the expected growth trajectories.

Furthermore, to investigate how these early developmental trajectories relate to later childhood outcomes, we assessed their cognitive flexibility at 3â€“5 years.

Results

We found that early physical growth in infancy drove optimal developmental trajectories of FC, which in turn predicted cognitive flexibility in later childhood. Specifically, more positive growth trajectory during the first 5 months of life predicted more mature patterns of interhemispheric frontal FC and bilateral short-range FC. Interestingly, delta WLZ after the 5th month of life were not associated with FC variability. Furthermore, long-range inter- and intra-hemispheric FC predicted stronger cognitive flexibility at preschool age.

In contrast to previously studied developmental populations in low-adversity contexts, in this Gambian population, we found that bilateral short-range FC increased with age and long-range interhemispheric FC decreased with age.

Conclusions

This work provides the first evidence of atypical longitudinal FC development between 0â€“2 years relating to infant growth. The delta WLZ-FC associations were statistically significant only when delta WLZ was calculated with neonatal measures. Changes in growth later in development did not show statistically significant impacts on FC. This suggests that undernutrition during the first months of life is more impactful on brain development than undernutrition later in infancy. While the impact of undernutrition on brain development has been already documented in LMICs (Xie, 2019), for the first time we provided empirical evidence that infant growth faltering specifically before the 5th months of age might impact FC development up to 24 months. This might also suggest that early undernutrition has a lasting impact on subsequent cognitive skills, even in children who show subsequent catch-up growth.

Our results highlight the measurable impact that poor growth in early infancy have on brain development, and the subsequent impact on pre-school cognitive development, underscoring the need for early life interventions in global settings of adversity.

2-B-4 - Precision Functional Mapping to identify stimulant treatment response in medication naive children with ADHD

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Details

Background: ADHD is a multifaceted neurodevelopmental disorder, with characteristics stemming from complex structural and functional disparities in the brain. Despite extensive research, identifying etiological biomarkers and predicting clinical outcomes remains challenging due to the heterogeneous nature of the disorder, which could be attributed to the unique brain functions of individuals. This heterogeneity also makes the disorder particularly hard to treat; some first-line treatments, like stimulant medications (e.g. methylphenidate, MPH), do not provide benefits to everyone. Response to such treatments must be monitored behaviorally, leading to an extensive process of trial and error, to

eventually land on an appropriate treatment. While there is heterogeneity in ADHD presentation, the ability to monitor brain effects prior to symptom changes for a given medication may help identify proper treatments for an individual faster. To test this idea, we took an individualistic approach and utilized precision functional mapping (PFM), with the aim of identifying neurological biomarkers that may predict treatment response in ADHD.

Methods: 37 medication-naÃ¯ve children with ADHD and 32 TD children (M age = 9.99, 33 female) were assessed. All participants completed two sessions of resting-state fMRI and go-no-go (GNG) task-based fMRI. Children with ADHD completed one scan session on methylphenidate (MPH) and one after being given a placebo; TD participants completed the exact same protocol, but they were not given MPH or placebo. Using PFM procedures outlined by Hermosillo et al. (2022), personalized networks were generated for each participant. Personalized networks were used to identify changes in functional connectivity in response to MPH that are individual-specific. The relationship between functional connectivity and behavior was assessed using a repeated measures correlation (rmcorr).

Results: The individuality of network organization identified using PFM provided the means to detect a network-specific response to MPH intervention for each individual child. Specifically, the ADHD participants with the largest improvements in performance on the GNG tasks following MPH intervention also displayed the largest changes in functional connectivity. On the group level, consistent changes in mean whole-brain functional connectivity were observed for ADHD participants compared to controls (who did not receive the intervention between sessions). These changes, importantly, were correlated with performance on the GNG task ($r = -0.678$, $p < 0.001$). To identify the brain networks driving the changes in functional connectivity and GNG scores, we repeated rmcorr analyses for each individual network pair. We found significant relationships between improved GNG performance after MPH intervention and functional connectivity within the Visual network (Vis) and between the Vis network and Somatomotor Dorsal (Smd) network ($r = -0.44$, $p = <0.001$; $r = 0.45$, $p < 0.001$). This pattern of results persisted when using the ADHD participants only (Vis-Vis: $r = -0.60$; Vis-Smd: $r = 0.55$), but did not persist using TD participants only. These findings suggest that the significant results observed at the whole-cohort level are driven by ADHD participants; therefore, the relationship between whole-brain changes in functional connectivity and improved GNG performance could be attributed to MPH intervention.

Conclusions: PFM is a viable methodology for identifying functional brain changes as a result of intervention (e.g., stimulant use). Additionally, PFM allowed for the identification of participant-specific connectivity changes that corresponded with behavioral changes; this result demonstrates the utility of PFM in assessing the impact of pharmaceutical interventions on brain connectivity. PFM could be used in future research to identify specific brain biomarkers of treatment response in individuals, eliminating the need for trial and error assessment.

2-B-5 - Functional network organization is atypical in patients with congenital heart disease

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Details

Children born with congenital heart disease (CHD) are at a higher risk of developing neurological and neurobehavioral deficits, with a predilection for executive function disorders, encompassing a constellation of neuropsychiatric disorders such as anxiety, depression, and attention-deficit/hyperactivity disorder (ADHD). To date, the underlying mechanisms linking CHD to these conditions remains unknown, and a deeper understanding of the relationship between CHD and neurodevelopment is critical for improving prognosis and planning effective treatment. Here, we conducted a preliminary exploration of functional connectivity differences between CHD and age matched healthy controls under the age of 25 using network-based models to better understand the functional organization of the CHD brain.

Resting State Blood Oxygen Level Dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) data was collected from a single-site population of patients with CHD and healthy controls (n=171). The available scans underwent rigorous preprocessing, including motion correction, brain extraction, artifact extraction, bandpass filtering, and scrubbing of volumes exceeding a framewise displacement of 0.5 mm. Patients were included if they were under 25 years age at the time of the scan and had at least 150 frames (~5 minutes) of data after scrubbing. The Automated Anatomical Labeling (AAL) template was then registered to BOLD space for segmentation.

A total of 72 subjects passed our QC thresholds (25 CHD, 47 controls). These subjects were used to construct adjacency matrices representing the Pearson correlation coefficient between average signals across the space of two brain regions over time. The correlational coefficients were binarized and used to create an undirected graph with edges between nodes representing functionally connected brain regions. The computed graphs were used to derive global and local network measures commonly used to characterize the nature of information travel and efficiency of a network. Global efficiency, assortativity, and density were selected global network measures that provide insight into the overall efficiency and organization of the brain network. Clustering coefficient, local efficiency, node betweenness, and degree were selected local metrics that can reveal specific regions that have high importance in the network. CHD patients were found to have higher clustering coefficients, degrees, and local efficiencies across several regions including the Cerebellum and Vermis. Six regions, including the Hippocampus and Insula, showed higher betweenness in Controls compared to CHD. In summary, our study found significant regional differences in network measures between CHD patients and controls, suggesting that these measures may have potential as biomarkers for tracking the neurological effects of CHD.

These findings lay a foundation for future hypothesis-driven research in CHD prognosis prediction by identifying potential biomarkers of CHD outcome. Further study is needed to determine the clinical significance and prognostic utility of graph measures with CHD, which will ultimately aid in the development of targeted studies, interventions, and improved patient outcomes. Future work to improve this analysis includes expanding our dataset to include a larger sample size. However, the current study is limited by a small population size, which is compounded by strict motion-related inclusion criteria. Therefore, further work is required to enhance our motion correction and scrubbing criteria. We aim to establish a threshold that allows us to retain the maximum amount of scan data while also ensuring its quality and the robustness of findings by minimizing motion artifacts.

2-B-7 - Functional connectivity patterns of the visual word form area are stable during learning

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Details

Reading entails rapid and efficient conversion of written symbols to sounds and meanings. This process depends on specialized circuitry in visual cortex, the Visual Word Form Area (VWFA; Dehaene and Cohen, 2011). Recent findings suggest that this word-selective cortex comprises at least two distinct subregions: the more posterior VWFA-1 is sensitive to visual features, while the more anterior VWFA-2 processes higher level language information. We've recently shown that these adjacent subregions also show distinct patterns of functional connectivity with distant brain regions, in children and adults (Yablonski et al., biorxiv). Here, we ask whether these connectivity patterns develop as a function of learning to read, or are a stable property of the reading network. To this end, we capitalize on a reading intervention program that was shown to drive significant improvement in reading skills (Donnely et al., 2019). In the current ongoing longitudinal study, children with a history of reading difficulty (N=28, age range 8-13y, 12 females, 16 males) participated in an intensive 8-week reading intervention over the summer. A battery of reading and cognitive measures was administered before and after the intervention to assess the magnitude and specificity of reading improvement. In addition, each child completed an MRI scanning session immediately before the intervention and 4 months after its completion. During the scan, children watched a nature movie that did not include any language content. These scans (2 runs of 5 minutes each, TR=820ms, TE=30ms, voxel resolution=2.4 isotropic) were preprocessed with fMRIprep (Esteban et al., 2017), and then denoised and analyzed using Nilearn (Abraham et al., 2014). We ran seed-based whole-brain correlation analyses using template regions of interest (ROIs; Kubota et al 2022) to investigate the functional connectivity patterns of VWFA-1, VWFA-2, and a frontal language region (IFC-text). We then calculated ROI-to-ROI correlations to evaluate whether connectivity strength between VWFA1/2 and the frontal lobe changes with time. Following the intervention, children significantly improved their reading skills, as indicated by an average increase of 9 standard score points on the Woodcock-Johnson (WJ) Basic Reading Skills composite index ($\bar{d}$ = 8.4, $t = 15.3$, $p<2e-16$). Math skills (as measured by the WJ Math Facts Fluency subtest) did not increase over this period, showing that the intervention had the desired targeted effect on reading. Whole-brain analysis revealed that VWFA-2 was strongly correlated with language regions in the frontal and lateral parietal lobes, particularly bilateral inferior frontal gyrus (IFG) and precentral sulcus. In contrast, VWFA-1 was more strongly correlated with bilateral visual regions including ventral occipitotemporal cortex and posterior parietal cortex. This replicates our previous findings and supports the distinction between these two sub-components of the VWFA. Importantly, this distinction was evident even before the intervention, when children had demonstrated poor reading skills. Longitudinal ROI-to-ROI analysis confirmed that a) across timepoints, VWFA-2 has significantly stronger connectivity with frontal language regions, compared with VWFA-1 or adjacent face-selective ROIs, and b) functional connectivity values remained stable over a time period of 6 months. Together, these findings suggest that functional connectivity of the reading circuitry is a relatively stable trait. We postulate that this functional organization of the ventral visual cortex is an intrinsic property of the brain that may scaffold the development of text-selective regions.

2-B-9 - Leveraging large-scale brain-wide association discovery in smaller samples: A polyneuro risk score approach to cognition in Kids2Health resting state data

Johannes Mohn [1], **Nora Byington** [2], **Ferdinand Hoffmann** [1], **Martin Bauer** [1], **Gracie Grimsrud** [2], **Felix Dammering** [1], **Lea Bentz** [1], **Katharina Pittner** [1], **Fiona O' Donovan** [1], **Jerod Rasmussen** [3, 4], **Damien Fair** [2], **Sibylle Winter** [1], **Sonja Entringer** [1], **Oscar Miranda-Dominguez** [2], **Claudia Buss** [1, 5], **Christine Heim** [1]

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Details

Cognitive abilities, including learning and memory, rely on distributed brain networks. However, it remains unclear which network connections support cognitive development across different ages and predict individual differences in children. Recent analyses have demonstrated that the reliable and generalizable estimation of brain-cognition associations require thousands of individuals. Few developmental studies can provide these sample sizes. Taking inspiration from genomics, the new framework of polyneuro risk scores (PNRS) leverages large-scale population-based studies to derive brain feature scores for application in smaller samples. This approach can derive such associations out of different types of brain features such as cortical thickness or resting-state functional connectivity. Interestingly, one recent study using resting-state functional connectivity data established that a weighted sum of network edges explained roughly 21% variance in general cognitive ability in adolescents and roughly 5% of variance in learning and memory.

The aim of this study is to test the generalizability of the PNRS method to the prediction of cognitive abilities in a pediatric sample with a wider distribution of ages. We plan to calculate PNRS for general cognitive ability and for learning and memory in the Kids2Health sample of children from Berlin (N = 331, ages 3-12) based on association strengths (beta weights) obtained from ABCD (discovery sample, N = 6507, ages 9-10). Data collection is complete, and neuroimaging data is undergoing ABCD-harmonized preprocessing at the time of submission. Scores for general cognitive ability and for learning and memory for every individual will be derived from a battery of tasks via dimensionality reduction.

We hypothesize that PNRS for learning and memory and for general cognitive ability and will explain variance in cognitive scores when applied to the Kids2Health sample. We further expect that the explained variance may be lower due to differences in site, procedures, cognitive assessments, and in developmental stage between discovery and target samples. Nevertheless, results may support aspects of the PNRS framework by showing robust associations in an independent sample that differs in age and cultural background. Multivariate regression models will be used to test these associations while controlling for confounding covariates.

This work will be critical in characterizing the development of the distributed resting-state functional connectivity patterns that are pivotal for cognitive development. These insights may further lay a basis for studies aiming to understand individual differences in functional brain organization that can arise in the context of developmental risk factors.

2-B-10 - Associations between changes in the immune environment across pregnancy trimesters and the developing human functional connectome

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Details

Objective: Maternal immune activation (MIA) during pregnancy is an example of an exposure prior to birth that influences later neurodevelopment. Typically, MIA measures are either collected only once during gestation or are averaged across collection time points to associate the average presence of some component of MIA to early neurodevelopment. However, MIA is known to be dynamic across pregnancyâ€"existing studies' use of MIA as a static temporal measure to assess offspring outcomes ignores critical periods of vulnerability and if different periods of exposures lead to different long term effects on offspring neurodevelopment. Therefore, we aim to explore the association between newborn functional connectivity and MIA during pregnancy as assessed by changes in 46 markers of activation between the second and third trimesters. This will build on existing analysis from the group exploring newborn functional connectivity and MIA in only the third trimester of pregnancy.

Methods: For the MIA component, 74 healthy women underwent blood draws 34â€"37 weeks into the gestation period. From this, 46 markers of MIA were assayed, including both innate (e.g., cytokines) and adaptive (e.g., IgG) markers. Each woman's markers are subdivided into second and third trimester blood draws to enable the comparison between two time points during pregnancy. Principal component analysis (PCA) was applied to the data across trimesters, enabling the reduction of the marker data for each woman to a single score for each trimester. For the functional connectivity component, 29 newborn infants between the ages of 2 to 6 weeks underwent MRI scans. The functional connectome edges will be correlated with the difference between scores in the third and second trimester, relating newborn functional connectivity to changes in MIA during pregnancy. Data collection is already complete, and analysis is currently in progress and will be complete by Flux.

Implications: Previous work has attempted to reveal associations between gestational MIA and early infant neurodevelopment, with the long-term goal of identifying how alterations in the maternal immune environment impact later diagnosis of neurodevelopmental conditions. Additionally, early interventions to prevent such conditions may result from work stemming from these concepts. The proposed study builds on this previous work, eschewing the treatment of MIA as a static metric in favor of analyzing how changes in MIA between the second and third trimester relate to newborn neurodevelopment via the functional connectome. To the best of our knowledge, this study would be the first to examine the relationship between changes in MIA and the human connectome across pregnancy. Research involving improved temporal resolution of MIA may lead to improved intervention strategies. Following this logic, this study would aid in framing fetal exposure to MIA as a dynamic process, leading the way for future research to delve into the effects of high temporal resolution trajectories of MIA, and potentially assisting in developing intervention strategies targeting specific trimesters in pregnancy to aid offspring development.

2-B-11 - Investigation of Affective Circuitry in Peri-adolescent Pubertal Development and Anxiety

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Details

BACKGROUND: Interactions between the medial prefrontal cortex (mPFC) and the amygdala are crucial in the processing of emotions. Several studies have found an association between anxiety and reduced mPFC-amygdala functional connectivity, coupled with heightened amygdala activation, in response to affective stimuli. These results have been interpreted to suggest poorer regulatory control over affective responses that may characterize anxious pathology. However, other studies have had mixed findings across different subclinical populations, anxiety diagnoses, and developmental cohorts. Importantly, mPFC-amygdala circuitry changes dynamically during the transition from childhood to adolescence, when many anxiety symptoms escalate. Specifically, studies have found a potential developmental shift from positive to negative mPFC-amygdala functional connectivity. However, it remains unclear how specific peri-pubertal changes in mPFC-amygdala circuitry are influenced by anxiety. While prior studies have made clear the important role that these regions play in anxiety across development, many have been limited by small sample sizes, a lack of information regarding pubertal status, or looked at a narrow population. By using a large sample of peri-adolescents at the inflection point of pubertal development and on a wide continuum of anxiety severities, we seek to address some of these limitations to better understand the development of affective circuits and identify important areas of intervention in the future.

AIM: To characterize functional connectivity patterns between the mPFC and amygdala in association with pubertal status and how they may be moderated by anxiety during the sensitive window of peri-adolescence. We specifically hypothesize that more advanced pubertal status will be associated with greater negative functional connectivity between the mPFC and amygdala in response to negative valence stimuli during the encoding phase of a mnemonic task. We also hypothesize greater levels of anxiety will attenuate the association between pubertal status and mPFC-amygdala functional connectivity.

PROPOSED METHOD: Neuroimaging and clinical data will be used from an ongoing large study (R01MH116005) of 200 participants aged 10-13 years with anxiety sensitivity ranging from severe to no anxiety. Participants completed two runs of an fMRI event-related design task in which they were presented with a series of neutral and negative pictures (on-screen for 2s) and random intervals (jittered ITI: 2-6s) and asked to label the valence of each image. Clinician- and self-reported measures of anxiety and pubertal status were collected, including the Screen for Child Anxiety Related Disorders (SCARED), the Pediatric Anxiety Rating Scale 6 (PARS-6), Anxiety and Related Disorders Interview Schedule-5 (ADIS-5), and Pubertal Development Scale (PDS). All data collection for this analysis has been completed.

PROPOSED ANALYSIS: Imaging data will be preprocessed with fMRIprep, and anatomical ROIs will be selected from FreeSurfer aparc+aseg labels (rostral anterior cingulate cortex and amygdala). Analysis will focus on beta series correlation to negative stimuli; beta values will be derived using a least square estimate approach. Correlation of beta series in each region will serve as the measure of functional connectivity between the rostral anterior cingulate cortex (i.e., mPFC) and amygdala. Principal components analysis will be used to create a composite anxiety score across child and parent SCARED and PARS-6 scales. Simple linear regression will analyze the association between pubertal status and mPFC-amygdala functional connectivity. Our composite measure of anxiety will be added as an interaction predictor to examine how anxiety severity moderates the association between pubertal status and mPFC-amygdala functional connectivity. Apart from data pre-processing, all analysis is pending and will be completed by conference time.

C – Brain function

2-C-12 - Longitudinal associations among the predictability of maternal behavior and infant brain function

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Details

The quality of the early caregiving environment has been shown to be predictive of variations in infant brain function during the first year of life, assessed via electroencephalography (EEG). Recent findings also implicate the predictability of maternal behavior as a key dimension of caregiving, but few studies have examined whether maternal predictability shapes infant brain function beginning in infancy. The current study will analyze associations among maternal predictability, infant EEG power spectral density (PSD), and infant cognitive and linguistic development in a sociodemographically-diverse sample of infants (N = 98 infants, 62 males; 52% Hispanic/Latino). At 3 months, the predictability of maternal behavior will be assessed by microcoding for transitions in maternal visual, auditory, and tactile signals offered to their infants during parent-child interactions. The predictability of maternal sensory signals will be indexed using Shannon's entropy. Infant resting EEG activity and measures of language, attention, and memory will be collected at 3 and 9 months. Analyses will test the following hypotheses: 1) higher maternal predictability will correlate with flatter PSD slopes, indicating greater relative EEG power in higher frequency bands; 2) maternal predictability will positively correlate with infant recognition memory, sustained attention, and expressive and receptive language at 9 months; 3) within-person changes in infant PSD slopes from 3 to 9 months will moderate associations among maternal predictability and infant neurocognitive outcomes at 9 months. These findings will provide novel insights into how the predictability of maternal behavior may impact developing cortical circuitry and cognitive systems beginning in infancy.

2-C-13 - Daily family assistance and behavioral and neural associations of giving to others

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Details

BACKGROUND: Family assistance is an essential aspect of family relationships across cultures and contexts exemplified by caring for siblings, running errands, and providing emotional and financial support (Telzer et al., 2010). Previous literature has suggested that family assistance is linked with positive aspects of psychological well-being and giving towards others (Telzer et al., 2010, Armstrong-Carter & Telzer, 2021), an essential aspect for developing and maintaining social relationships (Crone and Dahl, 2012). A few studies have suggested an increased differentiation of giving more to familiar others, including the family, than strangers across adolescence (Karan et al. 2022, van de Groep, et al. 2022). It is possible that daily family assistance promotes giving behavior towards the family and that youth who report more daily family assistance exhibit increased giving towards family in comparison to others. At the neural level, giving resources to family at a loss to oneself has been linked with neural activation in regions implicated in cognitive control and reward processing such as the dorsolateral prefrontal cortex (dlPFC) and ventral striatum (VS), respectively, which undergo significant change during adolescence (Karan et al. 2022, Crone and Fuligni, 2020). Thus, the goal of the present study is to investigate whether adolescents' daily family assistance is associated with more giving to family as compared to others during an fMRI task and concomitant neural activation in the dlPFC and VS.

METHOD: Data are drawn from the first wave of an ongoing longitudinal study of 180 young adolescents (Ages = 9-13 years) designed to assess the association between daily family assistance and giving towards family using behavioral and neural data. Participants completed a decision-making task in which they had the opportunity to give money to caregivers, friends, and strangers while undergoing functional magnetic resonance imaging (fMRI). Participants also completed daily diary checklists for 7 days, reporting whether they provided family assistance (i.e., cooking, cleaning, running errands, taking care of siblings) and the amount of time they spent doing so.

HYPOTHESES: It is hypothesized that daily family assistance will be associated with more giving towards caregivers at a cost to oneself in comparison to giving to a friend and a stranger. We also hypothesized increased activation in response to giving to a caregiver versus a control condition, and in comparison to giving to a friend and stranger versus control, with greater activation in regions in the cognitive control (dlPFC) and reward processing networks (VS). These predictions have implications for understanding the complexity of daily family assistance in social decision-making during adolescence (van de Groep et al. 2022).

ANALYSIS: Multiple regression analyses will be used to examine whether daily family assistance predicts giving behavior towards caregivers. For the neural data, a general linear model will be constructed for each participant in which the task was modeled as an event-related design. Each individual run (for caregiver and friend) will be entered into the model. The active condition (costly giving to caregiver versus control, in comparison to costly giving to friend and stranger versus controls) within a run will be modeled in separate regressors. Since trials in which offers were accepted are of primary interest in the present study, accepted trials for each condition will be modeled in separate regressors so they could be separately examined. Control trials will be modeled in a single regressor, regardless of whether the trial was accepted or rejected, given that the financial outcome in these trials was identical. Key contrast will compare accepted costly giving to caregiver trials to control trials in comparison to giving to friend and stranger trials to control trials. We will employ a region-of-interest (ROI) approach within the dlPFC and VS.

D – Brain structure

2-D-14 - Microstructural differences in the brains of young children with attention-deficit/hyperactivity disorder compared to typically developing children: Evidence from restriction spectrum imaging.

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Details

Attention-Deficit/Hyperactivity Disorder (ADHD) is the most common reason for early childhood mental health referral affecting between 10 to 25% of preschoolers. A prominent theory of ADHD is that the disorder is associated with dysfunction of dopaminergic (DA) circuits. For example, Nigg and Casey (2005) reviewed the potential association of basal ganglia (i.e., fronto-striatal) and cerebellar thalamocortical loop dysfunction with ADHD symptomology, noting the importance of DA in the modulation of function in both circuits. Indeed, stimulant medications, which block DA transporters to enhance extracellular DA, are a first-line treatment for ADHD. These medications modulate activity in these proposed basal ganglia and cerebellar thalamocortical circuits associated with symptoms and behaviors associated with ADHD, such as difficulty suppressing competing behaviors during goal-directed activity, impulsive behavior, poor sustained attention during complex tasks, and inefficient response to changing reward or learning contexts. The substantia nigra (SN) and ventral tegmental area (VTA) are central components of this circuit, and it is possible that early DA circuit dysfunction involving the SN is already present in young children with ADHD. This could be indicated if there are differences in cellularity of SN or VTA between medication naÃ¯ve ADHD and typically developing (TD) children before they are exposed to stimulants, which may affect cellularity in these regions. To establish whether there are existing diagnostic group differences, we employed a novel MRI method sensitive to *in vivo* neurite density. Method: The final participating sample consisted of 152 4-7-year-old medication naÃ¯ve children diagnosed with ADHD (dual clinician diagnosed) and 137 typical controls (M age = 5.50, SD = 0.87, and 69% male). All children were scanned in an MRI (3T Siemens Prisma) with a 102-direction multi-shell diffusion-weighted imaging acquisition. Restriction spectrum imaging (RSI; White et al., 2013) reconstruction of the diffusion signal was applied. The SN was identified using the Pauli atlas, and SN differences in restricted and hindered diffusion, which are sensitive to cellularity in grey matter (Palmer et al., 2022) were examined across age, with diagnostic group entered as a moderator. Results: In SN, we found a significant positive effect of age for restricted diffusion, but this effect was moderated by diagnostic group status (p = .02). Specifically, the slope for the ADHD group was significantly smaller than the TD group. In contrast, the age effect, which was also present in the VTA (p = .0004), was not moderated by group in this region (p = 0.33). Conclusions: Age-related differences in cellularity, evident in early adolescence using the RSI diffusion method (Palmer et al., 2022), are already indicated at earlier ages (4-7-years) in SN and VTA DA regions. The novel finding here, though, is that in SN these age-related differences proceed differently in children with ADHD relative to TD children. This indicates an early emerging structural difference in the DA circuit for children with ADHD that can be detected with novel diffusion imaging methods.

2-D-15 - Generalizable multivariate neuroanatomical correlates of psychiatric problems in preadolescence

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Details

Introduction

Associations between brain structures and child psychiatric problems have been extensively investigated across different disorders. However, findings were inconsistent, showed modest effect sizes in specific brain regions, and were prone to poor replicability. This lack of regional convergence could be due to (*i*) the categorical nosology that most studies were based on, which omits the dimensional nature of many child psychiatric problems. (*ii*) conventional mass univariate methods that do not account for the likely multivariate nature of associations and the embedded burden of multiple testing correction. (*iii*) small sample sizes and a lack of rigorous external validation in an independent sample. We aim to address these gaps by applying multivariate machine learning techniques to delineate robust and generalizable associations between brain structures and child psychiatric symptoms in two large neurodevelopment cohorts, the Adolescent Brain Cognitive Development (ABCD) Study in the US and the Generation R Study in the Netherlands.

Methods

A total of 11,271 structural MRI scans from the multi-site ABCD Study (ages 9-to-10 years from 21 study sites) and the single-site Generation R Study (ages 9-to-12 years) were included. Each brain structural measure (cortical and subcortical volumes, cortical surface areas, and cortical thickness) was normalized and residualized by regressing out potential confounders. Psychiatric symptoms were assessed using the eight syndrome scales of the Child Behavioral Checklist (CBCL). The ABCD sample was randomly split into a training set consisting of 17 sites and a test set consisting of 4 sites, a procedure that was repeated 10 times to reduce sampling bias. We applied a multivariate machine learning technique: sparse canonical correlation analysis (SCCA), in the training sets of ABCD and test *out-of-sample generalizability* in the test sets of ABCD. Importantly, *out-of-study generalizability* was further tested by applying the model weights in ABCD directly to Generation R, which is a highly stringent (gold-standard) generalizability test.

Results

We identified one brain-behavior dimension that was highly generalizable in test sets (*out-of-sample*) of ABCD as well as in Generation R (*out-of-study*). This brain-behavior dimension captured the correlation between higher attention-dominated externalizing problems and widespread reduced cortical/subcortical volumes and cortical surface areas, especially in frontal and parietal lobes. This association was highly consistent when we implemented traditional CCA without sparsity, when using more fine-grained measures (item scores of CBCL) of child psychiatric problems, and when removing the effects of head motion from the brain data. Moreover, the derived latent brain dimension was predictive of ADHD medication, child cognitive ability, and school achievement, with greater precision compared with total grey matter volumes of the brain.

Conclusion

By leveraging two independent large neurodevelopment cohorts, we identified one highly robust multivariate association between brain structural patterns and attention-dominated externalizing problems in the general population, which showed marked generalizability across different populations and study protocols. Our results showed the pervasiveness of reduced brain structures that are related to higher attention and social problems in preadolescence. Importantly, when using the gold-standard test, achieving a high level of generalizability is not common in existing brain-behavior association studies. This makes our results hold special values not only in illustrating the relationship of brain and child psychiatric problems, but also in providing methodological implications for replicable and generalizable multivariate prediction models. Future studies could extend the investigation into different development periods and the predictive values for diagnosis and disease trajectory in clinical samples.

2-D-16 - Concurrent and Predictive Associations Between Amygdala Volume and Scores on Subdimensions of the Autism Observational Scale for Infants

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Details

Background: Amygdala volume undergoes a period of accelerated growth between 6 and 24 months in infants at high familial likelihood for developing autism spectrum disorder (ASD), who are later diagnosed (HL+). Additionally, amygdala growth rate from 6 to 12 months is associated with increased social deficits at 24 months (Shen et al., 2022). Whether this neural phenotype, characterized by accelerated amygdala growth, is specific to ASD case-ness, or whether it is associated with variability in social communication function agnostic to DSM categorization is unknown. The Autism Observation Scale for Infants (AOSI; Bryson et al., 2000) provides an early measure of infant behavior that can be disaggregated into separate social communication (SC) and restricted and repetitive behavior (RRB) domains. Total scores on the AOSI consistently differentiate HL+ infants from HL- infants at 12 months. Here we used data from the Infant Brain Imaging Study (IBIS) network to derive subgroups based on SC scores from the AOSI and evaluated group differences in amygdala volume at 6, 12, and 24 months. Evaluation of amygdala development in the context of social communication ability on the one hand and ASD diagnostic status on the other will elucidate the relationship between amygdala volume and dimensional differences in social behavior, both within and across diagnostic categories.

Objective:

1. Evaluate the concurrent and predictive associations between SC scores derived from the AOSI at 6 and 12 months and amygdala volume at 6, 12, and 24 months.

Methods: SC and RRB domain scores from infants (*N* = 358, of whom 212 were males) at 6 and 12 months were derived from AOSI reports collected as part of the longitudinal, multisite IBIS. Infants with amygdala volume data (*N* = 264, of whom 162 were males) were divided into thirds based on SC scores. Amygdala volume at 6, 12, and 24 months was compared both across diagnostic categories (HL+ vs. HL-) and across terciles of SC scores (highest third, middle third, lowest third) calculated at 6 and 12 months. Finally, amygdala growth from 6 to 12 months and from 12 to 24 months was calculated and compared across SC terciles and diagnostic categories.

Results: Amygdala volume at 6 months did not differ between HL+ and HL- groups. Nor did amygdala volume at 6 months differ across terciles of SC scores. However, amygdala volume at 12 months did differ both between diagnostic groups and between SC terciles. At 24 months, amygdala volume differed between diagnostic groups but not across SC terciles. In sum, SC terciles based on the AOSI assessment at 12 months was associated with amygdala volume at 12 months, such that higher SC scores (indicating greater social communication deficits) were associated with larger amygdala volume. In contrast, diagnostic status differentiated amygdala volume measured at both 12 and 24 months, with HL+ infants showing larger amygdalae than HL- infants. While diagnostic status differentiated amygdala growth from 6 to 12 months in accordance with Shen et al. (2022), SC terciles at 6 and 12 months did not predict amygdala growth.

Conclusions: In accordance with previous findings, we observed evidence of enlarged amygdala volume at 12 and 24 months in infants at high familial likelihood for ASD who were later diagnosed with ASD (HL+) compared to infants with the same familial likelihood but who were not diagnosed with ASD (HL-). A measure of social communication function that was agnostic to DSM categorization was associated with amygdala volume at 12 months but not at 24 months, and it did not predict amygdala growth. In other words, while the SC measure was concurrently associated with amygdala volume at 12 months, ASD diagnostic status explained more variation in amygdala volume across development. This suggests that the neural phenotype characterized by periods of amygdala enlargement during early development is closely related to ASD case-ness, with variation in social communication ability being related but not predictive of amygdala volume.

2-D-17 - Weekday-to-Weekend Sleep Differences are Associated With Variations in Brain Morphology in School-aged Children

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Details

Short sleep duration has been identified as a significant risk factor for poor physical and mental health in youth (Chaput et al., 2016). Beyond insufficient sleep, other factors are increasingly recognized as characterizing unhealthy sleep behavior, including irregular sleep habits. The term social jetlag (SJL)

refers to the discrepancies between weekday and weekend sleep patterns due to social obligations (Wittman et al., 2006). For instance, school obligations may contribute to SJL in children, as earlier wake times likely create a buildup in sleep debt during the week that can be compensated by sleeping in during the weekend. Although SJL in youth has been linked to adverse health and behavioral outcomes (Randler et al., 2019), the potential implications on brain structure development remain poorly understood. To our knowledge, only two studies have documented these associations among adolescents, and found that later weekend awakenings were linked to smaller grey matter volumes (GMV) in medial brain regions (Lapidaire et al., 2021; Urrila et al., 2017). However, SJL was self-reported in both studies, increasing the risk of respondent bias (Jackson et al., 2018). Furthermore, no study has focused on these associations among preadolescents, despite the emergence of significant weekday-to-weekend sleep differences during childhood (Randler et al., 2019). This study examined the associations between objectively assessed SJL and whole-brain GMV in school-aged children.

At 10 years of age, 69 children (40 boys) underwent structural magnetic resonance imaging and sleep characteristics were assessed using actigraphy, which shows excellent convergent validity with polysomnography (Meltzer et al., 2016). Sleep duration refers to the time elapsed between sleep onset and sleep offset, excluding nocturnal awakenings. Sleep midpoint refers to the halfway point between sleep onset and offset. SJL was calculated by subtracting the mean weekend from the mean weekday values for sleep duration and midpoint. Preprocessing and whole-brain voxel-based morphometry analyses were performed using SPM12 software and the CAT12 Toolbox (12.8) running on MATLAB (R2019b). Statistical maps identifying voxel clusters significantly correlated with SJL values (duration and midpoint) were obtained by using permutation testing and threshold-free cluster-enhancement (TFCE). Due to the exploratory nature of this study, an uncorrected threshold of $p < .001$ with a minimum extent threshold of 100 voxels was initially used, then further tested with a conservative threshold of $p < .05$ corrected for multiple comparisons with Family Wise Error (FWE).

Children who tend to sleep more during the weekend relative to the week had smaller GMV in the bilateral lingual gyrus (MNI: $x = -3$, $y = -83$, $z = -11$; $k = 555$; TFCE = 942.87; p-unc $< .001$). A small cluster ($k = 23$) held at p-FWE $< .05$. Further, delayed sleep midpoint during the weekend was associated with smaller GMV in the left middle occipital gyrus (MNI: $x = -33$, $y = -84$, $z = 9$; $k = 433$; TFCE = 764.86; p-unc $< .001$).

Experiencing more SJL in late childhood was associated with reduced GMV in occipital regions. The lingual gyrus is involved in mental imagery generation, such as dreaming, imagination, and creative thinking (Fox et al., 2015; Jung et al., 2016). The middle occipital gyrus strongly co-activates with mnemonic regions such as the hippocampus during sleep, which enhances the retrieval and consolidation of emotional memories (Bennion et al., 2016). This study did not replicate associations previously documented in adolescents, possibly due to modest statistical power or methodological differences, notably the use of an objective sleep measure. This is nonetheless the first study to suggest that SJL shares associations with neural development even during childhood, before substantial age-related alterations in psychosocial (e.g., increased social engagement) and biological factors (e.g., puberty) set in.

2-D-18 - Effects of CPS involvement on white matter fiber density and morphology during middle childhood: A fixel-based analysis

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Details

Background

Experiences of early adversities have been associated with a reduction of fractional anisotropy (FA) across multiple major white matter bundles, including the corpus callosum, cingulum, fornix, inferior fronto-occipital fasciculus, superior longitudinal fasciculus, and uncinate fasciculus. A reduction of FA indicates decreased white matter integrity, which is associated with poor cognitive and socioemotional outcomes in children. Most studies have utilized a voxel-based analysis (VBA) approach that aggregates the degree of diffusion of multiple fibers within a voxel, despite the presence of multiple fibers within a voxel possibly superimposing on each other. To overcome this limitation, fixel-based analysis (FBA) can be used. A fixel can be thought as the smallest fiber bundle element within a voxel. The FBA approach computes fiber orientation distributions (FODs) using multi-tissue Constrained Spherical Deconvolution (CSD) algorithm, which in turn enables the analysis of fixels within a voxel that form different coherent bundles in their orientation space. In addition, a conventional diffusion VBA used scalar metrics (e.g., FA) to infer biological processes, such as maturation. However, FA along with other DTI metrics is sensitive to a variety of biological changes. The direct interpretation for biological processes using conventional DTI metrics is challenging. The FBA approach overcomes this limitation and provides biologically meaningful metrics, such as 1) Fiber density (FD), an estimate of the microscopic axonal density of fibers within a voxel; 2) Fiber cross-section (FC), an estimate of the macroscopic alterations that occur in the area perpendicular to the fiber bundle's orientation; 3) Fiber density and cross-section (FDC), a summary metric integrating FD and FC to provide simultaneous insights on both microscopic and macroscopic differences of the white matter tracts. To our knowledge, few studies have employed an FBA approach to understand the effects of early adversities on children's development of white matter microstructure.

Objective

In this study, we employed the novel FBA approach to examine the impact of experiences of early adversities on fiber density and macroscopic morphology using FD, FC, and FDC metrics.

Methods

Seventy children with and without histories of Child Protective Services (CPS) Involvement (45 and 25, respectively) underwent diffusion weighted imaging at age 10. The FBA was performed in MRtrix3, including generating a study-specific FOD template, performing a whole-brain probabilistic tractography, and filtering tractograms using Spherical-deconvolution Informed Filtering of Tractograms (SIFT) algorithm. The Connectivity-Based Fixel Enhancement (CFE) method was used to examine group differences in FD, FC, and FDC, while controlling for age when scanned and sex. The FBA results were produced with 5000 permutations, and family-wise error (FWE)-corrected statistical significance is reported at $p_{FWE} < .05$.

Results

Children with CPS involvement had significantly lower FD localized to the corpus callosum, cingulum, fornix, and inferior fronto-occipital fasciculus than children without CPS involvement. Additionally, children with CPS involvement had lower FC localized to the left uncinate fasciculus, as well as lower FDC localized in the right inferior longitudinal fasciculus.

Conclusion

Consistent with prior studies using the VBA approach, we found poorer white matter microstructure among children who had experienced early adversity. The differences found in white matter microscopic and macroscopic morphology may serve as potential mechanisms that explain the poor cognitive and socioemotional outcomes following early adversities. Finally, our study contributes to the growing literature using the FBA approach to understand the development of white matter microstructure in children.

2-D-21 - Sex-based dissociations of brain and behavioral measures of cognitive, motor, and emotional control in relation to externalizing and internalizing psychopathology across development

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Details

Objective: Neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD) emerge during early childhood and are more prevalent in males. In contrast, anxiety and mood disorders commonly emerge during adolescence and occur more in females. Our understanding of the mechanisms that underlie sex differences in the occurrence of psychopathology is limited, including whether behavioral or neuroimaging markers of internalizing (INT) and externalizing (EXT) psychopathology differ across development for girls and boys.

Methods: This study employed generalized linear mixed effects models to characterize developmental (i.e., age-related) changes in behavioral measures of cognitive (go/no-go task), motor (overflow), and emotional control and brain structure (regional volume and white matter microstructure) in relation to EXT and INT symptoms. Participants include 1,004 children and adolescents (ages 4-17) either with an initial diagnosis of ADHD (n=494, 157 girls) or typically developing (TD) controls (n=510, 167 girls) with MRI scans (anatomical and diffusion-weighted) collected at a single site. Longitudinal data were collected from a subset of the sample (n=339) at least 1 year apart.

Results: For behavioral measures, we found that poorer motor control is associated with higher EXT symptoms regardless of sex and age. For cognitive control, the relationship between task-based cognitive control (e.g., response inhibition errors on a go/no-go task) and EXT symptoms varied as a function of age and sex, such that boys showed a positive relationship, regardless of age, whereas younger girls showed a negative relationship and older girls showed a positive relationship. In contrast, response inhibition errors were positively associated with INT symptoms, regardless of age and sex, as was response variability (for both INT and EXT symptoms). Finally, for emotional control, the positive relationship between emotional lability and INT symptoms depended on age and sex, such that among

girls, greater emotional lability was more strongly associated with INT problems at older than younger ages, whereas boys showed consistently strong positive associations regardless of age.

Neuroimaging analyses revealed that within motor circuitry, fractional anisotropy (FA, higher values reflect the integrity of white matter tracts) of primary motor cortical region with sensorimotor striatum was positively associated with EXT symptoms, regardless of age and sex. In contrast, FA within the supplementary motor complex and sensorimotor striatum tract was positively associated with EXT in boys and negatively associated with EXT in girls, regardless of age. Volume of motor ROIs was unrelated to EXT symptoms. For cognitive control circuitry, volume of the anterior cingulate cortex and orbitofrontal cortex was unrelated to EXT symptoms, whereas dorsolateral prefrontal cortex (dlPFC) volume was negatively associated with INT symptoms, moderated by age (among older adolescents only). FA within fronto-subcortical tracts connecting the dlPFC with dorsal striatum were unrelated to EXT and INT symptoms. For emotional control circuitry, there was a trend for an age*sex interaction for FA within the orbitofrontal cortex and ventral anterior cingulate cortex to ventral striatum tract with INT symptoms, such that no relationship was observed among boys, and a stronger negative relationship was observed among girls at older rather than younger ages.

Conclusions: These findings suggest that motor, cognitive, and emotional control and structural integrity/volume of related neural circuitry are differentially related to EXT and INT symptoms across development in girls and boys, thereby elucidating the neurobehavioral basis for sex differences in psychopathology. Future studies of primarily longitudinal samples are needed to understand how these developmental trajectories unfold over time.

2-D-22 - Estimating BrainAGE with dynamic measures of structural brain development

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Details

The Brain-Age Gap Estimation (BrainAGE) has been proposed as one approach to assess the maturity of an individual's brain using cross-sectional data, as this measure reflects the difference between an individual's chronological age and their age as predicted by machine learning algorithms trained on neuroimaging dataâ€"often structural MRI (Brown et al., 2012; Franke et al. 2010). With this approach, an individual receives an estimated brain age that can differ from their chronological age. A positive BrainAGE, or a predicted brain age older than one's chronological age, has been interpreted as reflecting accelerated or advanced brain maturation in adolescent populations.

BrainAGE models harness the fact that brain structure changes throughout adolescence. However, substantial individual differences exist in static measures of brain structure for individuals of the same age during adolescence, and the pace of structural change also varies between individuals (Mills et al., 2021). The use of cross-sectional data to train and test BrainAGE models limits our ability to understand whether a more advanced BrainAGE reflects an adolescent having an accelerated or delayed trajectory of brain development, or simply having overall higher or lower measures while following a normative developmental trajectory. This is a particularly acute problem for studies using BrainAGE models to estimate brain maturity in the early- to mid-adolescent period, when we see high levels of inter-

individual variability in terms of the direction of structural change (Mills et al., 2021). Longitudinal data are able to capture these changes, indicating whether an individual's gray matter volume is stable, increasing, or decreasing.

In the current study, we trained a novel BrainAGE model using change scores calculated from two timepoints of data in early-to-mid adolescence, with the change in each structural measure used to predict age at the midpoint between waves of data collection. With this approach, we captured additional information about where an individual is on their trajectory of brain development. This is particularly important during this age range, as some individuals begin to show decreases in gray matter volume earlier than other individuals.

Midpoint age was predicted from 179 measures of cortical and subcortical volume and area. Participants ranged in age from 9-11 years old at T1, and 11-14 years at T2, and were all participants in the ABCD Study. The model was trained using data from 966 participants, and then used to predict BrainAGE in 6,466 participants. When predicting BrainAGE in a new sample, the model performed with a mean absolute error of 0.51 before bias correction, and 1.44 after bias correction. This is in line with existing adolescent BrainAGE models, which have performed with mean absolute errors in the one- to two-year range (Franke et al., 2012)

The novel model shows that BrainAGE can be accurately predicted from change scores in early to mid adolescence. Future work should examine how BrainAGE predicted with difference scores relates to other maturational metrics in adolescence.

2-D-23 - Subcortical Volume Differences in Monolingual and Bilingual Adolescents

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Details

Objective: Previous research suggests that bilingual experience may impact the development of subcortical regions, such that bilinguals exhibit greater subcortical gray matter volume than monolinguals. These differences may reflect age of L2 acquisition, language proficiency, or language control (i.e., selecting the appropriate language in the respective environment) . To date, most of the research on the relationship between bilingual experiences and subcortical regions has been conducted with adults. The current study uses the Adolescent Brain and Cognitive Development (ABCD) Study dataâ€"a large-scale longitudinal study collecting data from 21 sites across the United Statesâ€"to examine the relationship between subcortical volume and English vocabulary in bilingual and monolingual children, as well as volumetric differences between the language groups.

Method: The current study included 1,215 bilinguals and 5,894 monolinguals selected from the ABCD study based on parent-and-child-reported language background. The regions of interest included the bilateral cerebellum, thalamus, caudate, putamen, globus pallidus, and nucleus accumbens (NAc). To compare ~~the~~ bilinguals and monolinguals, we ran a hierarchal regression analysis controlling for relevant covariates (i.e., age, sex, handedness, pubertal status, parent education, household income, and non-verbal IQ). Model 1 included the unique effect of language group and English vocabulary, and model 2

included the main effects and the interaction between language group and English vocabulary. All analyses were False Detection Rate (FDR) corrected at alpha = 0.05.

Results: In model 1, results revealed smaller smaller bilateral cerebellums and larger bilateral putamens, right thalamus, right pallidum, and left accumbens in bilinguals compared to monolinguals. Greater English vocabulary was related to larger bilateral cerebellum, thalamus, caudate, putamen, NAc, and right pallidum in both monolinguals and bilinguals. In model 2, the same vocabulary-volume correlations were found, and bilinguals had larger bilateral NAc compared to monolinguals. In addition, there was an interaction in these regions, such that the positive relationship between English vocabulary and accumbens volume was stronger for monolinguals than bilinguals.

Conclusion: In general, there was a positive relationship between English vocabulary and subcortical volume in adolescents. This is consistent with findings suggesting the role of these regions in language proficiency. As children are gaining vocabulary and must learn to integrate them into daily speech, subcortical changes are likely occurring to accommodate this experience. In addition, there were language group differences such that bilingual adolescents had greater subcortical volume than monolingual adolescents. These findings are somewhat in line with existing literature on the dynamic volume adaptation of these brain regions due to bilingual experience, revealing expansion in subcortical structures in adulthood for bilinguals compared to monolinguals in the putamen, thalamus, globus pallidus, and NAc. Notably, prior research showed that accumbens volumes were positively correlated to bilingual experience in a non-linear pattern of increase followed by decrease. The English vocabulary-bilingualism interaction at the nucleus accumbens which showed a weaker vocabulary-volume relationship in bilingual than monolingual children may indicate a stage of this non-linear change being observed in adolescents, a developmental stage with dynamic changes in the environment and in the brain. Finally, one finding that does not fit in with previous studies was the reduced cerebellar volume in bilinguals relative to monolinguals. Prior findings suggest the opposite pattern. Future research is needed to further explore these regions in children and adults longitudinally across development to examine structural change in adolescent bilingual brains.

2-D-24 - Deep Learning and the Cortical Anatomy of Reading

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Details

Are there features of cortical anatomy that can reliably predict reading ability? Many studies have found associations between functional connectivity and reading, as well as white matter connectivity and reading. However, recent studies have provided conflicting evidence regarding whether the structural anatomy of the Occipitoteporal Sulcus (OTS) is associated with reading ability. In large part, these studies are limited by small sample sizes.

This open question motivates our main goal: investigate the association between OTS morphology and reading skill on a much larger dataset than has been previously attempted. This approach requires two ingredients: 1) data, and 2) automated rather than manual labeling and analysis of OTS anatomy. For the data source, we take advantage of the Healthy Brain Network IHBN) dataset, which contains MRI and

behavioral data for thousands of heathy children participants. For the analysis, such scale requires an automated method to parse OTS anatomy, which we provide in the form of a convolutional deep neural network. This network and the procedure to train it consitute a key component of this work.

The resulting network is capable of learning to label OTSs in previously unseen brains with a fidelity of 0.8 (evaluated against human expert labels), which permits a large number of analyses that were previously infeasible. In particular, the pretraining procedure of this network is generally useful and novel strategy for pretraining networks in the specific domain of neuroimaging.

Our main brain-behavior result clarifies contradictory literature: we find in HBN that there is a small but significant corrleation between OTS morphology and reading ability, as measured by TOWRE scores. In smaller samples, studies to date have found either large effects or null effects; a small effect size, as validated on a large sample, would help to explain to explain this discrepancy.

2-D-25 - Changes in Brain Energy Metabolism Across Childhood and Adolescence: A Multi-Occasion 31P Magnetic Resonance Spectroscopy Study

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Details

Child and adolescent development are associated with pronounced changes in various brain properties. *In vivo* structural MRI measures have revealed a nonlinear pattern of developmental change, with initial increases in grey matter volume giving way to shrinkage, along with myelination and the strengthening of long-range brain connections. Relative to the gross structural changes in the cortex, other aspects of the brain development are not as well documented, and the neurobiological mechanisms underpinning the development of the cortical mantle and their temporal dynamics have not been thoroughly examined *in vivo.* Given that the bulk of grey matter observed on MRI is neuropil â€“dendrites and unmyelinated axonsit is plausible that grey matter changes are related to neuropil transformations. Changes in the neuropil may be examined by assessing the metabolites that are associated with membrane phospholipids (MPL) involved in the expansion and contraction of the membranes - MPL precursors phosphocholine (PC) and phosphoethanolamine (PE), and MPL breakdown products glycerophosphocholine (GPC) and glycerophosphoethanolamine (GPE). While PC and PE levels are higher during growth spurts than during periods of relatively slow development, greater GPC and GPE levels are observed at sites of neuropil contraction.

We used phosphorus magnetic resonance spectroscopy (^{31}P MRS) to measure *in vivo* longitudinal changes in the levels of MPL precursors PC and PE, and breakdown products GPC and GPE in 49 children and adolescents aged 6 to 15 years at baseline who underwent up to three assessments, approximately one year apart. As MPL maintenance and the sculpting of brain connections incur substantial energetic costs, we also assessed brain energy metabolites through ^{31}P MRS-derived measures of phosphocreatine (PCr) and adenosine triphosphate (ATP), a key source of energy in the brain.

Based on the evidence demonstrating developmental thinning of the cortical mantle, we hypothesised that PE, PC, and ATP levels will decrease over time, whereas breakdown products levels will increase, albeit at a potentially slower rate. We expected that metabolite changes will be greater in regions demonstrating pronounced structural change across childhood and adolescence, including lateral prefrontal and inferior parietal regions, the neostriatum, the hippocampus and the thalamus. In addition, we sought to characterize changes in MPL metabolites in major white matter tracts, the forceps major and the forceps minor. Multi-level models on the metabolites revealed that the MPL precursors, PE and PC, decreased across all brain regions. In contrast, GPE and GPC changes depended on the baseline age: breakdown products levels in the PFC increased in children who were younger at baseline but decreased in their older counterparts. ATP decreases over time were heterochronic and regional: ATP decreases in the PFC were more pronounced for children who were younger at baseline, whereas ATP decreases in the hippocampus were larger for older children at baseline. In contrast, hippocampal PCr levels decreased in younger children but increased in their older counterparts. There were no reliable changes in PCr levels in the remaining brain regions.

Our results demonstrate longitudinal dissociations across metabolites that are relevant to neuropil contraction, expansion, and maintenance. The age-related discrepancy in PFC breakdown products change over time suggests differences in neuropil contraction at earlier and later stages of maturation. The dissociation between PFC and hippocampus vis a vis ATP change points to potentially different energy demands contributing to brain development across late childhood and early adolescence. Thus, in vivo ^{31}P MRS opens a new window into developmental shifts of the neuropil expansion and contraction equilibrium that can further our understanding of brain development across childhood and adolescence.

2-D-26 - Longitudinal effects of prenatal alcohol exposure on visual structural neurodevelopment over infancy

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Details

Background/Objective

Globally, 9.8% of pregnant people endorse alcohol use during their pregnancy, with prenatal alcohol exposure affecting neurodevelopment in over 59 million individuals. Prior literature using dichotomous categorization of alcohol use and/or samples with heterogeneous substance exposure has significantly limited knowledge of how the timing and level of alcohol exposure specifically impact human neurodevelopment. Additionally, limited studies index neurophysiological changes over the infant windows in which rapid development occurs.

This study addresses these key gaps by focusing on structural brain changes supporting visual development over infancy. Over the first six postnatal months, rapid functional development of the primary visual cortex through sensitive periods supports dramatic changes in visual capabilities. Structurally, myelination acts as a 'brakeâ€ on this plasticity and 'locks inâ€ prior visual learning with consequences on sensory functioning lasting across the lifespan. Occipital lobes are thus largely myelinated by 5-6 months. Animal model literature and human histology studies suggests that myelination is impacted by prenatal alcohol exposure. While human neuroimaging studies have shown prenatal exposure influences myelin in children 5 years and older, it is important to measure when myelin is developing to understand how and when these differences come to be.

Methods

We will address this question using longitudinal data from an ongoing project with families recruited from Gugulethu, an informal settlement in Cape Town, South Africa. In this sample, 73 mothers endorsed alcohol use at any point in pregnancy without comorbid substance use. We will test how timing and level of prenatal alcohol exposure impact early postnatal neurodevelopment to support emerging visual abilities by tracking myelination in the visual cortex from 3 to 6 months of age.

T1- and T2-weighted images were collected with a 3T scanner during natural sleep at both timepoints. We will use the T1- and T2-weighted MRI myelin mapping technique to measure cortical myelin with traditional volumetric images. These data have been collected and we are in the process of data analysis.

Hypothesis

We expect that increased exposure to alcohol prenatally will result in decreased change in myelination in the visual cortex from 3 to 6 months, as indexed by T1/T2 ratio values.

Proposed Analyses

We plan to analyze dose-related changes across trimesters by modeling the change in structural indices of myelin integrity from 3 to 6 months (while controlling for myelination at 3 months) as a function of the number of weekly drinks in each trimester using multiple regression.

Maternal age at infant birth, education, income, and depression scores will be considered as potential covariates of drinking scores.

Impact of the Study

This research has the potential for far-reaching impacts to improve the lives of pregnant people and their children globally. The study design allows us capture outcomes over the spectrum of possible prenatal alcohol exposure with increased ecological validity and accuracy. This work can be used to inform recommendations and guidelines as to how best support prenatal and postnatal development. Future work can explore factors that buffer against the effects of prenatal alcohol exposure on structural measures established in this study.

2-D-27 - Gray Matter Volume, Antisocial Behavior, and Callous-Unemotional Traits

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Details

Background: Antisocial behavior (e.g., rule breaking, aggression) has tremendous individual and societal costs. Previous studies have found that antisocial behavior peaks during adolescence. While many adolescents engage in some form of antisocial behavior, some engage in more severe forms. One leading theory is that the presence of callous-unemotional traits moderates the etiology of antisocial behavior, and moreover, there may be neural differences in individuals with or without callous-unemotional traits. Recent research has found that antisocial behavior and callous-unemotional traits are associated with differences in grey matter volume, particularly in regions associated with emotion regulation and salience detection such as the amygdala, insula, fusiform gyrus, and frontal gyrus (Rogers and De Brito, 2015).

Study Objectives: We aim to investigate whether there are gray matter volume differences associated with dimensional measures of antisocial behavior, callous-unemotional traits, and their interaction in an understudied population of youth. Moreover, as exploratory aims, we will test: (1) whether gender moderates associations between grey matter volume, antisocial behavior, and callous-unemotional traits, and (2) whether gray matter volume is differentially associated with proactive and reactive aggression.

Methods & Analysis Plan: We will test these questions in a subsample of 190 adolescents from the Future of Families and Child Wellbeing Study (FFCWS), a well-sampled longitudinal study of families enriched for exposure to poverty. At age 15, adolescents participated in a structural MRI and semi-structured clinical interview (K-SADS). Moreover, they completed self-report measures of aggression, callous-unemotional traits, and antisocial behavior. We measured antisocial behavior and callous-unemotional traits using latent factors. We hypothesize: Aim 1 - Antisocial behavior and callous unemotional traits will each be associated with reduced gray matter volume including in the amygdala, insula, frontal gyrus, and fusiform gyrus (Rogers and De Brito, 2015). We expect individuals with high levels of antisocial behavior and low levels of callous-unemotional traits will have a greater reduction in grey matter volume compared to those with high levels of callous unemotional traits, specifically in regions associated with emotion and salience processing (e.g., amygdala, putamen). Previous literature is mixed on differences in gray matter volume for boys and girls, and there were few studies evaluating proactive and reactive aggression (Michalska, Decety, Zeffiro, & Lahey, 2015; Naaijen et al., 2020). Thus, for our exploratory aims, we hope to add to budding literature by investigating these questions in a new, unique sample. We will analyze these data using the CAT12 toolbox for SPM, while controlling for pubertal status, gender, race, primary caregiver education, family income, and total intracranial volume.

Preliminary Analysis and Implications: Thus far, we have completed preliminary models for antisocial behavior, callous-unemotional traits, and aggression, and we are currently in the process of analyzing the gender moderation models. Preliminary analyses indicate grey matter volume is not associated with reactive or proactive aggression. Furthermore, neither antisocial behavior nor callous-unemotional traits

on their own were associated with differences in grey matter volume. However, the interaction between antisocial behavior and callous-unemotional traits is significantly associated with grey matter volume. Follow-up analyses are currently being conducted to examine the interaction. By Flux Congress, we expect to have completed all analyses. Through this study, we aim to better understand associations between grey matter volume and antisocial behavior and thus, better understand the etiology of antisocial behavior which may help improve prevention or treatment efforts in the future.

2-D-28 - Impact of in alcohol use on adolescent brain maturation in a longitudinal cohort

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Details

Adolescence is a time of behavioral change, brain maturation and increasing incidence of psychiatric illnesses. Adolescent exposure to alcohol is associated with increased risks for adverse outcomes, including increased risk for development of alcohol use disorder. During adolescence the brain undergoes a period of accelerated thinning of the cerebral cortex. The impact of adolescent alcohol use on brain maturation is poorly understood. Few studies have examined brain structure and alcohol use at more than two time points, which permits the disaggregation of within- and between-person effects. We used a longitudinal design and participants from a population-based cohort study (n>3800) to study substance use, mental health, and brain maturation. Participants completed annual assessments for 5 years starting at age 13. Participants in the neuroimaging sub-cohort (n=150) completed structural MRI scans at three time points for each participant (at ages 13, 15, and 17). MRI images were processed using the Freesurfer longitudinal pipeline. We will apply random effects linear mixed models to investigate between- and within-person contributions to relationships between alcohol use and brain structure. We hypothesize that within-person increases in alcohol use will affect the normal trajectory of age-related change in cortical thickness such that increased alcohol exposure will be associated with greater cortical thinning. We hypothesize the within-person effect will be observed across most brain regions, whereas the between-person effect which may reflect a common vulnerability to alcohol use will be strongest in frontal brain regions. This analysis examines the relationship between alcohol use and brain structure, including contributions of sex, alcohol use patterns, concurrent cannabis use, and risk factors for problematic substance use (e.g., sensation seeking, impulsivity). Overall, this analysis will contribute to our understanding of the impact of alcohol exposure on adolescent brain maturation.

2-D-29 - The role of stress on early thelarche & brain structure: Evidence from the ABCD® Study

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Details

Objectives: Stress has been implicated as a causal factor in early puberty for adolescent females, including the declining age of thelarche, or breast bud development. Global trends indicate a reduction in the age of thelarche by approximately 3 months per decade since the 1970s; this trend was amplified during the COVID-19 pandemic. Early thelarche is associated with significantly greater circulating hormone levels, specifically greater estradiol levels. Estradiol is neuroprotective, acting to increase neuroplasticity of the hippocampus. Sustained secretion of glucocorticoids in response to stressors during development has implications for development of the corticolimbic system, which is rich in glucocorticoid receptors. Indeed, childhood adversity has been implicated in reduced hippocampal volume and growth during adolescence in the ABCD[SM] Study. Animal models suggest that puberty may be protective for females: Brydges et al (2018) identified that adult male rats, but not adult female rats, experienced reduced adult hippocampal neurogenesis following persistent pre-pubertal stress. To date, no one has addressed hippocampal growth in human females to identify whether early thelarche is adaptive, in order to protect the hippocampus against early childhood stressors.

Hypotheses: We predict that early thelarche will be protective against the effects of stress on hippocampal growth.

Analysis Plan: The Adolescent Brain Cognitive Development[SM] Study provides a large dataset of neuroimaging, self-reported thelarche, estradiol measures, and youth-reported adverse experiences. Self-report of thelarche includes endorsement on an ordinal scale, including, no changes yet; breasts have barely started to grow; breast growth underway; breast growth is complete. Pubertal hormones measured include estradiol levels. Adverse childhood experiences reported in the demographics, life events and Kiddie Schedule for Affective Disorders and Schizophrenia will be included as stressors of interest. Utilizing Linear Mixed-Effects Modeling, we will examine the effect of adverse childhood experiences on baseline hippocampal volume and hippocampal volume changes within-subjects from baseline to Year 2 mediated by the impact of pubertal construct variable combining thelarche report and measured estrogen levels.

Significance: Given the role of the hippocampus in learning and memory in early adolescence, it is critical to understand how puberty may be protective against common, but significant, stressors, like childhood adversity among a cohort of adolescent females.

2-D-30 - Do subcortical volumes decline with age more precipitously in middle-aged and older adults with autism spectrum disorder

Michaela Cordova [1], **Kathryn Porter** [2], **Ralph-Axel Müller** [1], **Gioia Tori** [2], **Annika Linke** [1], **Adam Schadler** [3], **Kalekirstos Alemu** [4], **Stephanie Pedrahita** [1], **Molly Wilkinson** [1], **Jiwan Kohli** [1], **Janice Hau** [1], **Inna Fishman** [1], **Ruth Carper** [1]

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Details

Significant differences in volume of the striatum (caudate, putamen, and nucleus accumbens) and thalamus in people with autism spectrum disorder (ASD) - in comparison to age-matched peers without

ASD - have been linked to differences in ASD-related behaviors and neurobiology across the lifespan, including repetitive behaviors, atypical responsivity of reward neurocircuitry, and challenges relating to others. In typical control groups, volumes of these subcortical nuclei usually decrease with age across adulthood, with associated decline in memory, attention, and processing speed. Together, these findings suggest that age effects on subcortical volumes may have important implications in autistic individuals. Specifically, compared to typical individuals, middle-aged and older autistic adults could be susceptible to earlier onset, or accelerated subcortical volume decline. In this pre-registered cross-sectional study, we hypothesize steeper age-associated subcortical volume decline among middle-aged and older adults with ASD, in comparison to an age-matched group of typically developing (TD) adults. Data were collected on adults (40-70 years old), with ASD and TD participants enrolled in an ongoing longitudinal study on aging in ASD. Individuals with self-reported history of neurologic (e.g. epilepsy, head injury) or genetic (e.g. fragile X, Rett syndrome) conditions other than ASD were not included. ASD diagnoses were confirmed by an expert clinician using DSM-5 criteria, supported by the Autism Diagnostic Observation Schedule 2nd edition. TD participants had no family or personal history of ASD or other neurologic conditions or serious mental illness. Magnetic resonance imaging (MRI) data were collected on a 3T GE Discovery MR750 scanner with a 32-channel head coil at the Center for Functional Magnetic Resonance Imaging at UC San Diego. T1-weighted anatomical images (acquired with TR=8.78ms, TE=3.66ms, resolution=0.8mm^3) were visually inspected for noise, motion artifacts, and brain coverage. For the current project, an automated subcortical segmentation approach (SynthSeg, Freesurfer 7.3.1) will be used to parcellate subcortical regions. Briefly, SynthSeg employs a convolutional neural network previously trained on randomized synthetic data, to segment regions of interest (ROIs) within the brain from raw T1 MRI data and then estimates volumes for all ROIs. Bilateral thalamus, caudate, putamen, nucleus accumbens and pallidum will be selected from SynthSeg. Accuracy of SynthSeg parcellations will be reviewed using a 4 point scale (4 = excellent, 1 = unusable). Images with a rating of 4 will be included in analyses, with a rating of 3 warranting review by an independent rater for consideration of inclusion. Groups will be matched on age, sex, non-verbal IQ, and ethnicity. Data from approximately 30 ASD and 40 TD participants will be available for this project. General linear models will be applied to test for age-by-diagnosis interaction effects, as well as main effects of diagnostic group or age on each subcortical ROI, while controlling for the effects of total brain volume. We anticipate that subcortical volumes will decrease with age for both groups, with a steeper decline in the ASD group. Subcortical nuclei play a role in many of the symptoms of ASD, and they are known to decrease in size during typical aging. If our hypothesis is supported, it may be indicative of reduced resilience to typical neurodegenerative processes and raise the possibility that those with ASD may have increased vulnerability to age-associated cognitive changes previously linked to such decline in subcortical volumes.

2-D-31 - Trajectories of subcortical volume development in the Baby Connectome Project

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Details

Introduction: The first years of life represent a dramatic period of nonlinear subcortical brain development, co-occurring with a time of blossoming cognitive and behavioral skills. Densely sampled

data throughout early development is needed to capture these nonlinear trends of subcortical volume development. Previous studies of this development have focused on just the first two years of life or have been limited by small sample sizes or cross-sectional designs, making it hard to fully delineate growth trajectories during this period of rapid development. Studies are also limited by the availability of manually-corrected, early life, human brain segmentations; thus gold standard segmentations for the developing human brain remain absent. The Baby Connectome Project (BCP) and a new open repository of manually-corrected segmentations developed from it represent an exciting opportunity to evaluate subcortical volume trajectories in the first years of life.

Objective: This project aims to elucidate specific subcortical volume developmental trajectories in typically developing infants and young children, 0-5 years of age, using data from the BCP.

Methods: The BCP is a longitudinal study designed to characterize brain and behavior development in typically developing infants and young children 0-5 years old (Howell et al., 2019). T1 and T2 MRI scans were collected from infants and children using an accelerated longitudinal design, with participants completing up to six neuroimaging sessions. A subset of these scans were utilized to create an open, editable repository of manually segmented brain regions in infants and young children ('BOBs repositoryâ€), which will become available soon (also see submitted Flux Abstract: Feczko et al. 2023). For this project, all available T1 and T2 images from the BCP will be processed with a Human Connectome Project - style pipeline. This pipeline was modified to account for developing brains and will take advantage of the manual segmentations from the BOBs repository. Subcortical volumes will be pulled from this processed data, including the thalamus, caudate, putamen, pallidum, amygdala, hippocampus, and nucleus accumbens of each hemisphere.

Analysis Plans: To model trajectories of growth for each subcortical structure, generalized additive models for location, scale and shape (GAMLSS) will be used. The GAMLSS framework allows for complex nonlinear models, has been used for recent large studies of structural brain growth over the lifespan (ex. Bethlehem et al., 2022), and is recommended by the WHO for modeling growth curves. Model distributions within the 'gamlssâ€ package in R will be tested and a best fitting distribution will be selected by Bayesian Information Criteria (BIC) and Akaike Information Criteria (AIC). Spline models will be fit for each region to allow for flexible modeling of nonlinear trends and inflection points. Model goodness of fit will be checked to evaluate if fits are appropriate and meet model assumptions. If spline models do not converge or pass goodness of fit tests, alternative models will also be tested. Separate models will be fit by sex and with volumes corrected and uncorrected for total brain volume.

Hypothesis: Region-specific trajectories will be found for each subcortical structure evaluated. We hypothesize that these trajectories will differ by region, hemisphere, sex, and whether the volumes are adjusted for total brain volume.

Implications: A more complete understanding of each subcortical structure's growth trajectory will provide a foundation for future research into structural correlates of brain function and related behaviors. Identified inflection points will warrant further research as potential critical periods for development. Overall, these growth rates will become important normative data to compare with other populations of interest, such as infants born prematurely or populations at risk for developmental disorders.

2-D-32 - Cortical thickness trajectories associated with changes in language skill

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Details

Background

Cortical thickness (CT) increases rapidly in the first year of life, peaking regionally between 12-14 months before slowly decreasing over the lifespan (Bethlehem et al., 2022). Infancy is an especially important time for language development. To understand the relationship between CT and language, Qi and colleagues (2019) calculated CT in 11 language-related regions of interest (ROIs) from the Desikan-Killiany (DK) atlas and reported language improvement is influenced by a larger degree of cortical thinning in the left triangular inferior frontal gyrus as compared to the right ($r = -0.42; n = 76$).

Analysis Plan

The Baby Connectome Project was a large, accelerated longitudinal study of infant and toddler development between birth and 5 years. Currently, there are more than 500 anatomical images (8 months - 5 years) that have been processed with an in-house version of the Human Connectome Project pipeline.

With regards to language, the Mullen Scales of Early Learning (MSEL) are normed across development and test for receptive and expressive language. We will test trajectories of growth in receptive language against language areas defined by the authors (Day et al., 2023), as the DK ROIs are large. We will include trajectories over the 11 DK areas for comparison purposes. This also indicates an almost 10-fold increase in sample size.

For each longitudinal participant ($n = 148$), we will calculate mean MSEL percentile score. At each session ($n_{ses} = 420$), we will calculate the difference between the session-level CT and MSEL raw scores and the participant mean for each measure. Therefore, regressing CT on mean MSEL and MSEL change score estimates the effect of between-participant language level as well as the within-participant effect of changing language level on CT trajectories.

In addition to the analysis described above, we will control for age, hemisphere, brain-wide mean CT, total brain volume, sex, site (Minnesota, North Carolina), and the random effect of participant among right-handed participants. A model including non-right-handed participants will be considered exploratory.

Hypothesis

We hypothesize that greater language skills will be associated with greater decreases in cortical thickness, with a significant effect of hemisphere such that decreases are greater on the left. Language skills will not be associated with changes in control ROIs.

Preregistration

We are preregistering this analysis because there is anatomical processing remaining; that will only increase our power by increasing the number of sessions and number of participants with longitudinal data. A power analysis suggests that we have sufficient power (>0.9) to detect an association with an effect size (r of 0.4 = f^2 of 0.19) comparable to the findings of Qi and colleagues between change in language skill and CT using effect sizes reported by Qi and colleagues, even assuming a large correlation between brainwide CT and LH CT.

Furthermore, currently sessions below 0;08 are not available. This encompasses the ages of linear decrease, but including sessions below 0;08 will allow us to model the quadratic effect of age in an exploratory analysis. However, the CDI is not normed below 0;08 so this will be a structural approach only.

Conclusions

We have begun to understand the effect of language development on the structural properties of the brain. Performing this analysis in the largest sample yet of typically developing infants and toddlers will further elucidate CT trajectories and their influence on behavior.

References

Bethlehem et al. (2022). *Nature;* Day et al. (2022). *Flux 2022*; Desikian et al. (2006). *NeuroImage*; Qi, Schaadt, & Friederici (2019). *Dev Cog Neuro.*

E – Clinical populations

2-E-33 - Differences in intra- and interhemispheric white matter connectivity in children with down syndrome and autism

Dea Garic [1], **Rebecca Grzadzinski** [1], **Khalid Al-Ali**, **Robert Mckinstry** [2], **Kelly Botteron** [3], **Natasha Marrus** [2], **Stephen Dager** [4], **Annette Estes** [5], **Guido Gerig** [6], **Heather Hazlett** [7], **Martin Styner** [1], **Joseph Piven** [7], **Robert Schultz** [8], **Juhi Pandey** [9], **Tanya St. John** [5], **Mark Shen** [7]

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Details

Background: Down syndrome (DS) is the most common genetic cause of intellectual disability, with a prevalence rate of 1 in 700 live births. Despite this, our understanding of white matter (WM) connectivity in DS remains limited, with only about six diffusion weighted imaging studies with matched controls conducted to date. Most reports are in adults with DS, who have widespread reductions in WM integrity as indexed by fractional anisotropy (FA). Only one study has examined WM microstructure in children with DS compared to typically developing (TD) children, with results suggesting lower FA particularly in the bilateral uncinate (UNC) and right inferior longitudinal fasciculus (ILF). The modest sample size of that study (n=10 DS, aged 2-4 years) requires further investigation.

Another limitation of previous WM microstructure studies in DS is the reliance on diffusion tensor imaging (DTI), which is unable to parse out crossing fibers and disentangle microstructural characteristics (e.g., myelination, axonal and neurite density). With multishell diffusion acquisition, it is possible to generate more sensitive microstructural data from High Angular Resolution Diffusion Imaging (HARDI) and Neurite Orientation and Dispersion Imaging (NODDI) models.

We included another comparison group, children with autism, since DS and autism have significant shared symptomatology but potentially divergent brain development, with DS typically associated with decreased brain volume, while autism has been linked to early brain overgrowth. By leveraging data from concurrent clinical cohorts scanned under identical imaging protocols in the Infant Brain Imaging Study, we aim to compare WM structural differences across multiple diffusion models in children with DS, autism, and typical development.

Methods: The sample consisted of 103 children (DS=25, autism=27, TD=51) between the ages of 7 to 12 years (*M*=9.85, *SD*=1.06). Nine major intrahemispheric fiber pathways were examined: bilateral frontotemporal arcuate (arcuate FT), temporoparietal arcuate, cingulum, parietal corticofugal, fornix, inferior fronto-occipital fasciculus (IFOF), optic radiation, ILF, and UNC. Two interhemispheric pathways were examined: splenium and tapetum. Analysis of variance models were conducted to first examine group differences on average DTI, HARDI, and NODDI values in core intrahemispheric WM (aggregate of all nine intrahemispheric pathways per hemisphere), then for each tract individually. All analyses covaried for age, sex, and intracranial volume. Significance values were adjusted for multiple comparisons using False Discovery Rate.

Results: The DS group had lower FA, generalized FA (GFA), axial diffusivity (AD), and higher orientation dispersion (ODI) in left core intrahemispheric WM than both the autism and TD groups. The right hemisphere had similar patterns, but only AD reached significance. Core intrahemispheric group differences were driven by differences in the bilateral IFOF, left ILF, right UNC, and right arcuate FT. The fornix was observed to have a unique pattern, with higher MD, RD, AD, and lower ODI in the DS group, which will be further discussed. On the other hand, interhemispheric connectivity showed an opposing pattern: children with DS had higher FA, GFA, and neurite density (NDI) in the tapetum compared to other groups. This same pattern was also observed in FA and NDI of the splenium. No significant differences were found between the autism and TD groups.

Conclusion: Taken together, results suggest that children with DS have a pattern of less coherent intrahemispheric connectivity, but denser neuronal packing and greater WM integrity within interhemispheric pathways, compared to children with autism and TD. These findings provide early insight into WM development in school-aged children with DS and have the potential to further elucidate microstructural differences than what has previously been observed through DTI models alone.

2-E-34 - Alterations in Visual Oscillatory Dynamics in Children with Mild-to-Severe Hearing Loss

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Details

Objective: Hearing loss has been associated with a wealth of language and academic delays in children. Interestingly, prior work suggests that there is a compensatory enhancement of bottom-up visual processing in deaf individuals compared to those with normal hearing, but that this is coupled with decrements in visual selective attention ability. In other words, while deaf individuals excel in broad visual perceptive ability, they have difficulty selectively focusing attention and inhibiting distracting information. However, whether these differences in visual perception are also found in children with more moderate degrees of hearing loss, commonly termed children who are hard of hearing (CHH), remains to be clarified. The current study sought to identify the neural dynamics that underlie visual processing in CHH and a matched group of children with normal hearing (CNH).

Methods: A total of 46 children, including 25 CHH aged 7-15 years with mild-to-severe hearing loss (i.e., better-ear pure tone average between 20 and 79 dB) and 21 CNH participated in this study. Participants were told to fixate on a crosshair presented centrally. After a baseline period, an 8x8 checkerboard grid was presented for 800 ms at one of four positions relative to the fixation: above right, below right, above left, or below and to the left. The left/right orientations were defined as a lateral offset of 75% of the grid from the center of fixation. Participants were instructed to respond whether the grid was positioned to the left or right of the fixation point. These responses served to ensure that the participants were paying attention. All MEG data was transformed into the time-frequency domain, and significant oscillatory events were imaged using beamforming. The resulting SPMs were compared between groups using independent samples t-tests. Groupwise difference maps were thresholded at $p < .01$ and corrected for multiple comparisons using a cluster-based method based on the theory of Gaussian random fields.

Results: Participants performed this task generally well, and there were no significant differences in accuracy or reaction time in CHH compared to CNH. Time-frequency results indicated a strong, transient theta (4-8 Hz) ERS immediately after grid onset, followed by a sustained alpha ERD (9-14 Hz), and gamma ERS (66-84 Hz) bands, which temporally corresponded to visual processing prior to the behavioral response. Independent-samples t-tests showed frequency-specific alterations in these responses between CHH and CNH, where CHH showed increased gamma ERS activity in superior parietal regions relative to CNH, coupled with significant decreases (i.e., more negative) in parieto-occipital and temporo-parietal alpha ERD in regions (all p's < .01, corrected). There were no differences in theta ERS activity between groups.

Conclusions: These results provide preliminary tevidence of altered visual processing in CHH compared to CNH, in line with studies of individuals with severe-to-profound loss. Future work should investigate whether these alterations in visual processing predict performance on behavioral tasks, and whether alterations in visual processing transcend into higher-order visual selective attention ability.

2-E-35 - Neural Mechanisms of Sensory Over-Responsivity Across Clinical Groups

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Details

Intro: Sensory over-responsivity (SOR) is a heightened response to sensory stimuli, which can cause significant impairments in daily functioning. SOR is common across a wide variety of clinical groups including autism (ASD), anxiety disorders (ANX), and those who experience early caregiving adversity (ECA). Despite its transdiagnostic prevalence, little is known about the similarities and differences in the neurobiological processes underlying SOR across these groups. Research has indicated that in ASD, higher levels of SOR correlate with an over-active neural response to sensory stimuli in salience and sensory-processing related brain regions, however, limited research exists on SOR outside of ASD. Understanding neural mechanisms of SOR across clinical groups is important to developing tailored interventions for SOR in different populations.

Aim: This study aimed to investigate commonalities and differences in neural responses to aversive sensory stimuli and their relationship to SOR symptomatology in ASD, ANX, and ECA youth compared to typically developing youth.

Methods: We will report on two unpublished studies, one comparing 27 children and adolescents with ECA, 30 youth with ASD, and 26 non-adopted, typically developing controls (TD). The second compared 19 ANX with 20 TD youth. Groups were matched on age and sex. IQ was included as a covariate in group analyses where groups were not matched on IQ (i.e., ECA and TD). Participants, ages 8-18 years, were presented with 6 15-sec blocks of mildly aversive tactile (scratchy fabric rubbed on the forearm) and auditory (pulsing white noise) stimuli during fMRI. Parents completed the Sensory Processing 3-Dimensions (SP3-D) Inventory to report on their chil's SOR. FMRI analyses were performed at a threshold of $Z=2.3$, $p>.05$. SOR scores were entered into bottom-up regressions with anxiety symptoms (parent report on the SCARED) covaried to examine how SOR behaviors uniquely predict brain responses in each group.

Results: Clinical groups showed increased SOR scores compared to TD: ASD ($M=8.67$, $p<.001$), ANX ($M=7.12$, $p= 0.01$), ECA($M=4.35$, $p=.03$). Compared to rest, ASD, ANX, and ECA groups all exhibited increased neural activity during sensory stimulation compared to the TD group. The ASD group demonstrated widespread areas of increased activity while the ANX and ECA groups showed more limited overactivation in sensorimotor and frontal cortices (orbital frontal cortex in ANX and supramarginal gyrus in ECA). In the ASD group, higher SOR related to increased activation, particularly in visual processing regions (left precuneus and lateral occipital cortex). In the ANX group, SOR correlated with activity in frontal regions (e.g., superior frontal gyrus, anterior cingulate cortex). The ECA group showed a unique pattern in which *lower* SOR corresponded to increased activation in subcortical (thalamus, limbic regions, and basal ganglia) and cortical regions (prefrontal cortex, precuneus, and sensory cortices).

Conclusion: All three clinical groups demonstrated hyperreactivity across brain regions during aversive sensory stimuli compared to TD peers, consistent with higher SOR seen in these groups. More widespread hyperactivity and correlations with SOR in the ASD youth is consistent with the highest levels of SOR in this group. The other two groups showed more specific regions of hyperactivity, particularly in sensorimotor and frontal cortices. Limited correlations with SOR in the ANX group suggests that other symptoms, such as anxiety, play a role in the strong neural response to sensory stimuli. The ECA group's unique pattern of higher SOR correlating with lower reactivity could reflect that the highest levels of SOR in this group were relatively mild, or might suggest mechanisms of resilience toward SOR in ECA youth. Taken together, these findings indicate potential differences in underlying mechanisms of SOR across groups and reaffirm the importance of investigation into SOR across diagnoses.

2-E-36 - Maturational trajectories of the acoustic radiations, and links with sensory sensitivities and sleep problems in young children with autism

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Details

Thalamocortical projections relay sensory information from the periphery to primary sensory cortices and play a crucial role in early cortical development and sleep regulation. Atypical functional connectivity (FC) between the thalamus and sensory cortices has been reported in autism spectrum disorder (ASD) across the lifespan and is linked to sensory and sleep problems in young children with ASD. Atypical maturation of the acoustic radiations (AR), the primary auditory tract (connecting the thalamus and auditory cortex), has been reported in school-aged children with ASD. The present multimodal study will be the first to examine the ARs in young children with ASD, and relationships between structural and functional auditory-thalamic connectivity, atypical auditory processing, and sleep problems. We hypothesize the following: (H1) Toddlers and preschoolers with ASD will show increased AR fractional anisotropy (FA) derived from tractography compared to typically developing children (TD), (H2) an increase in FA with age will be observed within the TD group but not in the ASD group, and (H3) increased AR FA in the ASD group will be linked to increased thalamocortical FC, higher sensory sensitivities and greater sleep problems. Archival data from 38 children with ASD and 27 TD children, between ages 1.5-5 years, enrolled in the longitudinal SDSU Toddler MRI Project will be analyzed. The two groups will be matched at group level on age, sex, socioeconomic status (e.g., household income-to-needs ratio), and MRI data quality. Measures of sensory sensitivities and sleep problems will be derived from caregiver reports (Sensory Profile, Child Behavior Checklist, and an in-house sleep questionnaire). Multiband diffusion (93 directions at b = 1500 and 3000s/mm^2 and 6 b0s, 1.7 mm isotropic resolution, 2x7min.) and functional (TR=800ms, 2 mm isotropic voxel size, 2x6min.) Magnetic Resonance Imaging (MRI) data were acquired during natural sleep. Diffusion Magnetic Resonance Imaging (dMRI) data will be preprocessed using eddy from FSL. Tissue-specific fiber orientation distributions (FOD) will be estimated using constrained spherical deconvolution and normalized across tissue types using MRtrix3. Anatomically constrained probabilistic tractography will be run on white matter FODs (see regions of interest [ROIs] below). Functional Magnetic Resonance Imaging (fMRI) data will be preprocessed using SPM12 and the conn toolbox. AR tractography (5000 seeds per voxel, combining reversed trackings between ROIs) will be assessed between two ipsilateral ROIs: Heschl's gyrus (HG) and the thalamus as defined by the Harvard-Oxford atlas. Microstructural measures will be obtained by sampling values from scalar maps (i.e., FA and mean diffusivity derived from the DTI model, and neurite density and orientation dispersion derived from the NODDI model) along streamlines and averaging them for the tract. We will test (H1, H2) for differences in AR microstructure using a general linear model including the main effects of diagnostic group, age, and group-by-age interactions (controlling for in-scanner-head motion [RMSD]). Associations between AR microstructure and functional connectivity (Fisher-z-transformed Pearson correlation of fMRI time series between ROIs derived from tractography endpoints) as well as associations with sensory sensitivities and sleep problems (H3) will be assessed within the ASD group only using partial correlations (controlling for age and RMSD). A threshold of p<.05 FDR-adjusted to determine significance will be utilized.

Understanding how atypical thalamocortical connectivity is related to sleep and sensory problems may have implications for infants at risk of ASD as the auditory system is among the earliest to mature and is vulnerable to disrupted thalamocortical development. This study may contribute to designing early interventions during the critical period when they are most effective.

2-E-37 - Relating Parental Buffering of their Child's Neural Reactivity to Threat to Family Accommodation of Anxiety

Elizabeth Kitt [1], **Alexis Broussard** [1], **Sadie Zacharek** [2], **Cristina Nardini** [3], **Grace Hommel** [4], **Maya Barr** [1], **Gillian Weeks** [1], **Alison Magnotti** [1], **Paola Odriozola** [5], **Carla Marin** [4], **Wendy Silverman** [4], **Eli Lebowitz** [4], **Dylan Gee** [1]

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Details

Childhood anxiety disorders are highly common and are associated with significant distress and impairment in youth's daily lives. Parenting behaviors play a critical role in childhood anxiety disorders. Parental neural buffering can regulate anxious children's responses to major stressors, and parental presence has been found to encourage approach-related behaviors that are important for treatment. However, overreliance on parents has long-term consequences for anxious children's fear reduction. The majority of parents of youth with anxiety disorders report engaging in accommodation of their chil's anxiety (i.e., changing their own behaviors and schedules in an attempt to diminish or prevent their chil's distress). It is possible that this behavioral overreliance on parents is accompanied by an overreliance on parents to buffer children's responses to fear at the neural level. However, neural processes that may relate to family accommodation are unknown. Examining how parental neural buffering relates to family accommodation could improve our understanding of how laboratory-based, neural measures relate to observable, clinically relevant behaviors.

Using a sample of 168 children (ages 6-12) with primary anxiety disorders, this study will examine the ways in which neural measures of parental threat buffering relate to parental accommodation of their chil's anxiety. Families first complete an initial screening visit, during which they complete the child- and parent-reported versions of the Family Accommodation Scale for Anxiety. Following this screening visit, families return for a separate MRI scanning visit, during which they complete two runs of an event-related fMRI task measuring parental modulation of children's neural reactivity to fearful versus neutral face stimuli. In each run, participants view a series of face stimuli (24 with a fearful expression, 24 with a neutral expression) selected from the NimStim set of facial expressions. Child participants complete two runs of this task: one while alone in the scanner room ('Parent-Absent Conditionâ€) and one while their parent is physically present in the scanner room holding their chil's hand ('Parent-Present Conditionâ€). The order of these two task conditions is counterbalanced across participants. Data collection is ongoing but will be completed before the conference.

We hypothesize that higher levels of family accommodation will be associated with elevated parental modulation of activation in the amygdala, insula, anterior cingulate cortex, and ventromedial prefrontal cortex. In addition, we predict that elevated family accommodation will be associated with altered

connectivity between these regions. To test these hypotheses, we will run a general linear model testing associations between family accommodation and parental neural buffering (the contrast between neural activation in the Parent-Present Condition and the Parent-Absent Condition) across the whole brain. We will then use psychophysiological interaction (PPI) analysis with the left and right amygdalae as seed regions of interest to examine accommodation-related patterns of connectivity across the brain. All analyses will control for child sex and age. All analyses will be completed before the conference.

This study has the potential to bridge two growing lines of research on parental neural buffering and family accommodation of anxiety. While parental behaviors intended to reduce their chil's anxiety are common in families with anxious youth, no study to date has examined neural patterns associated with these behaviors. Relating parental neural buffering to family accommodation will provide novel insight into how basic neural mechanisms of fear responding may translate into maladaptive behavioral patterns.

2-E-38 - Comparing Brain Laterality in Children with Neurodevelopmental Disabilities: A Reproducible Study

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Details

Brain laterality (BL), defined as the asymmetric size of cortical areas devoted to a given task between the left and right brain hemispheres is a property of functional and structural brain organization linked to cognitive, motor, language, and visuospatial functions. Over the years there has been a tremendous amount of work on BL that has found inconsistent results regarding BL, its developmental trends, and its associations with developmental disabilities. Recent findings suggest that some of these inconsistencies might be due to small sample sizes, insufficient statistical power, and heterogeneity in methodology and experimental designs. Additionally, BL measures typically have focused on a few regions, rather than examining how BL from multiple regions may contribute to developmental outcomes. Therefore, there is a need to validate and reevaluate the current fMRI results with adequate sample size, threshold, and accurate inferential techniques.

Objective: Here, we will explore BL in the typical population and then explore whether BL is similar in neurodivergent groups. **Methods and analysis:** For this purpose, we will examine four large and distinct resting-state fMRI datasets: *Adolescent Brain Cognitive Development (ABCD),* a longitudinal study, with over 11,000 typical children, ages 9 to 19, *the Healthy Brain Network (HBN)* with over 3,000 subjects (ages 5-21) from multiple sites and multiple respondents (child, parent, teacher) for clinical, cognitive, and behavioral phenotypes; *the* Oregon's longitudinal *ADHD and ASD datasets* with 300 subjects (ages 7-21) with over 1200 longitudinal scans along with phenotype data (age, gender, diagnosis score and status, IQ). We will compare BL patterns among neurotypical (using ABCD) and neurodiverse (HBN, Oregon's ADHD, and ASD) children and investigate the effect of demographic variables, age, gender, and diagnosis on BL. Our analysis steps are as follows: The ABCD-BIDS pipeline will be used to process the data. We will use a homotope matching method (i.e., matched left and right brain regions) to select regions that we will use.

To calculate laterality, a novel package based on mixing source time series will be applied, namely the Crossotope_mapping package. An Integrated Laterality Index (ILI) will be created based on cubic fit integration. Then, the correlation between ILI and age will be computed in our main datasets (autism, ADHD, and typical group) to explore the predictability of age. **Hypothesis:** Our hypothesis is that there will be differences in BL patterns between neurodiverse and neurotypical group. We also anticipate that age will play a significant role in BL, with older children showing more developed BL patterns. **Implications:** The project will help us to better understand how BL patterns develop in children and young adults with neurodevelopmental disabilities compared to typical children. This will provide new insights into the clinical phenotypes of these conditions, which can be heterogeneous in terms of disability.

2-E-39 - The impact of methylphenidate on the functional hubness of striatal regions in children with ADHD

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Details

Psychostimulants, such as methylphenidate (MPH), are a highly effective first-line treatment for ADHD. MPH is well-known to block dopamine reuptake in the striatum, but the mechanism by which this improves symptoms of ADHD is unclear. Theoretical models and empirical findings point to alterations in functional connectivity (FC) as one possible mechanism, yet results have been heterogeneous and mixed. One promising analytic technique to characterize changes in FC after the administration of MPH is graph theory. Graph theory allows us to characterize how brain regions targeted by MPH may act as hubs at the network level, contributing to changes in both local and global topology. Thus, this study will aim to characterize how the topological roles of regions of the striatum in functional networks in children with ADHD change after MPH administration and will further compare their roles to those in typically developing (TD) children.

Participants 8-12 years old participated in this study (n = 36 psychostimulant-naÃ¯ve children with ADHD and 30 TD children). Participants received two fMRI scans, and those with ADHD were administered MPH or placebo at the two MRI sessions in a double-blind, crossover design. Participants completed resting state scans, as well as a series of cognitive tasks, including standard and rewarded versions of a go/no-go task, in the scanner. Functional connectivity will be estimated from time series concatenated across all tasks. For the task runs, task events will be included as nuisance regressors to remove task-induced signal, resulting in a single time series per session assessing background functional connectivity. A functional brain atlas including cortical and subcortical with 300 spherical regions of interest (ROIs) will be used (Seitzman et al., 2020). Time series data will be averaged within each ROI and correlation matrices from these averaged time series will be generated. The optimal partition of communities will be determined individually for each correlation matrix using the consensus clustering method. Finally, hub characteristics of the 14 striatal ROIs (2 ventral striatum, 4 caudate, and 8 putamen) within the whole-brain network will be calculated using the Brain Connectivity Toolbox. First, degree strength, betweenness centrality, and nodal efficiency will be used as measures of overall hubness of the nodes. Next, within-module degree (WD) and participation coefficient (PC) will be calculated to assess the degree of network segregation (WD; within-network connectivity) and network integration (PC;

between network connectivity). The three groups (ADHD on MPH, ADHD on placebo, and TD) will be compared using mixed effects models, using age, biological sex, and mean FC as fixed effects. For each graph metric and node, one model will compare participants with ADHD on and off MPH and the other model will compare participants with ADHD to TD participants.

We hypothesize that striatal nodes will be more hub-like, with higher degree strength, betweenness centrality, and nodal efficiency, in children with ADHD on placebo compared to MPH and children with ADHD on placebo compared to TD children. We further hypothesize that both WD and PC will be higher in children with ADHD on placebo compared to both children with ADHD on MPH and TD children. The findings of this study will contribute to the ongoing literature exploring the neural underpinnings of ADHD and the impact of psychostimulants on brain network architecture, aiding efforts to improve the diagnosis and treatment of ADHD.

2-E-40 - Developmental trajectories of fronto-amygdala and hippocampal-dorsal anterior cingulate cortex neural circuitry and associations with anxiety in early adolescence

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Details

Adolescence is a peak time for the onset of psychiatric illnesses, with anxiety disorders being the most common and affecting as many as 1 in 3 youth (Kessler et al., 2005). Although evidence-based interventions such as cognitive behavioral therapy (CBT) can be highly effective for many youth with anxiety disorders, up to 50% of both clinically anxious youth and adults do not benefit sufficiently from CBT (e.g., Creswell et al., 2020). Furthermore, interventions for youth with anxiety are largely based on treatment principles studied and implemented in adulthood that fail to account for the dynamic changes that occur in relevant neural circuitry during adolescent brain development.

Extensive research across species has shown that cortical-subcortical interactions primarily involving the amygdala, ventromedial prefrontal cortex (vmPFC), dorsal anterior cingulate cortex (dACC), and hippocampus are central to fear learning and extinction (e.g., LeDoux, 2000). In adolescence, projections from the vmPFC to the amygdala undergo protracted development (Cunningham et al., 2002). These projections are involved in fear extinction learning (Davis & Whalen, 2001), which is diminished during adolescence across rodents and humans (Pattwell et al., 2012). In parallel, projections between the prelimbic cortex (PL) in rodents, which corresponds to the dACC in humans, and the amygdala are involved in fear maintenance (Burgos-Robles et al., 2009) and are augmented in adolescent rodents (Pattwell et al., 2016). Similarly, projections from the hippocampus to the PL are strengthened in adolescence relative to adulthood in rodents (Pattwell et al., 2016). However, the developmental course of these fronto-amygdala and hippocampal-dACC pathways have not yet been investigated in human youth.

In the proposed study, we will use longitudinal data from the Development of Anxiety in Youth Study (GalvÃ¡n & Peris, 2020), a prospective longitudinal study of n=120 youth (ages 9-13 at baseline) across the anxiety spectrum who were followed annually for 3 years. We will use seed-to-seed functional

connectivity analyses applied to resting state fMRI data to investigate the developmental trajectories of fronto-amygdala and hippocampal-dACC circuitry. In addition, we will investigate associations between the developmental trajectories of this neural circuitry and anxiety symptoms using the Screen for Child Anxiety Related Disorders (SCARED) child report questionnaire. We will use a mixed effects regression analysis with *lme4* implemented in R to model longitudinal changes in functional connectivity of each seed-to-seed pair while controlling for sex differences. Finally, we will conduct a separate time-varying effect model to examine the relation between changes in functional connectivity and anxiety symptoms over time. Data collection is ongoing but is ~97% complete and will be finalized by June 2023; data compilation, cleaning, and preprocessing has been completed for existing data and will be completed for any new data acquired; analyses have not been conducted to date, but will be completed by the 2023 Flux Congress.

We hypothesize that, as in rodents, youth will show increasing functional connectivity in both hippocampus-dACC and dACC-amygdala pathways over development. We also hypothesize that higher anxiety between-subjects will be related to weaker hippocampal-dACC functional connectivity but stronger dACC-amygdala functional connectivity.

Delineating the developmental timing of fronto-amygdala and hippocampal-dACC circuitry is particularly important for understanding developmental differences in fear learning and extinction, which are core components of anxiety. During adolescence, when fear extinction is diminished and fronto-limbic circuitry is undergoing substantial changes, it may be especially beneficial to develop or optimize neurodevelopmentally informed interventions for anxious youth that acknowledge the biological state of the developing brain.

F- Education

2-F-41 - Educational Environment is Related to White Matter Development

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Details

Introduction

Students who are fortunate to attend high quality schools demonstrate better performance across academic domains including reading and math. Furthermore, educational intervention studies have shown that changes in the educational environment can drive both learning and lead to changes in white matter properties (Huber et al., 2018). In contrast, demographic factors, such as parental income and education, have been shown to relate to white matter development. We used longitudinal data from the ABCD dataset to explore whether the educational opportunities afforded to an individual relates to the development of white matter tissue properties above and beyond other demographic factors.

Methods

We used data from the Stanford Education Data Archive (SEDA), which provides measures of the quality of each participant's educational context. SEDA uses standardized test scores from nearly every school in the United States to generate achievement scores for each school relative to the national average. This score can be thought of as the quality of educational opportunity afforded by the school. We performed a median split using SEDA scores to classify each participant as belonging to relatively high or low quality educational environments.

We also leveraged the preprocessed longitudinal diffusion MRI data available in the ABCD dataset. Tractography was performed on these data using DIPY (Garyfallidis et al. 2014) and tractometry was performed using pyAFQ (Kruper et al., 2021). We first conducted univariate comparisons of the diffusion kurtosis imaging metrics between SEDA groups across a left-lateralized network of white matter tracts that have been linked to academic skills, as well as their right lateralized counterparts. We then trained a machine learning model (XGBoost; Chen & Guestrin, 2016) on diffusion and demographic data to explore high-dimensional predictions of SEDA scores. Finally, we constructed longitudinal growth models to examine the relationship between SEDA scores and change in fractional anisotropy.

Results

A comparison of white matter properties across SEDA score groups revealed group differences in diffusion properties, as well as correlations between white matter properties and SEDA scores. Furthermore, machine learning models suggested that the addition of white matter features to the model slightly increased the explained variance in SEDA scores, above and beyond what is explained by other demographic factors alone. We then leveraged the longitudinal ABCD data to explore intraindividual change in the white matter while controlling for parental education, income, and broader demographic factors. Not surprisingly, growth models replicate past findings that show developmental changes in the white matter as a function of age. However, these models also revealed a significant age by SEDA interaction in a series of left-lateralized bundles that have been implicated in reading and math skill in the past. Decomposing this interaction revealed that white matter development is accelerated in the left arcuate, SLF, and ILF for individuals in schools with higher SEDA scores, even when controlling for known demographic effects.

Conclusions

The present analysis found both cross-sectional and longitudinal links between the quality of an individual's educational environment and their white matter in a large, diverse sample. Multivariate models suggested that a chil's educational environment is related to white matter development above and beyond the influence of other demographic factors. Furthermore, growth modeling suggested the rate of white matter maturation in the left arcuate, left SLF, and left ILF is higher in individuals from schools with higher SEDA scores. Together, these findings suggest that the quality of an individual's school environment may lead to measurable differences in white matter properties and that differences in educational quality shape developmental trajectories in white matter.

2-F-42 - White Matter Plasticity in Response to Educational Intervention in Reading Disability

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Details

Background and Objectives: Reading disabilities are the most common learning disability, impacting an estimated 15% of school-age children. Summer reading interventions for children who struggle to read may help in mitigating skill regression associated with breaks in formal education, reducing the skill gap between high- and low-achieving readers. Reading is a complex task enabled by a distributed left-lateralized network in the brain, and white matter tracts are responsible for communication between nodes in this network. As a skill that must be explicitly learned, reading offers a unique and educationally relevant window into learning-driven neural plasticity. Diffusion-weighted imaging (DWI) can be used to non-invasively infer microstructural properties of white matter *in vivo*. Few studies have examined how such white matter properties change in relation to intensive short-term structured reading instruction, and those study results have not converged. In this study, we examined longitudinal cognitive and DWI data from 41 children (ages 7-9; starting grades 2-3) with reading disabilities who were (n = 26) or were not (n = 15) randomly assigned to a summer reading intervention, investigating whether improvements in reading were associated with changes in white matter properties. Notably, the educational curriculum was the same as that employed in another DWI reading intervention study (Huber et al., 2018, 2021), allowing an opportunity to more directly explore the generalizability of previous findings.

Methods: Standardized reading assessments and DWI data were collected before and after an intensive 6-week reading intervention (Lindamood-Bell Seeing StarsÂ® Program). The Symbol Imagery Test (SIT), which is a measure of phonological-orthographic associations closely linked to the intervention approach, was used as a proximal outcome. A reading composite index of four timed and untimed word reading age-normed subtests (*Woodcock Reading Mastery Test, 3rd Edition,* Word Identification and Word Attack subtests; *Test of Word Reading Efficiency 2nd Edition*, Sight Word Efficiency and Phonemic Decoding Efficiency subtests) was used as a distal outcome. From the DWI data, fractional anisotropy (FA) and mean diffusivity (MD) were calculated at each time point for 7 white matter tracts: the splenium of the corpus callosum and bilateral arcuate fasciculi (AF), inferior longitudinal fasciculi (ILF), and corticospinal tracts (CST). The CST and right-lateralized tracts were chosen as control tracts that are not expected to be sensitive to variation in reading skills, while the remaining bundles are thought to directly support reading. We ran ordinary least squares models to relate change scores in reading measures with changes in tract properties, controlling for age at first scan, sex, and image quality at each time point.

Results: The reading intervention group had gains in reading scores compared to the non-intervention group, who declined in performance. Across all participants, decreases in MD in the left AF ($p = 0.037$), ILF ($p = 0.010$), and splenium ($p = 0.082$) were associated with improved SIT scores. Increases in FA in the left CST ($p = 0.034$) and left AF ($p = 0.094$) were associated with improved SIT scores as well. However, for the composite reading index, there was only a trend of lower MD in the splenium ($p = 0.066$) relating to improvements in reading scores.

Conclusions: Our findings suggest that changes in core reading circuitry are associated with proximal, but not distal, outcomes related to reading intervention. These results partly converge with prior findings of widespread global changes in MD in relation to the composite reading index (Huber et al.,

2018). While studies with larger samples may resolve inconsistencies in findings, it is also possible that neural correlates of reading intervention may vary in relation to the specific characteristics of individuals participating in different studies.

G – Environment (Stress, SES)

2-G-43 - 'Namaskaar! Namaste! Konnichiwa!': What do we know about Multilingualism In Deaf & Hard-To-Hear Children And Their Language Development?

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Details

Language development is crucial in a chil's early life. It can impact many cognitive skills if delayed or deprived of exposure to them. If a child at an early age is not exposed to their first language, in that case, it can lead not only to language deprivation but also cause a delay in memory organisation and numerical manipulation (Humphries et al., 2012). Around 80% of developed countries have access to different hearing aids that can help a child listen and talk (Humphries et al., 2012). However, it is tougher for those from a lower socioeconomic (SES) background to access such services (Ambrose SE, Walker EA, Unflat-Berry LM, et al; Meinzen-Derr et al., 2018). It becomes important to look at how deaf and hard-to-hear children (DHH) from a multilingual environment learn and process language. Literature from the past few years has suggested mixed observations of understanding communication impairments in DHH multilingual children and the impact it has on overall development. (Crystal, 2003; Romaine, 2013; Cannon et al., 2016; Crowe & Guiberson, in press). As young children grow up, they rely heavily on sounds to hear, understand, and speak different words from an early age. However, since most studies are reported to have been conducted in the Global North, this review focuses on studies from the Global South, which is believed to be rich in and home to many multilingual individuals, and yet is underrepresented in research (Draper et al. 2022). With the limited research conducted on the DHH children, the objective of this review, which is currently on-going, is to examine how the DHH children from a multilingual environment from the Global South learn and process language. The second aim of this review is to investigate the role played by socioeconomic status (SES) in how DHH children acquire and process multiple languages from their environment. Research in this area is seldom conducted or reviewed, given that this is a unique challenge, and yet an important area in understanding the DHH community. This review shall follow the methodology of conducting a systematic literature search with a set of keywords (Multilingualism, SES, DHH, Language Processing, Language Acquisition, Language development, global South) which will result in a comprehensive evidence map (Miake-Lye et al., 2016) that will help formulate an overview of DHH children in the context of language acquisition. Once all the papers are collected and screened by abstracts, they would then be screened by full papers subsequently and will be segregated by applying pre-defined inclusion/exclusion criteria, which would then finally be followed by data categorization and extraction for a holistic and systematic analytical review. Insights from these would be used to inform original empirical research for effective interventions and policy formulation to aid the integration of this population, which has been historically understudied and underrepresented in research in spite of the unique characteristics they possess, into the mainstream.

2-G-44 - Associations of Mother-Child Closeness, Adolescent Symptomatology and Structural Brain Networks

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Details

Introduction: Mother-child closeness is an essential aspect of positive parenting that reflects the quality of the caregiver-child relationship. Prior research suggests that greater mother-child closeness is associated with lower rates of adolescent internalizing symptoms, yet multi-informant approaches to examining closeness across multiple time points in population-based samples are lacking. Moreover, while some preliminary studies have explored the relationship between positive parenting and the brain, no research has investigated the neural correlates of mother-child closeness. Caregiving practices are critical to support the development of neural structures, specifically white matter structures that facilitate information transfer in the brain. Such investigations can advance our understanding of potential biological mechanisms relating to mother-child closeness and adolescent mental health. Our study consisted of two aims. First, we examined the associations between mother-child closeness and internalizing symptoms in a population-based sample. Second, we investigated the associations between mother-child closeness, neural network architecture, and internalizing symptoms in a subsample.

Methods: In the first analysis (N=3872 from The Future of Families and Child Wellbeing Study), we examined whether mother-child closeness is linked to adolescent internalizing symptoms. Then, in a subgroup of the full sample (Study of Adolescent Neurodevelopment; N=237), we examined whether mother-child closeness was associated with adolescent internalizing symptoms and white matter structural network organization. Mother-child closeness was assessed by averaging mothers' and children's self-reported ratings of their level of closeness with each other at ages 9 and 15. Adolescent internalizing symptoms were measured using latent variables constructed from children's self-reported depression and anxiety at age 15. Structural network organization was assessed by applying graph analysis on diffusion MRI-based white matter connectomes at age 15. The analysis focused on topological properties of structural networks using measures of global network efficiency (how quickly information transfers from one end of the network to the other), transitivity (how nodes are clustered together), and modularity (how easily it is for the network to be subdivided into segregated groups). All analyses were adjusted for covariates, including average household income from birth to age 15, maternal marital status at birth, maternal educational status and depression at age 15, children's sex at birth, race, and pubertal development at age 15.

Results: There was a negative relationship between mother-child closeness and adolescent internalizing symptoms. Greater mother-child closeness was associated with lower internalizing symptoms (full sample: $\hat{I}^2 = -0.234$, $p < 0.001$; sub-sample: $\hat{I}^2 = -0.171$, $p = 0.008$). There was a positive relationship between mother-child closeness and two network metrics. Greater mother-child closeness was associated with greater global network efficiency ($\hat{I}^2 = 0.186$, $p = 0.009$) and greater transitivity ($\hat{I}^2 = 0.189$, $p = 0.008$), but not with modularity. There were no associations between network metrics and internalizing symptoms.

Conclusion: Our study utilized a population-based sample to investigate the link between mother-child closeness and internalizing symptoms, followed by examining its association with whole-brain neural network architecture in a sub-sample. Greater mother-child closeness is associated with lower internalizing symptoms in adolescence. Additionally, greater mother-child closeness is related to greater global efficiency and transitivity. Our findings are the first to indicate that differences in structural network organization may emerge from parent-child closeness. Future studies with larger neuroimaging data are necessary to generalize these findings.

2-G-45 - Examining the Relation of Depriving and Threatening Childhood Experiences to Mechanisms Underlying Reading Skill and Anxiety Symptoms in 7–12-year-old Children

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Details

Objective: Children vary in their language skills, emotion regulation, and working memory. Investigating the sources of this variability is crucial as these processes are potential mechanisms implicated in reading disabilities and anxiety disorders, which often co-occur. Early adversity is known to affect emotion, cognition, and behavior, but more research is needed on the distinct effects of varying types of adversity. The dimensional model of adversity groups experiences postulated to be alike in their consequences and includes the dimensions of threat, experiences of harm or threat of harm, and deprivation, a lack of social and cognitive input (Sheridan & McLaughlin, 2014). This project investigates how threat and deprivation are related to reading skill, anxiety symptoms, and related processes. We aim to examine deprivation as a potentially unique factor underlying reading and language skill, threat as a potentially unique factor underlying anxiety and emotion regulation, and the relation of both, but perhaps deprivation more strongly, to working memory.

Methods: 35 children, 7-12 years (M_{age}=10.2), completed standardized measures of word reading skill (WJ-ID) and anxiety symptoms (SCARED), as well as an experimental rhyming task. The task manipulated lexical processing (low- vs. high-frequency words), valence reactivity (negative vs. neutral images), and working memory (2- vs. 1-back load). Parents completed surveys on the chil's experiences of threat (VEX-R) and deprivation (ECLS).

Results: Using hierarchical regressions, we examined unique variance explained by threat and deprivation, above and beyond age and the other, in reading, anxiety, lexical processing, valence reactivity, and working memory. We discuss trends with Î”R^2>2.5% as weak evidence and Î”R^2<2.5% as no evidence.

For the standardized measures, we see weak evidence of the relation of deprivation to reading above threat (Î”R^2=2.54%, *F*(1,31)=1.53, *p*=0.23) and no evidence for the relation of threat to reading above deprivation (Î”R^2=0.10%). We also see weak evidence for the relation of threat to anxiety above deprivation (Î”R^2=7.54%, *F*(1,31)=2.63, *p*=0.11), and no evidence for the relation of deprivation to anxiety above threat (Î”R^2=1.00%). Altogether, these results are consistent with the dimensional model of adversity.

For the experimental task, we see weak evidence for the relation of threat, above deprivation, to RT for lexical processing (Î”R^2=6.57%, *F*(1,31)=2.77, *p*=0.11), valence (Î”R^2=3.86%, *F*(1,31)=1.51, *p*=0.23), and working memory (Î”R^2=6.32%, *F*(1,31)=2.29, *p*=0.14). Though, we see no evidence of the relation of threat, above deprivation, for accuracy across conditions (lexical processing: Î”R^2=0.13%; valence: Î”R^2=0.45%; working memory: Î”R^2=0.18%). We see weak evidence for the relation of deprivation, above threat, to valence accuracy (Î”R^2=2.75%, *F*(1,31)=0.91, *p*=0.35), though we see no evidence of this relation for RT (Î”R^2=0.14%). In addition, we see no evidence in support of the relation of deprivation, above threat, to lexical processing (accuracy: Î”R^2=2.30%; RT: Î”R^2= Î”R^2=0.01%) or working memory (accuracy: Î”R^2=1.42%; RT: Î”R^2=1.80%). Altogether, these results suggest that threat is generally related to reaction time.

Conclusions: Overall, we see weak evidence for the unique relation of deprivation to reading and threat to anxiety, in line with a dimensional model of adversity. Inconsistent with this model, we see weak evidence for the relation of threat to RT across experimental task conditions. Prior literature suggests early violence exposure may have long-term effects on executive functioning, and specifically, components influenced by attention and processing speed (Clark et al., 2022). A child who takes longer to process information may exhibit a slower RT across the more challenging task conditions. To further investigate the dimensional model, we are examining the neural correlates of lexical processing, valence reactivity, and working memory using fMRI.

2-G-46 - Associations among exposome factors, personalized functional brain network topography, and cognitive functioning in youth

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Details

Cognitive functioning during childhood is associated with critical socio-economic, physical and mental health outcomes across the lifespan. To comprehensively understand how individual differences in cognitive functioning emerge during childhood, one must account for both the unique features of an

individual chil's neurobiology and the unique features of each chil's environment and experiences. Despite the long-recognized importance of the environment in shaping unique patterns of functional neurodevelopment and cognition, challenges have remained in 1) defining reliable individual-level functional brain organization in large-scale datasets of youth, and 2) measuring and characterizing the many inter-connected aspects of an individual chil's environment and experience. Here, we overcome these challenges by leveraging the largest long-term study of brain development and child health in the United States and two previously validated unsupervised machine learning algorithms: non-negative matrix factorization (Cui et al., 2020) to define personalized functional networks (PFNs) and longitudinal bifactor analysis (Moore et al., 2022) to define exposome factors in individuals from the Adolescent Brain Cognitive Development study.

We identified a general exposome factor (exp-factor) capturing a range of socio-economic domains, as well as specific exposome sub-factors capturing experiences at school, family values, family turmoil, dense urban poverty, extracurricular activities, and screen time from our data-driven bifactor analysis. Using linear mixed effects models, we first sought to relate individual differences in these exposome factors to individual children's cognitive functioning across five cognitive tasks from the NIH Toolbox (Weintraub et al., 2013), while accounting for age, biological sex, family structure, and site covariates. Reproducibility of findings was determined by repeating our analyses across matched discovery (*n*=5,139, 48.5% female) and replication (*n*=5,137, 47.1% female) samples (Feczko et al., 2021; Cordova et al., 2021). We found that exp-factor was associated with cognition across all five cognitive tasks in 9-10 year olds (B_s = 0.15 0.50, *p*s<0.001). Specific exposome sub-factors capturing variability in family values and screen time were consistently associated with performance on specific cognitive tasks across both samples (Family Values/Picture Vocabulary: $B_{Disc.}$ = -0.10, $B_{Rep.}$ = -0.10, *p*s<0.001; Screen Time/Reading Recognition: $B_{Disc.}$ = -0.08, $B_{Rep.}$ = -0.06, *p*s<0.001). Moreover, exp-factor measured at baseline assessment predicted cognitive performance two years later when children were 11-12 years old (*n*=5,632), over and above effects of baseline cognitive performance (B_s = 0.08 0.24, *p*s<0.001).

Next, we quantified the total spatial representation of seventeen individually-defined PFNs for each child from prior work (Keller et al., 2022) as the sum of vertex-wise loadings for each network at baseline assessment. Neuroimaging data were drawn from the ABCD BIDS Community Collection (ABCC, ABCD-3165) and preprocessed according to the ABCD-BIDS pipeline. We hypothesized that the association between exposome factors and cognitive functioning would be mediated by the total cortical representation of individually-defined fronto-parietal PFNs. In line with this hypothesis, we found that the total cortical representation of all three fronto-parietal PFNs was positively associated with performance on two cognitive tasks (Picture Vocabulary: $B_{Disc.}$ = 0.04, $B_{Rep.}$ = 0.03, *p*s<0.001; Reading Recognition: $B_{Disc.}$ = 0.03, $B_{Rep.}$ = 0.04, *p*s<0.001) and partially mediated the association between exp-factor and cognitive performance on these tasks (bootstrapped indirect effects: all *p*s<0.001).

Together, the findings of this study represent a critical advance in our understanding of the link between early childhood environments, personalized functional brain network organization, and individual differences in cognition in youth. By identifying replicable brain-behavior associations using a personalized neuroscience approach, our work lays a strong foundation for future studies to further investigate environmental influences on individual-specific patterns of neurocognitive development.

2-G-47 - Exploring neural correlates of behavioral and academic resilience among children in poverty

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Details

Children in poverty must contend with systems that do not meet their needs. We explored what, at a neural level, helps explain children's resilience in these contexts. Lower coupling between the lateral frontoparietal network (LFPN) and default mode network (DMN)â€"linked, respectively, to externally and internally directed thoughtâ€"has previously been associated with better cognitive performance. However, we recently found the opposite pattern for children living in poverty: higher LFPN-DMN connectivity associated with better test performance (Ellwood-Lowe et al., 2020). Here, we investigated trajectories of LFPN and DMN network coupling over childhood and early adolescence, and their relation to children's cognitive, behavioral, and academic outcomes. Additionally, we explored if these relations differed meaningfully between children whose families lived above and below poverty.

In a pre-registered study, we analyzed longitudinal data from the Adolescent Brain Cognitive Development Study. Our sample comprised 8366 children at baseline (T0, ages 8.9-11.1y), *n*=7935 and *n*=4727 at two-year follow-up (T2, ages 10.6-13.6y). Of these children, 1303 were living below poverty at T0. Over the two-year period, there was not consistent LFPN-DMN connectivity change across the full sample. As predicted, higher LFPN-DMN connectivity was linked to better grades and fewer attentional problems for children living below poverty, while the opposite was true for children above poverty (interactions: $c^2(1)=7.94$, p=.005; $c^2(1)=6.61$, p=.010). This interaction between LFPN-DMN connectivity and poverty related to children's grades two years later; however, it was attenuated when controlling for baseline grades and was not related to attention longitudinally. Together, these findings suggest that network connectivity is differentially related to real-world settings for children above and below poverty.

2-G-48 - Impact of childhood adversity on white matter development from late childhood to early adolescence

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Details

Objective: Exposure to adverse childhood experiences (ACEs) may confer risk for neurocognitive development. Research has demonstrated that ACEs are associated with structural and functional alterations in prefrontal brain regions, which may occur due to regional sensitivity to chronic stress (i.e., greater glucocorticoid receptor density). This is one proposed mechanism linking ACEs to poorer mental health outcomes. Fewer studies have investigated potential changes in white matter (WM) microstructure, despite WM's role in brain network communication and evidence that myelination is sensitive to chronic stress. Studies have shown reduced fractional anisotropy (FA) in fronto-limbic and occipital visual tracts in individuals exposed to adversity, but findings have been limited to small, cross-sectional samples or primarily investigated in adult samples. Examining stress' impact on neurocognitive development in large, diverse samples across adolescent development will clarify mechanistic pathways

and inform intervention and prevention efforts. To address these gaps, the current study aimed to examine the relationship between ACEs and WM microstructure in frontal, fronto-parietal, and fronto-limbic tracts from late childhood to early adolescence.

Methods: Participants included 10,537 youth (age range= 9-14 years old, 48% female; 68% non-Hispanic White) enrolled in the Adolescent Brain Cognitive Development Study from baseline to 2-year follow-up (FU). Cumulative ACEs scores were calculated based on the youth's and caregiver's report of the youth's exposure to adverse events from baseline to 2-year FU. Imaging data was collected at baseline and 2-year FU. Diffusion tensor imaging (DTI) was used to calculate fractional anisotropy (FA) and mean diffusivity (MD), and AtlasTrack was used for WM tract segmentation. WM tracts examined in the current analyses include the uncinate fasciculus (UF), forceps minor (FM), superior longitudinal fasciculus (SLF), and the inferior frontal to superior frontal cortical (IFSF) tract. Separate linear mixed effect models were conducted to examine the association between ACEs and DTI indices (FA and MD) in each tract while controlling for age, sex at birth, race, ethnicity, caregiver education, household income, pubertal status, internalizing mood symptoms, and random effects of family/twin status and scanner manufacturer model. Post-hoc brain-behavior correlations were conducted between significantly predicted tracts and UPPS-P Impulsive Behavior subscales to aid in interpretation.

Results: Significant ACE-by-time interactions were revealed. Specifically, youth with lower ACE scores demonstrated a more robust increase in FA in the left UF (p=.01) at 2-year FU. Behaviorally, greater FA was significantly correlated with less positive urgency and more perseverance (p's <.05). Bilaterally across all tracts, youth with greater ACEs showed higher MD at baseline and a more robust decrease in MD levels (p's < .001) across time. Brain-behavior correlations demonstrated that decreases in MD in all tracts except the FM were correlated with less negative and positive urgency and more perseverance and planning (p's <.05).

Conclusions: Our FA findings in the left uncinate are consistent with literature suggesting that ACEs are associated with disruptions in white matter development; in contrast, the greater rate of change in MD across examined WM tracts suggest potential for resiliency in youth with greater ACEs. Further, results demonstrate that indices of white matter microstructure are correlated with adaptive behavioral outcomes. Overall, our findings highlight the need for longitudinal investigations of ACEs and white matter maturation to clarify brain development trajectories. Further investigation across additional time points is warranted to better characterize both risk and resiliency in white matter development after exposure to childhood adversity.

2-G-49 - Early life adversity, sleep disturbances, and depressive symptoms during adolescence: The role of the cingulum bundle

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Details

Adolescence is a period during which there are normative increases in sleep disturbances, typically characterized by decreases in sleep duration and greater variability in sleep duration and timing. While normative, these sleep disturbances can have significant adverse effects on the developing brain,

particularly in white matter tracts that have been implicated in affective and cognitive regulation, such as the cingulate portion of the cingulum bundle (CGC) and the uncinate fasciculus (UF). Although there is a growing body of research examining the links between sleep disturbances and white matter development during adolescence, few studies have delineated the longitudinal relations between sleep problems and white matter development during adolescence and how they may differ by severity of exposure to early adversity. In the current study, measures of self-reported sleep disturbances (a composite of sleep-related questions from the Youth Self Report), self-reported depressive symptoms (total score from Child Depression Inventory), and indices of white matter microstructural integrity (from diffusion-weighted MRI scans) were obtained at two timepoints once during early adolescence (9-13 years; Time 1 [T1]) and again approximately four years later (13-17 years; Time 2 [T2]) from at least 77 youth (about 50% female) who varied in exposure to early life adversity (ELA). We tested whether sleep problems at T1, and changes in sleep problems from T1 to T2, were related to changes in depressive symptoms from T1 to T2 and also to changes in fractional anisotropy (FA) of the CGC and UF from T1 to T2; we further tested whether these effects differed by levels of ELA. For associations in which ELA moderated the effect of sleep problems on changes in both depressive symptoms and FA, we conducted moderated mediation analyses. We found that higher initial (T1) levels and increases in sleep problems were related to increases in depressive symptoms across a four-year period; these effects did not vary by ELA exposure. In youth who experienced lower levels of ELA, higher initial levels of sleep disturbances were associated with greater increases in CGC FA, which, in turn, were associated with greater increases in depressive symptoms. In contrast, in youth who experienced higher levels of ELA, higher initial levels of sleep disturbances were associated with greater decreases in UF FA and no changes in CGC FA. Sleep problems were not associated with changes in UF FA in youth with lower ELA. Moreover, independent of ELA level, changes in UF FA were not associated with changes in depressive symptoms. These findings highlight the importance of sleep quality in shaping frontolimbic white matter tract development and the course of depressive symptoms during adolescence. Findings from the moderated mediation analysis suggest that changes in CGC FA are a mechanism by which sleep quality is related to depressive symptoms in youth with lower ELA, but not in youth with higher ELA.

2-G-50 - Integrating Dimensional Models of Early Adversity: Relative Contributions of Caregiver and Environmental Risks

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Details

During early childhood, rapid brain development occurs in areas responsible for goal-directed behaviors, emotion processing, and self-regulation abilities (Gilmore et al., 2018). Exposure to adversity during this sensitive period may alter typical developmental trajectories, placing individuals at increased risk for impaired functioning and psychiatric disorders (Bick & Nelson, 2015). To understand effects of adversity on youth neural and psychosocial development conceptual frameworks have considered multiple dimensions of adversity and developmental context. Models such as threat-deprivation (Sheridan & McLaughlin, 2014) and harshness-unpredictability (Ellis et al., 2009) have linked specific stressful experiences with alterations to brain structure and function. Specifically, threat (exposure to perceived or actual harm) has been associated with reduced volumes in limbic areas, associated with emotion regulation and threat sensitivity, while instances of deprivation (a lack of necessary input) have been

associated with reduced thickness and volume in pre-frontal regions implicated in executive functioning (Sheridan & McLaughlin, 2014). Unpredictability (inconsistency in expected developmental experiences) has been associated with alterations in emotion and cognitive processing and increased risk for psychopathology (Chen & Baram, 2016). Early childhood may be a period where youth are particularly impacted by caregivers, who may amplify or mitigate the effects of adversities occurring outside the home across these dimensions (Tottenham, 2020; Hostinar & Gunnar, 2015) and have marked consequences for brain structure and function (Smith & Pollack, 2020).

The present study builds off previous work, integrating dimensional models of adversity (Usacheva et al., 2022; Ellis et al., 2022), exploring how dimensions of adversity function differentially across contexts, with the idea that experiences of adversities (or lack thereof) in caregiving will be most salient in early development phases. Specifically, we differentiate between cues of threat vs. safety, deprivation vs. enrichment, and unpredictability vs. stability in caregiving compared to more distal contexts. We expect that especially in early childhood, greater exposure to threat, instability, and deprivation in early social relationships will explain more variance in neurodevelopment in frontal and limbic circuitries.

Our sample consists of 122 children ages 3-7 years old (M= 4.75, SD=.87, 47% male) from diverse racial/ethnic and socioeconomic backgrounds. Parents completed measures on adverse experiences occurring within the home and in the broader developmental context, relating to threat (parenting practices, department of social services involvement, trauma exposure), deprivation (income to needs ratio, use of welfare benefits), and unpredictability (food insecurity, number of moves) dimensions. Children underwent MRI scans and T1-weighted images were processed to obtain structural measures (cortical thickness, surface area (SA), volumes, convexity, and curvature). All data has been collected and is being cleaned for analysis. We hypothesize that increased rates of adversity across domains will be related to decreased in SA and thickness in frontal areas and lower hippocampus and amygdala volumes. Additionally, we hypothesize that during early childhood, adverse caregiving experiences will be uniquely predictive of brain development over and above environmental risk.

Our findings extend existing work by including under-explored neuroimaging metrics, such as convexity and curvature, with comprehensive measures of adversity exposure in a diverse sample of children during a critical developmental period. This work examines caregivers as gatekeepers of environmental risk, who can be targeted for prevention and intervention strategies.

2-G-51 - Early life adversity reveals adaptive use of absorption in music

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Details

Early life adversity includes experiences with dimensions of deprivation, threat, and unpredictability in the environment and are associated with downstream effects into adulthood, such as difficulties with mood regulation and the presence of psychopathology. For this reason, individuals who have faced early life adversity may use adaptive behaviors to assist with self-regulation. One such adaptive behavior is absorption in music. Mindful music-listening is shown to down-regulate negative affect following an acute stressor, as indicated by both self-report and increased functional connectivity between the

amygdala and medial prefrontal cortex. However, it is unclear how experiences of early life adversity might alter engagement with the regulatory uses of music in adulthood. We examined the effects of exposure to early life adversity on individual differences in music usage and resilience in adulthood. In our first study, 254 participants (ages 18-65) completed the extended Barcelona Music Reward Questionnaire (eBMRQ) and the Healthy-Unhealthy Music Usage Scale (HUMS) to measure differences in music usage, and the Connor-Davidson Resilience Scale to measure resilience. Additionally, to capture early life adversity along its constituent dimensions, participants retrospectively reported the Questionnaire of Unpredictability in Childhood (QUIC), measures of threat and deprivation, and the Confusion, Hubbub, and Order Scale (CHAOS) for childhood and adolescence. All adversity measures were significantly positively correlated with the eBMRQ absorption subscale, which measures the tendency to be immersed in music listening. Absorption was significantly positively correlated with music usage as well as with resilience, suggesting that a degree of absorption in music listening is adaptive. In Study 2, we tested the hypothesis that absorption in music serves an adaptive purpose for individuals with adverse home environments by offering a means of escapism. Participants (n=288; ages 18-65) completed the Absorption in Music Scale (AIMS), a more robust measure from which the eBMRQ absorption subscale was derived, and the Escapism Scale to measure the use of music as a means of escapism. Additionally, participants retrospectively reported the same adversity measures as in Study 1. As expected, AIMS absorption scores were significantly positively associated with escapism. We replicated the significant positive relationships between absorption and resilience, as well as absorption and developmental CHAOS, threat, and deprivation adversity dimensions. Further, mediation analyses showed that accounting for absorption accentuated the negative relationship between early adversity and resilience, particularly for those with higher levels of developmental deprivation and chaos. This result suggests that absorption in music serves as a psychological buffer and regulatory tool for those with prior developmental adversity. Through investigating music usage tendencies, our results highlight lasting adaptive behaviors linked to early life experiences.

2-G-52 - Adolescent Caregiving Quality and Neurodevelopmental Recovery Following Severe Early Childhood Psychosocial Deprivation

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Details

Severe early psychosocial deprivation experienced in institutional settings is related to alterations in cortical structure that can be observed into adolescence (Sheridan et al., 2022). Evidence from the Bucharest Early Intervention Project (BEIP), the only randomized control trial of foster care intervention for institutionalized youth, suggests that removal from institutional care and placement in high quality foster care in early childhood, a period of heightened neurodevelopmental sensitivity to environmental experience, may partially remediate the effect of early childhood psychosocial deprivation on cortical development (Sheridan et al., 2022). Less is known about the potential for caregiving experiences in adolescence, another putative sensitive period, to contribute to neurodevelopmental recovery following childhood caregiving adversity. Emerging evidence from the BEIP suggests that associations of caregiving

quality and recovery in executive function, reward sensitivity, and psychopathology may be strongest in adolescence relative to earlier caregiving experiences (Colich et al., 2020). The present study aims to further examine the developmental timing of caregiving experiences from early childhood to adolescence and their association with cortical structure. We hypothesized that there would be a lasting association of the earliest caregiving experiences with cortical structure in adolescence, as well as a concurrent association of greater caregiving quality with thinner cortex and greater cortical surface area in adolescence in the BEIP across all randomized conditions.

At baseline, 136 institutionalized children and 72 community comparison children aged 6-30 months were recruited in Bucharest, Romania. Half of the institutionalized participants were randomly assigned to a high quality foster care intervention and half were randomly assigned to care as usual (i.e., remained in institutional care). Early childhood caregiving quality was rated by BEIP staff using a standardized observational measure at baseline, 30 months, and 42 months. BEIP staff made post-hoc ratings of caregiving quality at ages 54 months, 8 years, 12 years, and 16 years based on further observation. At age 16, 103 participants (52 female) completed a structural MRI scan.

We estimated linear growth curve models to characterize change in caregiving quality over the course of early childhood and separately from middle childhood through adolescence. Random effects estimates from each model were extracted and used to examine associations with cortical structure at age 16. All analyses controlled for age, sex, and group assignment.

Results revealed that, on average, early childhood caregiving quality increased across assessments. On average, caregiving quality was stable across middle childhood through adolescence, but there was significant variability in individual trajectories. Better caregiving quality at baseline (prior to random assignment) was uniquely associated with thinner cortex in areas of the medial and lateral prefrontal, inferior temporal, and the lateral occipital cortices in adolescence. Finally, increasing caregiving quality across adolescence was associated with greater cortical surface area in the superior parietal and inferior temporal cortices at age 16.

Taken together, these findings suggest that, while early childhood caregiving is strongly associated with adolescent neural structure, particularly cortical thickness, adolescence may also represent a developmental window where caregiving experiences influence neurodevelopmental outcomes, predominately through effects on cortical surface area.

2-G-53 - Neural Correlates of Resilience to Trauma During Adolescence: A Multi-Modal Study

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Details

The neurobiology of resilience, which refers to the process of 'bouncing back' from experiences of adversity, has been of research interest in recent years. Our recent systematic review on the topic revealed a general lack of consistent findings for neural biomarkers of resilience in children and adolescents, although some consistency suggested resilience may be associated with prefrontal and subcortical structure/connectivity. Limitations within the field were also highlighted in our review, such

as a lack of whole-brain and multimodal neuroimaging research efforts, as well as oversight of sex differences in prior research. To address these limitations, the current study aims to examine the neural correlates of resilience in adolescents across structural and functional (resting-state) imaging modalities using a whole-brain approach. Based on findings from our review, we hypothesize that structure/connectivity in prefrontal and subcortical regions will be associated with resilience to internalizing and externalizing symptoms in adolescents. The current study also aims to explore any sex differences in the neural correlates of resilience in adolescents. Given limited prior research examining sex differences in neural correlates of resilience during adolescence, we have no hypothesis for this aim. To examine these aims, we will use second-year follow-up data from the large-scale U.S.-based Adolescent Brain Cognitive Development Study, which contains imaging, mental health, and environmental data from over 10,000 adolescents (11-12 years of age at second year follow up). The current study will first conduct latent profile analysis to identify groups of resilient (high adversity, low symptoms), high-risk (high adversity, high symptoms), healthy (low adversity, low symptoms), and susceptible (low adversity and high symptoms) adolescents based on reports of traumatic events and internalizing/externalizing symptoms. Mixed effects modelling will then be conducted to examine differences in white and gray matter structure and resting-state connectivity between the groups to identify neural characteristics that are uniquely associated with resilient group membership. For our exploratory aim, we will include sex and its interaction with imaging independent variables to the mixed effects models conducted for the main analyses to examine any differential neural correlates of resilience in female and male adolescents. The results of the current study will provide valuable insights into the multimodal neural characteristics that uniquely associate with resilience to trauma during adolescence, as well as any potential sex differences. The study is currently in progress to submit for pre-registration, we plan to begin analysis in mid-May and have results completed by the Flux congress in September.

2-G-54 - Threat experiences moderate the link between hippocampus volume and depression symptoms prospectively in adolescence

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Details

Objective: Identifying neuroimaging risk markers for depression has long been an elusive goal in psychiatric research. Smaller hippocampus volumes have been among the most consistent correlates of depression symptoms across the lifespan (Schmaal et al., 2016), though the effects have been modest and cross-sectional. The clinical utility of such effects is limited, suggesting new approaches to seeking risk markers for depression are needed (Herzberg, 2022). One such approach is enhancing specificity by evaluating the role of environmental heterogeneity. For example, recent research has shown that smaller hippocampus volume was associated with depression symptoms in high- but not low-income youth, suggesting low income youth may not display this effect in the context of a more persistently high stress environment (Herzberg et al., 2022). The current study aimed to replicate and extend these effects in a larger independent sample using multiple indices of socioeconomic status.

Methods: Data from the Adolescent Brain Cognitive Development study (ABCD; N = 6,693) was used to evaluate the moderating effects of socioeconomic status on the link between baseline hippocampus

volume and depression symptoms assessed two years later. Analyses were pre-registered on OSF (osf.io/6g9ab; currently embargoed). Socioeconomic status was indexed using a continuous measure of family income-to-needs ratio. Additionally, moderated nonlinear factor analysis (MNLFA; Bauer, 2017) was used to establish invariant dimensions of more proximal experiencesâ€"namely, economic deprivation, psychosocial threat, and caregiver social supportâ€"that adjusted for demographic bias (DeJoseph et al., 2022). Right and left hippocampus volumes from ABCD release 4.0 were analyzed separately. Zero-inflated Poisson multi-level regression models were used to estimate the interaction between baseline hippocampus volume and socioeconomic experience as a predictor of 2-year depression symptoms assessed using the child behavior checklist. Covariates included age, sex, race, parental education, and intracranial volume.

Results: Psychosocial threat moderated the association between baseline right hippocampus volume and depression symptoms two years later such that a negative association was evident at low-, but not mean or high-levels of threat (std. beta=0.15, 95% CI [0.05, 0.24], simple slope estimate=-0.18, *p* =0.01). When baseline depression symptoms were added to the model as a covariate the interaction was no longer significant. However, in a follow-up analysis using only participants who endorsed one or more depression symptoms at baseline the interaction term was significant when controlling for baseline depression symptoms (std. beta=0.13, 95% CI [0.03, 0.23]). Decomposition of this interaction term again indicated that the negative association between hippocampus volume and depression symptoms was present only in low-threat contexts (simple slope estimate=-0.15, *p*=0.05). Neither family income-to-needs ratio nor the two remaining dimensional scores followed the same pattern.

Conclusions: Better characterizing the impact of environmental heterogeneity on the associations between brain structure and depression may improve the specificity of neuroimaging risk markers. In this study, larger right hippocampus volume was associated with fewer future depression symptoms only in the context of low psychosocial threat, consistent with the findings in the prior study. Among only individuals endorsing depression and experiencing low threat at baseline, there was a negative association between hippocampus volume and the change in depression symptoms from baseline to 2-year follow-up. These results suggest that hippocampus volume may not be a consistent correlate of depression symptoms in high risk environments and emphasize the importance of including measures of environmental heterogeneity when seeking risk markers for depression.

2-G-55 - Neighborhood air pollution is negatively associated with neurocognitive change in early adolescence

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Details

Introduction: The ability to maintain focus and process task-relevant information continues to develop during adolescence and predicts desirable education and health outcomes. Many aspects of cognitive development are associated with the neighborhood one lives in, but the specific physical environmental factors that influence cognitive development above and beyond socioeconomic factors remain poorly characterized. One candidate factor is air pollution. Evidence suggests that air pollution, especially small

particulate matter (PM2.5) and nitrogen dioxide (NO2) concentration in the air, is associated with negative impacts on cognitive development in childhood. In the current study, we assessed neighborhood air pollution's relationship with developmental change in attention and working memory performance, as well as the brain networks supporting cognitive performance, in the large Adolescent Brain Cognitive Development (ABCD) Study sample.

Methods: We utilized the neighborhood socioeconomic and air pollution variables in conjunction with behavioral (n = 5256) and neuroimaging (n = 878) measures of attention and memory from the baseline time-point (ages 9-10) and the two-year follow-up time-point (Y2; ages 11-12) releases of the ABCD Study. Performance in the n-back task was used to operationalize cognitive performance at baseline and Y2 for each participant. To capture the neural development of the brain networks supporting cognitive performance, we quantified the strength of a publication pre-registered predictive brain network, the youth cognitive composite Connectome-based Predictive Model (ccCPM), in both baseline and Y2 for each participant using their fMRI connectivity during the n-back task. The ccCPM includes two sets of functional brain connections that predict higher or lower performance in NIH-Toolbox cognitive battery and was previously trained in ABCD Study baseline fMRI connectivity data in a leave-one-site-out procedure. The ccCPM brain expression score was calculated from baseline and Y2 data for participants from the left-out sites to estimate the developmental change in the strength of functional network predictors of attention and working memory between the two ages.

Results: In the *behavioral* domain, multiple linear regression showed that developmental change in n-back task performance was negatively associated with neighborhood air pollution ($\hat{I}^2$ = -.044, t = -3.11, p = .002), adjusted for covariates capturing baseline cognitive performance of the child, their parental income and education, family conflicts, and their neighborhoo's population density, crime rate, perceived safety, and Area Deprivation Index (ADI). The strength of the adjusted association for air pollution was similar to parental income, family conflict, and neighborhood ADI. In the *neuroimaging* domain, we again found that decreased developmental change in the strength of the ccCPM from pre- to early adolescence was associated with neighborhood air pollution ($\hat{I}^2$ = -.110, t = -2.69, p = .007), adjusted for the covariates mentioned above and head motion. Finally, we found that the developmental change in ccCPM strength was predictive of the developmental change in n-back performance (*r* = .157, p < .001), and there was an indirect-only mediation where the effect of air pollution on change in n-back performance was mediated by the change in the ccCPM strength ($\hat{I}^2_{\text{indirect effect}}$ = -.013, p = .029).

Conclusion: We found that neighborhood air pollution is associated with decreased development of youth working memory and sustained attention abilities, as well as decreased strengthening of the brain networks supporting these abilities over time.

2-G-56 - Brain volumes at birth mediate the relationship between prenatal social disadvantage and socioemotional, but not other developmental abilities at age 2 years

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Details

Objective: Early social disadvantage is consistently associated with poorer cognitive function and socioemotional difficulties. Previous work has also shown that prenatal social disadvantage is associated with volumetric brain reductions at birth in total cortical grey matter (GM), total white matter (WM), cerebellar, total subcortical GM, total brain volume (BV), and cortical folding (gyrification index; GI). Thus, we sought to investigate whether (1) any of these disadvantage-associated volumetric reductions at birth predicted later cognitive and socioemotional outcomes at age 2 years and (2), if so, did they mediate the relationship between social disadvantage and outcomes?

Methods: Participants consisted of 286 pregnant women and their 288-singleton offspring followed longitudinally. In each trimester of pregnancy, information was collected about material (i.e., income-to-needs ratio, national area deprivation index) and social (i.e., education and health insurance status) resources, which was combined into a latent variable: Prenatal Social Disadvantage (pSD). At birth, T2-weighted images (Siemens Prisma 3T Scanner; TR=3200/4500ms, TE=563ms, 0.8mm^3 isometric voxels) were collected from sleeping, non-sedated neonates. At age 2 years, toddlers returned for developmental assessment (Bayley Scales of Infant and Toddler Development, 3rd Edition) and parents completed socioemotional questionnaires (Infant-Toddler Social and Emotional Assessment). Regressions tested whether disadvantage-associated volumetric reductions at birth predicted age 2 outcomes. For birth metrics that significantly predicted year 2 outcomes, formal mediation models tested whether brain volume at birth mediated the relationship between pSD and age 2 outcomes. All reported results were significant at FDR corrected ($q<.05$).

Results: Volumetric reductions at birth in total cortical GM, total BV, total WM, subcortical GM, total cerebellum, and mean GI were associated with greater externalizing symptoms at age 2. Similarly, reductions in each of the pSD-associated metrics, except mean GI, were associated with greater dysregulating symptoms at age 2. Lower cognition scores were only associated with volumetric reductions in total cerebral WM and total brain volume at birth; language scores were not associated with any brain volume metrics at birth.

pSD was associated with greater externalizing and dysregulating behaviors, and lower cognition and language scores at age 2 years. The relationship between greater pSD and higher externalizing symptoms at age 2 was partially mediated by volumetric reductions in: total cortical GM (95% CI: .005 to .099), total cerebral WM (95% CI: .003 to .131), and total BV (95% CI: .007 to .126). The relationship between greater pSD and higher dysregulation scores at age 2 was partially mediated by volumetric reductions in total cortical GM at birth (95% CI: 0.001 to 0.086). Brain volume at birth did not mediate the relationship between pSD and developmental outcomes (cognition or language).

Conclusions: Findings shed light on mechanisms through which social disadvantage influences socioemotional (e.g., externalizing, dysregulating symptoms) and developmental (e.g., cognition, language) outcomes. Results suggest that gross volumetric reductions at birth are more strongly associated socioemotional than with cognitive and langauge outcomes at age 2. This study highlights that brain alterations associated with later socioemotional difficulties begin *in utero*. Given that early socioemotional difficulties are predictive of later psychiatric disorders, this finding could have important implications for identifying and targeting early risk factors.

2-G-57 - The role of developmental timing of adverse childhood experiences in shaping brain structure: A systematic review

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Details

Background: Adverse childhood experiences (ACEs) are widely reported to be associated with a range of alterations in the brain. Many developmental neuroscience researchers have highlighted the importance of considering the developmental timing of ACEs, given the likely presence of sensitive periods, during which the brain is most vulnerable to the effects of ACEs. In one influential model, known as the Life Cycle Model of Stress, sensitive periods were suggested to occur during periods of rapid brain development (Lupien et al., 2009). Specifically, this model proposed that the sensitive periods for the hippocampal, amygdala, and frontal cortex are around infancy (birth to 2 years old), early to late childhood, and adolescence, respectively. In this pre-registered systematic review (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=284727), we aimed to explore the role that the developmental timing of ACEs might have on brain structure (we also aimed to explore brain function and hypothalamic-pituitary-adrenal axis function, although we do not report on these here). We aimed to synthesise the empirical evidence for sensitive periods and determine whether they align with those presented in the Life Cycle Model of Stress. **Method:** Literature searches on MEDLINE (OVID), PsycINFO, Scopus, and Web of Science yielded 2,132 articles, with a total of 70 studies included in the final review (22 of which investigated brain structure). **Results:** There were two main findings: (1) Among studies that conceptualised timing as duration of exposure or age of onset, longer duration of exposure and/or earlier age of onset tended to be associated with larger ventricles, and smaller intracranial, cerebral, cerebellar, grey and white matter volumes; (2) among studies that investigated ACEs exposure across various developmental timepoints (e.g., exposure during each year of childhood, exposure during childhood versus adolescence), we found little consistency in findings, with no clear pattern of sensitive periods for different brain regions. Sensitive periods suggested by study findings did not necessarily align with those presented in the Life Cycle Model of Stress. For example, some studies identified early childhood as the sensitive period for the hippocampus (consistent with the model), while others identified later childhood or adolescence as sensitive periods. Similar patterns were observed for the amygdala and frontal cortex findings. **Discussion:** Methodological factors may have contributed to inconsistent findings, including heterogeneous conceptualisations of ACEs, varying statistical approaches to test sensitive periods, and sample characteristics (e.g., adult versus paediatric samples, clinical versus community samples). Studies also differed in the age range of ACEs exposure that they explored, limiting conclusions about certain ages (e.g., early childhood) that some studies did not capture.
Conclusion: Further studies are needed to investigate the factors that might have contributed to inconsistencies in findings regarding the influence of developmental timing of ACEs and brain structure. A mega-analysis combining all data across all existing studies may also be beneficial to advance our understanding regarding sensitive periods for the effects of ACEs on the brain.

2-G-58 - Early life stress alters the development of task-rest neural flexibility of the reward network and its association with depressive symptoms in adolescents

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Details

Introduction. Experiences in early life are a critical source of information that guides the development of brain architecture. Unfortunately, over half of youth are exposed to early life stress (ELS), which significantly increases their risk for subsequent emotional problems, including depression, that often emerge in adolescence. Indeed, adolescence is a particularly vulnerable developmental period, given the dramatic physical, social, and emotional changes that occur at this time. In order to adapt to changing environmental contingencies, the brain is required to efficiently reconfigure itself to subserve flexible cognitive and affective processing, a process referred to as neural flexibility. It is important to recognize that large-scale functional brain networks involved in cognitive and affective processing are still developing during adolescence; it is possible that ELS disrupts the normative development of neural flexibility, increasing adolescents' risk for the development of emotional problems. At this time, however, we do not know how pervasive or persistent the influence of ELS is on the development of neural flexibility and risk for subsequent psychopathology in adolescence. In this study, we examined the effects of ELS on the development of neural flexibility over the course of adolescence, and the association between neural flexibility and depressive symptoms, by combining resting-state and task-based fMRI data.

Method. A community sample of 150 adolescents spanning ages 9-19 years (92 girls; mean age of 12.63Â±2.11 years) completed a comprehensive interview-based assessment of early life stress, the Children's Depression Inventory, and resting-state and task-based fMRI scans. Neural flexibility was operationalized by measuring similarity in the functional connectivity (FC) during resting-state and during the Monetary Incentive Delay (MID) task to capture the flexibility with which the brain reconfigures itself from resting-state to a task-state. We regressed out task events from the MID timeseries data to generate a â€˜reward processing task-state' time course that was comparable to resting-state. Using a functional atlas, we extracted timeseries data from 300 regions of interest (ROIs) across the entire brain and computed functional connectivity among the ROIs, resulting in separate FC matrices for resting-state and task-state. For each participant, we calculated the similarity in the FC of the ROIs in the reward network during resting-state and reward processing task-state using Pearson's correlation, thereby generating a reward network neural flexibility score. We then conducted two linear regression analyses to examine 1) moderating effects of ELS on age predicting NF, and 2) NF predicting depressive symptoms. Both models controlled for sex and race.

Results. We found that ELS moderated the age-related trajectory of neural flexibility of the reward network over adolescence. Whereas adolescents exposed to lower levels of ELS exhibited greater neural flexibility with age, adolescents exposed to higher levels of ELS had less neural flexibility with age ($F(4,149)=3.807$, $p=0.006$). We also found a significant negative association between reward network flexibility and depressive symptoms in adolescents who had experienced greater severity of ELS ($p<.0001$).

Conclusion. Our findings indicate that exposure to high levels of ELS adversely affects adolescents' ability to efficiently recruit the functional brain network necessary to meet demands of a task. This neural flexibility is inversely related to their levels of depressive symptoms. Intervention strategies

designed to increase neural flexibility may mitigate the adverse effects of ELS on functional brain development and on risk for psychopathology in adolescents.

2-G-59 - Examining evidence for the intergenerational transmission of resilience: A 3-cohort infant neuroimaging study (Pre-registration)

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Details

Objective: A growing body of research has tied subjective and objective stress during pregnancy to neonatal brain development. Yet the potential interaction of subjective and objective stress in has been less studied. Indeed, many individuals exposed to objective stressors, such as neighborhood disadvantage, do *not* report high levels of subjective distress and instead display psychological resilience. Children and adults who experience adversity but who do not develop psychiatric symptoms have been reported to show increased connectivity of cognitive control networks, such as stronger frontoparietal connectivity. The goal of this project is to examine whether similar neural patterns can be detected in infants born to resilient mothers living in disadvantaged neighborhoods during pregnancy.

Methods: We applied similar preprocessing methods to neonatal resting-state functional MRI (rsfMRI) data from three longitudinal birth cohorts in Atlanta, Detroit, and New York City respectively (n=122). Participant addresses were geocoded to quantify neighborhood disadvantage (*Area Deprivation Index*) during pregnancy. Mothers also completed measures of perceived stress, depression, and anxiety in each cohort, which were standardized and averaged to create a composite measure of subjective distress during pregnancy. Analyses will compare neonatal functional connectivity patterns between 3 groups: a **resilient group** with high neighborhood disadvantage but low maternal subjective distress (n=37), a **vulnerable group** with high neighborhood disadvantage and high subjective distress (n=37), and an **advantaged group** with low neighborhood disadvantage (n=48; see Figure 1). Preliminary analyses confirm resilient and vulnerable groups are matched on neighborhood disadvantage (t=1.52, p=0.14), but differ on subjective distress ratings (t=11.23, p<0.001). Data for these analyses are collected, quality assured, and in the final stages of preprocessing. Group-level analyses have not yet been conducted.

Hypothesis: Executive control networks will show stronger within and between-network connectivity in neonates of resilient mothers compared to neonates of vulnerable mothers.

Analytic Plan: After preprocessing, ComBat will be used to account for site-related heterogeneity. Region of interest (ROI) parcels will be grouped into networks using a community detection algorithm, and we will calculate functional correlations of ROIs within a given network to represent within-network connectivity. Functional correlations between ROIs assigned to different networks will be used to derive between-network connectivity. One-way ANOVAs will be used to compare within and between network connectivity strength between groups, controlling for motion during the scan, number of resting-state functional volumes, infant age, and infant sex. Significance thresholds will be FDR-adjusted to correct for multiple comparisons. We will employ cross validation to assess replicability of in-sample effect sizes.

Implications: If neonates of resilient mothers display different neural connectivity patterns compared to similarly exposed vulnerable mothers, it will provide initial evidence that subjective perceptions moderate the cross-generation impact of objective adversity. No differences between the resilient and vulnerable groups could suggest that neighborhood disadvantage yields strong impacts on the developing brain, regardless of a mother's subjective distress. In either case, the findings from this project hold potential to advance our understanding of individual differences in the cross-generation transmission of adversity, which is a potent factor that shapes child psychological and behavioral outcomes.

2-G-60 - Associations between early life trauma and gray and white matter brain age during childhood and adolescence

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Details

Background/Study objective:

The developing brain is in part shaped by variability in early-life risk and protective factors. Scientific studies have highlighted the potentially harmful impact of early life adversity (ELA) related to trauma (e.g., physical and emotional abuse) on brain maturational patterns, with evidence of trauma being associated with early (accelerated) maturation [1]. However, existing literature still lacks a comprehensive understanding of the extent of effects on the developing brain and the potential protective role of social resilience in moderating said effects. The current study aims to extend our existing knowledge of whether and to what extent early life adversity related to trauma is associated with accelerated brain maturation and to investigate the potential moderating effect of social resilience as a protective factor.

Method:

Population: Children and adolescents (age range 9-14) from the Adolescent Brain and Cognitive Development (ABCD) Study (N = Ëœ11,800 at baseline). The design will be mixed cross-sectional and longitudinal.

MRI measure(s): Tabulated T1-weighted and diffusion data.

Adversity measure(s)*:* abcd_ptsd01 is a parent questionnaire that includes traumatic events that are part of the PTSD diagnostic interview. Measures of interest include sexual and physical abuse, and exposure to violence.

Protective factor(s): srpf01 is a questionnaire that includes school risk and protective factors. Measures of interest include teacher attentiveness, involvement in clubs, feeling safe at school, and doing well in class.

Statistical analysis: All statistical analysis and visualisation of results will be carried out in R. Brain-age prediction will be carried out using eXtreme Gradient Boosting (XGboost), where we will predict gray and white matter brain age at baseline and follow-up.

To investigate whether and to what early life trauma is associated with brain age, we will use linear mixed effects (LME) models to test main effects of trauma on the difference between predicted age and chronological age, i.e., brain age gap (BAG), and interaction (longitudinal) effects of time (interval between TP1 and TP2) and sex. Additionally, moderation analysis will be carried out to test the moderating effect of social resilience on the association between trauma on BAG. For each model, we plan to control for genetic ancestry factors, scanner effects, and sex and timepoint where appropriate.

Hypotheses:

Based on existing literature, we hypothesise that factors related to early life trauma will be associated with larger (positive) brain age gaps (i.e., older-looking brains indicative of accelerated maturation). We also hypothesise evidence of protective factors related to social resilience to moderate the deleterious effects of trauma on the youth brain.

2-G-61 - Characterizing unique profiles and correlates of multi-domain resilience to neighborhood disadvantage in youth: A person-centered approach

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Details

Background:

Resilience is a dynamic process defined as positive adaptation in the face of adversity. Early work predominantly characterized resilience as the *absence* of a *single* negative outcome (e.g., lack of psychopathology), yet research increasingly suggests that there are multiple separable domains of resilience (e.g., social and academic) that encompass both the absence of negative outcomes *and* the presence of positive outcomes. Notably, rates of resilience are reported to be lower when characterizing resilient outcomes across multiple areas of functioning relative to single domain resilience, which suggests that youth may show distinct patterns of resilience in different domains of functioning. Person-centered approaches, such as latent profile analysis, offer a powerful tool for identifying unique patterns of resilient functioning. However, previous work has largely utilized latent profile analyses to extract profiles of risk rather than resilience. In addition, research outlining the neural patterns that support resilience is just beginning and no work has characterized neural correlates of resilience using person-centered profiles.

Methods, Analysis Plans, and Hypotheses:

The current study will examine resilience profiles in a sample of 708 adolescent twins (7-19 yrs, M_{age} = 14.6yrs) recruited from neighborhoods with above average poverty levels. This study will encompass two aims, for which all data has been collected. First, we will conduct a latent profile analysis of parent, teacher, and adolescent reports to extract unique profiles of resilience across psychological, social, and academic domains. Given the data-driven nature of this approach, we do not hypothesize an exact number of latent profiles. However, we anticipate that profiles may encompass youth with high resilience across all domains, low resilience across all domains, and unique combinations of resilience across pairs of domains or single domains. Second, we will examine neurobiological correlates of each resilience profile. We plan to explore associations with neural functioning using task-based fMRI activity during relevant tasks (e.g., socioemotional processing, reward responsivity, inhibitory control) within regions implicated in emotion regulation and self-control (e.g., amygdala, ventral striatum, inferior frontal gyrus). We will derive evidence-based hypotheses in accordance with the data-driven resilience profiles and relevant neural correlates (e.g., inhibitory control-related prefrontal activation may be associated with academic resilience).

Implications:

This project will provide a data-driven approach toward refining our understanding of resilience profiles in youth. Through these analyses, we aim to identify person-centered features of multi-domain resilience and highlight neurobiological factors underlying resilience to neighborhood disadvantage.

2-G-62 - Environmental impacts on adolescent excitatory and inhibitory processes in frontal cortex

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Details

Mechanisms of critical period plasticity in prefrontal cortex, specifically changes in excitatory and inhibitory processes, are thought to contribute to the maturation of cognitive function through adolescence. Heightened plasticity during adolescence could render the frontal cortex more susceptible to environmental influences, as well as environmentally-driven changes in neural inputs from downstream brain regions that mature in earlier childhood. Life stressors are one such environmental factor known to affect neurodevelopmental trajectories and increase risk for psychopathology. Childhood stress has been conceptualized as adversity that has unique dimensions of threat and deprivation. Prior work has indicated that an individual's neighborhood environment can provide an effective index of one aspect of deprivation. However, it is not yet known how an individual's neighborhood impacts development of neurophysiological mechanisms that develop through adolescence, such as frontal excitatory and inhibitory processes. In this study, we will use already acquired longitudinal data in a sample of 162 10 30 year olds with up to 3 visits per participant. At each visit, we obtained 7T Magnetic Resonance Spectroscopic Imaging (MRSI) data using a J-refocused

spectroscopic imaging sequence (TE/TR=35/1500ms) to examine inhibitory GABA and excitatory glutamate across multiple regions of frontal cortex. An oblique MRSI slice was obtained of 24x24 voxels (1.0x0.9x0.9mm), encompassing dorsolateral prefrontal cortex, anterior cingulate cortex, and medial prefrontal cortex. In order to obtain information about participants' neighborhoods, we will also use the Area Deprivation Index (ADI), derived from American Community Survey data by the University of Wisconsin Neighborhood Atlas, to obtain information about the participant's neighborhood. We will first investigate how excitation and inhibition change through adolescence by looking at how glutamate and GABA change with age across regions in our sample. Based on prior literature and our prior cross-sectional studies (Perica et al., 2022), we hypothesize that glutamate will decrease with age and GABA will increase with age in our sample, and that glutamate and GABA will become more correlated, or balanced, through adolescence. We will then investigate how neighborhood deprivation could impact developmental trajectories of glutamate and GABA and thus the timing of frontal critical period plasticity. We hypothesize that greater neighborhood deprivation will be associated with less correlated glutamate and GABA across frontal cortex suggesting a change in the trajectory of critical period plasticity. These results will inform a model of how environmental factors of deprivation can impact developmental trajectories of prefrontal plasticity, which could impact cognitive development as well as risk for psychopathology.

2-G-63 - Associations between neighborhood socioeconomic status and infant brain activity

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Details

Increasing evidence suggests that socioeconomic status (SES) is associated with individual differences in children's brain activity as indexed by electroencephalography (EEG). For example, family-level socioeconomic disadvantage has been associated with lower frontal gamma power in the first year of life (Tomalski et al., 2013), and a recent randomized control trial found that a poverty-reducing intervention caused increased high-frequency (beta and gamma) power at 12 months of age (Troller-Renfree et al., 2022). However, less is known about how neighborhood SES may be associated with infant resting EEG power during early childhood. The goal of this study is to examine the association between neighborhood socioeconomic disadvantage and resting EEG power in infants ranging from 6-9 months of age. The data for this study will come from an ongoing longitudinal study of a cohort of 115 mother-infant dyads, who were recruited prenatally and are being followed longitudinally through age 3, to better understand links among socioeconomic factors, children's experience, and brain and behavioral development. Data from a subgroup of these participants will be used for the present study, and the analytic sample will include 6-9 month-old infants (current n=79; we anticipate data from up to 9 additional infants by the time of the Flux conference). Neighborhood SES will be measured using participant addresses to obtain an Area Deprivation Index (ADI) score, which examines the overall income, education, employment, and housing quality of a neighborhood (Kind & Buckingham, 2018). Resting EEG data will be collected from these infants, and will be preprocessed using the MADE pipeline and decomposed into the following frequency bands: theta (3-5 Hz), alpha (6-9 Hz), beta (13-19 Hz), and gamma (21-45 Hz) (Debnath et al., 2020). Multiple linear regression analyses will be used to examine the relationship between participant ADI score and EEG power in each of the frequency bands while controlling for child age, sex, and parental education. We hypothesize that lower neighborhood SES,

indexed by a higher ADI score, will be significantly associated with increased relative low-frequency power (theta) and decreased relative high-frequency power (alpha, beta and gamma). Subsequent research in the current longitudinal cohort, outside of the scope of the present analyses, will further investigate whether the association between neighborhood disadvantage and infant brain activity changes across the first three years of life. Altogether, this work will contribute to the scientific understanding of how environmental factors might contribute to brain activity in infants.

Citations

Debnath, R., Buzzell, G. A., Morales, S., Bowers, M. E., Leach, S. C., & Fox, N. A. (2020). The Maryland Analysis of Developmental EEG (MADE) Pipeline. *Psychophysiology, 57*(6). https://doi.org/10.1111/psyp.13580

Kind, A.J.H.,& Buckinghman, W. (2018). Making neighborhood disadvantage metrics accessible: The neighborhood atlas. *New England Journal of Medicine*, *378*, 2456-2458. doi: 10.1056/NEJMp1802313

Tomalski, P., Moore, D.G., Ribeiro, H., Axelsson, E.L., Murphy, E., Karmiloff-Smith, A., Johnson, M.H., & Kushnerenko, E. (2013). Socioeconomic status and functional brain development - associations in early infancy. *Developmental Science*, *16*(5), 676-687.

Troller-Renfree, S.V, Costanzo, M.A., Duncan, G.J., Magnuson, K., Gennetian, L.A., Yoshikawa, H., Halpern-Meekin, S., Fox, N.A., & Noble, K. G. (2022). The impact of a poverty reduction intervention on infant brain activity. *Proceedings of the National Academy of Sciences*, *119*(5). https://doi.org/10.1073/pnas.2115649119

2-G-64 - Interference Processing following evidence of childhood maltreatment in ABCD

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Details

Study objectives: Child maltreatment (CM) is a serious, widespread problem, with an estimated 37% of children referred to child protective services (CPS) for investigation in their lifetimes. CM often leads to long-term deficits in cognitive functioning broadly under the umbrella of inference processing. In fact, children with exposure to maltreatment have twice the rate of referral for special education and show deficits in achievement and IQ as well as in multiple domains of cognitionâ€”particularly in attention and executive functioning. Understanding developmental changes in cognition post-CM would have consequential benefits to society through the development of targeted interventions.

Identification of cognitive developmental mechanisms of CM is hampered by the size of cognitive developmental cohorts with CM. Recent work in neuroscience has shown the need for data from thousands of people to contend with individual variability in brain function and structure. CM neuroscience research tends to rely on small sample sizes due to the relative rarity of the experience

being studied. The proposed study confronts this problem in the field with a subsample within the larger ABCD study (~12,000) with CM exposure (n=4520).

Method: The ABCD study is a longitudinal study of normative cognitive development with a large national cohort of approximately 12,000 participants, aged 9-10 at baseline. Our CM baseline cohort includes subtypes of CM physical neglect (n = 2372); psychological (n = 1,033), physical (n=134), and sexual abuse (n = 72); and witnessing intimate partner violence (IPV, n = 2575), with significant subtype overlap. Subtype determinations were based on the Coleman CM definitions.

We will compare interference functioning during The Stop Signal Task (SST) between CM and control and to total cumulative exposure to CM. The SST is a measure of the ability to inhibit a prepotent response when the signal to stop is unpredictable. The task is designed to have a high failure rate with approximately 50% unsuccessful stops in this population, allowing researchers to examine response time (RT) and contrast successful and unsuccessful stops.

We hypothesize that the CM baseline cohort will have higher rates of behavioral failure during the inhibition of a prepotent response (H1). We also hypothesize that lateral prefrontal (lPFC) and anterior cingulate cortex (ACC) functioning will be disrupted in the CM cohort (H2) during inhibition. We further hypothesize that cumulative exposure to CM at baseline will be negatively associated with behavioral failure to inhibit a prepotent response (H3) and with disrupted lateral prefrontal and anterior cingulate cortex function (H4).

Analysis plans:

In behavioral analyses, we will compare SST successful and unsuccessful stops and response times (RT) using ANOVA (H1 and 3). fMRI statistical analysis will use a modified General Linear Model.49-50 Contrasts will be constructed at the individual participant level and then entered into a second-level random effects analysis to compare participant groups. The primary analysis will contrast correct interference trials with control trials to isolate the effects of interference resolution on fMRI BOLD signal in the lateral prefrontal cortex and anterior cingulate cortex (H2 and 4). To test the hypothesis that cumulative exposure is associated with poorer behavioral performance and greater neural functional dysfunction, cumulative exposure will be measured with total exposure to all varieties of CM.

General Implications: One of the core reasons that CM is so costly to society is the association of CM with decreased behavioral, cognitive, and/ or social functioning across the life course, which leads to lower academic attainment, employment trajectories, and lifetime loss of income. Identifying a cognitive mechanism would assist in the development of new preventive interventions.

H – Executive functioning

2-H-65 - Alpha and Theta Oscillations Support Verbal Working Memory Processing in Typically Developing Youth

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Details

Background: Working memory or the capacity to maintain and manipulate information for the purpose of goal-directed behavior, supports learning, reasoning, and language comprehension. Neuroimaging studies have shown that this ability improves across childhood and have identified the frontal-parietal network as integral to its function. Magnetoencephalographic (MEG) studies of verbal working memory in typically developing youths are rare, but the few existing studies have shown decreased alpha power within left-lateralized language regions during encoding and increased alpha power in parieto-occipital cortices during maintenance.

Methods: Herein, we used MEG to examine the oscillatory dynamics supporting working memory in a cohort of 66 youth, aged 6 to 14 years old, with a modified Sternberg working memory task. The resulting data were transformed into the time-frequency domain and the windows of interest within the alpha (8-12 Hz) and theta (4-7 Hz) ranges were determined using a data-driven approach and imaged using a beamformer. Task behavior was examined using correlation analyses, and voxel-wise whole-brain correlations were performed, followed by voxel-wise Fisher Z tests to examine possible age-by-sex interactions.

Results: During encoding, decreased alpha power was seen in occipital cortices and left-lateralized language regions. During maintenance, increased alpha power was seen in parietal-occipital cortices, while decreased alpha power was seen in left-lateralized language regions including inferior frontal cortices. During both encoding and maintenance, increased theta power was seen in cingulate cortices. Behaviorally, increased age was correlated with increased accuracy and decreased reaction time. Developmentally, alpha power during encoding was positively correlated with age in the right superior frontal cortex and negatively correlated with age in the right superior parietal cortex. Theta power was positively correlated with age in visual cortices during encoding. When examined for sex differences, females exhibited increased alpha power with age in the right frontal and right parietal cortices, while males exhibited the opposite relationship. The voxel-wise, whole-brain correlations between theta and age did not significantly differ by sex.

Discussion: Stronger visual theta with age may suggest that older youth utilize visual circuits to a greater extent during stimulus coding. The developmental changes in alpha activity in frontal and parietal regions may indicate significant optimization of networks supporting working memory during late childhood and adolescence. Additionally, the sex differences in alpha power with age may suggest an earlier maturation of frontal-parietal networks in females. These data support previous work by showing alpha oscillations within occipital and left-lateralized regions and add to the developmental literature by showing a strong increase in theta oscillatory power in cingulate cortices.

2-H-66 - Neurobiological differences in inhibitory control in preschool-aged typically-developing children and children with ADHD assessed by a continuous performance task.

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Details

Attention-Deficit/Hyperactivity Disorder (ADHD) and associated symptoms are a common reason for early childhood mental health referral, affecting between 10 to 25% of preschoolers. One persistent feature of ADHD is poor inhibitory control. However, little is known about how neural circuits supporting inhibitory control in this age range differ between typically developing (TD) children and children with ADHD. To examine this, we compared TD and ADHD children during task-based functional MRI as they completed a modification of the Kiddie Continuous Performance Task (KCPT). In the KCPT, children press a button when a picture is shown, but withhold responding if the picture is a soccerball. Withholding the response requires inhibitory control. Method: The final participating sample consisted of 56 4-7-year-old children diagnosed with ADHD (dual clinician diagnosed) and 78 typical controls (M age = 5.51, SD = 0.99, and 68% male). All children were scanned in an MRI (3T Siemens Prisma; whole-brain EPI T_2* BOLD scan, TR/TE = 1000/30 ms; FOV = 216 x 216; FA = 52; 2.4 x 2.4 x 2.4 mm; 60 slices no gap). Standard image post-processing corrected for movement (FD = .9 mm) and a voxelwise GLM analysis was applied. Whole brain analysis of baseline showed robust activity above resting baseline in bilateral visual and left motor cortex, in bilateral anterior insula associated with visual attention, in right middle/superior frontal cortex and parietal regions associated with working memory, in midline cingulate, pre-SMA, and SMA regions associated with motor planning and execution, and in subcortical thalamic and striatal regions associated with motor execution ($p < .005$, cluster corrected). These network activations are robust across groups, suggesting engagement with the task demands as expected. Whole brain analysis of group (ADHD vs TD) showed evidence of greater activation for the TD group in regions of the inhibitory control network, including bilateral inferior frontal gyrus, right pre-SMA and anterior cingulate cortex, and bilateral caudate. We examined whether there were age differences in brain activity collapsed across groups. The principal finding was a cluster of activity in right substantia nigra. This revealed increasing activity in this region as a function of age (controlling for sex, parent education, and movement), irrespective of diagnostic group status. We additionally examined the association between brain activity in our identified ROIs and behavioral measures of the computerized KCPT administered outside the MRI scanner. Significant main effects were found in right anterior insula for Hit RT and RT Variability measures. No significant group-by-region interaction effects were found. The results show that a) a validated measure of inhibitory control can be applied with preschool children in the MRI environment; b) the task is sensitive to group differences between TD and ADHD-diagnosed children in canonical executive function regions that are also identified in adults; c) functional activity in right substantia nigra may change over the course of development in response to tasks that require inhibitory control d) there is a significant association between right anterior insula activity and KCPT scores.

2-H-67 - School's Out for the Summer: Modeling Time-Of-Year Effects on Children's Cognition Using Cyclical Splines Across Large-Scale Datasets

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Details

Children's cognitive abilities vary substantially across both short and long timescales, from circadian fluctuations to year-by-year developmental changes. Temporal changes in cognitive functioning are typically assessed by treating time as a continuous linear variable, potentially masking cyclical fluctuations such as time of day, day of the week, or month of the year. Given that the academic school year may be a particularly dominant force in shaping children's' cognitive functioning, here we focus on understanding cyclical patterns of variability in children's cognition across the calendar year. To do so, we leverage generalized additive models (GAMs) that model the time-of-year of the assessment date with a cyclic smoothing spline. We fit these models in two large-scale datasets of youth: the baseline assessment of the Adolescent Brain and Cognitive Development (ABCD) Study (*n*= 11,042; ages 9-11y), and the Philadelphia Neurodevelopmental Cohort, (PNC; *n*=9,416; ages 8-22y). Cognitive performance in the ABCD dataset was quantified as scores on the first three principal components capturing broad domains of general cognition, executive functioning, and learning/memory derived from performance across nine cognitive tasks as derived in prior work. Cognitive performance in the PNC was quantified as factor scores on five cognitive factors (overall cognition, executive functioning, complex cognition, social cognition, and memory) as previously reported. We assessed the association between time of year (date of cognitive assessment, as day-of-year) and each cognitive measure using GAMs that modeled time of year with a cyclic smoothing spline and included covariates for age and sex. For the ABCD dataset, random intercepts for family and site were also included. For the PNC dataset, we included an interaction term for age and time of year to account for changes in nature of the time-of-year from late-childhood to early-adulthood. We found significant associations in ABCD between time of year and performance for all cognitive measures, with the lowest cognitive performance observed between August and September (general cognition: min=Sep-21, CI=[Sep-05, Oct-09]; executive functioning: Sep-07, [Aug-19, Sep-23]; learning/memory: Sep-08, [Aug-16, Sep-28]). In the PNC dataset, we found that the association between time of year and cognitive performance varied depending on age. At the median age of the ABCD sample (age 9.9y), we observed the same pattern as in the ABCD dataset (lowest scores between July and September; overall cognition: Aug-26, [Jul-22, Sep-22]; executive function: Sep-14, [Aug-16, Oct-07]; complex: Aug-17, [Jul-02, Sep-25]; social: Jul-24, [Jun-08, Sep-17]; memory: Aug-25, [Jul-19, Sep-26]). However, for adults, there was no defined minimum in performance during the year. Given that school-age children typically experience vacation from school during the summer months (June to August in North America), these findings suggest a small but consistent and reproducible effect of time of year on cognitive performance that may be related to this common, cyclical change in children's lifestyle or experience. Although relatively small in size (max $h^2_{partial}$ = .01), this effect was consistent across cognitive domains as well as across multiple large-scale samples of youth collected across the United States. Follow-up work may further explore the many possible factors that could contribute to this effect, including differences in social, environmental, physical, or affective experiences that may vary between the school months and summer months. More broadly, future studies examining variation in children's cognitive performance may want to account for this cyclical variability in cognition across the year, particularly as more large-scale datasets collect cognitive measures across year-long or longer study time frames. The extent to which this effect is present in datasets from countries with different academic calendars will also be important to assess.

2-H-68 - Affective-related impulsivity mediates relationship between internalizing symptoms and alcohol sipping initiation in youth

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Details

Objective: It has been demonstrated that early onset of alcohol use increases one's risk for developing drinking problems later in adulthood (Grant & Dawson, 1997; DeWit et al., 2000; Deutsch et al., 2015). Furthermore, average age of onset has significantly reduced in the last few decades, now regularly occurring during adolescence (Lim et al., 2012). Understanding risk factors for early alcohol use is therefore of critical importance for minimizing negative outcomes. Much research on incipient alcohol use in youth has focused on direct comparison of theorized developmental risk trajectories, namely the externalizing and internalizing pathways. Due to its more robust findings (e.g., King et al., 2004; Farmer et al., 2016), the externalizing pathway to substance use has received more attention in the literature. Evidence suggesting that internalizing symptoms can precede this pathway, however, substantiates the need for a deeper investigation into the internalizing pathway, as this could facilitate earlier prevention efforts for some youth. Additionally, there is a need to further observe interactions between elements of these two pathways to delineate time course trajectories and potential compounding risk.

Methods: 11,876 youth aged 9-10 were enrolled in the Adolescent Brain Cognitive Development study, a nationwide longitudinal study of brain development and child health. At each yearly visit, the youth and parent are administered a battery of measures, which includes self-reports of alcohol sipping and impulsive behavior from the youth, as well as parent reports of internalizing symptoms observed in the child. Alcohol sipping was recoded into a dichotomous variable, where a child was deemed an initiator once they had reported drinking at least 3 sips. A logistic repeated-measures Generalized Estimating Equation (GEE) was run to determine if the parent-reported Child Behavior Checklist internalizing subscales (anxious/depressed, withdrawn, and somatic complaints) predicted alcohol initiation while controlling for demographic and alcohol-related covariates. Dimensions of impulsivity, which included positive and negative urgency, lack of perseverance, sensation seeking, and lack of premeditation, were measured using the UPPS-P Impulsive Behavior scale. These subscales were each individually tested as mediators in a reduced GEE model via bootstrapping within the PROCESS mediation macro for R.

Results: Anxious/depressed symptoms emerged as the sole internalizing predictor of alcohol initiation in the full GEE model, which included all three subscales of the CBCL. Removing the two non-predictive subscales made this finding more robust and increased the overall fit of the model. This reduced model was used to test for mediating effects of the dimensions of impulsivity on the relationship between anxious/depressed symptoms and alcohol use onset. Positive urgency, negative urgency, and lack of perseverance each significantly regressed on anxious/depressed symptoms and fully mediated the relationship between that and alcohol initiation. When expanding the model to include all three

significant mediators, only the indirect effects of negative urgency and lack of perseverance remained intact.

Conclusions: Overall, our findings provide support for an internalizing pathway, but also suggest links between internalizing and impulsivity symptoms in the prediction of early alcohol use. The finding that only anxious/depressed symptoms predicted alcohol use onset suggests that internalizing composite scores, which are commonly used in the literature, are not sufficiently precise for detecting these effects. Our results suggest a possible combined internalizing/externalizing pathway for early alcohol use, with affect-related impulsivity increasing one's susceptibility to early alcohol experimentation. Further investigation is needed to continue characterizing these relationships over time, as substance use trajectories develop into adolescence.

2-H-69 - Household cognitive enrichment is associated with visual working memory function in pre-schoolers

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Details

Objective: Exposure to high-quality resources and activities in homes is critical for promoting children's school readiness, yet the effect on neurocognitive function remains unclear. The current study investigated the association between home enrichment and visual working memory (VWM) processing in pre-schoolers.

Methods: One hundred and twenty-six 4.5-year-olds children participated in the study. Home enrichment was assessed using an adapted version of the Home Observation Measurement of the Environment (HOME) Interview, conducted with one parent of each child. Parent responses to the adapted HOME interview were examined using inductive content analysis. From the responses, codes were created for resources/activities that promoted literacy (12 codes, e.g., books) and mathematics (11 codes, e.g., counting using fingers) development. These codes were quantified by summing parental endorsement to yield a home enrichment score, which was used in further analyses. Here, a higher home enrichment score suggested greater access to, and use of resources/activities thought to promote literacy and mathematics development. VWM was assessed in children using a colour change detection task while brain activation was recorded using portable functional near-infrared spectroscopy. fNIRS image reconstruction was implemented to transform channel-based fNIRS into a volumetric representation. Finally, a linear mixed effects model was run to examine the association between home enrichment and brain function in the VWM task.

Results & Discussions: Greater home enrichment was not directly linked to VWM performance. Instead, home enrichment modulated a right-lateralized fronto-parietal VWM network. Greater home enrichment was associated with increased activation in right angular gyrus (AG), important for guiding visuo-spatial attention and WM maintenance. Greater home enrichment was associated with suppression in right

inferior frontal gyrus (rIFG), important for re-orienting attention to distracting events. Critically, this home enrichment-modulated rIFG suppression was linked to better VWM performance. Taken together, our findings suggest that better home enrichment might provide children with more diverse opportunities to repeatedly engage in activities that improve sustained attention and suppressing distraction.

Conclusion: This work sheds light on potential mechanism(s) through which home enrichment during the preschool years might be linked to the development of critical cognitive systems.

2-H-70 - Development, Reward, and Motor Prepotency Effects on a Go-No-Go Task in HCP-D

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Details

Objective

One key feature of cognitive development is the capacity to select and execute one's actions according to the superordinate goals of the environment, which draws on a collection of cognitive processes generally referred to as cognitive control. As individuals grow from childhood to adulthood, there is broad-scale improvement in the capacity to control one's own behavior. The need for cognitive control is not equal in all situations. There are some environmental cues that particularly challenge cognitive control such as salient, value-laden cues. Diminished adolescent cognitive control under 'hotâ€ conditionsâ€"such as those involving rewardâ€"has been conceptually linked to risk taking behaviors in adolescence and young adulthood. However, these studies often juxtapose the cognitive control demands and the active presence of rewarding information, which limits the ability to isolate the specific changes in cognitive processes under reward conditions. In addition, rewarding information is frequently learned from direct, repeated experience with environmental cues. To mirror this process, the Conditioned Approach Response Inhibition Task (CARIT) specifically evaluates the influence of prior learning on subsequent cognitive control.

In these analyses, we characterize the task dynamics of the CARIT version of a go-no-go task to examine the effect of age and response prepotency on reaction time and errors, and unpack the implications for our understanding of the development of cognitive control. We then seek to examine the influence of previously conditioned reward and punishment cues on these task features to understand the development of the impact of reward learning on cognitive control.

Method

We use behavioral data from the Human Connectome Project Development's CARIT collected with the help of 1,173 participants (age 5-22 years). For each of two runs, participants responded to 92 trials, 68 go trials and 24 no-go trials. One of the two no-go cues had been previously associated with a reward (monetary gain; N = 12), while the second had been associated with a punishment (monetary loss; N = 12). We create a series of Bayesian hierarchical linear models using the probabilistic programing language, Stan, via the brms package in R to estimate the effect of smooth functions of age, motor

prepotency (i.e., number of previous contiguous successful go trials), and previous conditioning on reaction time during successful go trials (Hits) and on the error rate for no-go trials (False Alarm rate).

Results

We observe a gradual decline in reaction time to Hits and False Alarm error rate across age. The number of previous contiguous Hits (i.e., prepotency) *increased* reaction time. There was no correlation between individual differences in prepotency effects and error rate. However we observed a negative correlation between reaction time and error rate, and a positive correlation between reaction time and prepotency. We observed a very small reduction in error rate to previously rewarded cues.

Conclusion

Speed and accuracy on this cognitive control task gradually improve over the course of childhood and adolescence, with an average effect of prepotency suggesting participants strategically use the number of previous go trials to gauge the likelihood of encountering a no-go trial. Even after adjusting for age, individual differences correlations indicate those with faster reaction times tend to be more accurate overall, and evince less of a strategic slowing with number of go trials. The very small reduction in error rate to previously rewarded versus punished cues was not credibly different across ages, and was potentially so small as to be practically zero. This would be consistent with either a slight strategic increase in attention and performance to rewarded stimuli, or no effect.

2-H-71 - An examination of the longitudinal development and construct validity of Go/No-go task-related neural activation during successful inhibition across adolescence and early adulthood

Katie Paige [1], **Mary Heitzeg** [2], **Lora Cope** [2], **Jillian Hardee** [2], **Craig Colder** [3], **Mary Soules** [2], **Alexander Weigard** [2]

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Details

Objective: Poor cognitive control is thought to be a primary risk factor for adolescent substance use and poor social adaptation. Indeed, adolescents who engage in substance use and have difficulties with parents, peers, and school tend to exhibit poor behavioral performance on the Go/No-go (GNG) task, a measure of cognitive control. Notably, neuroimaging studies using the GNG have provided mixed results regarding the association between neural activation and problem behavior. These mixed results raise concerns about what GNG task-related neural activation measures and warrant further examination of its predictive validity with clinical outcomes. We used longitudinal factor analysis and computational modeling to examine the development of neural activation from the GNG, as well as its associations with substance use, social adaptation, and the cognitive mechanisms that underlie behavioral performance.

Method: The current study (*N*=215) used functional magnetic resonance imaging (fMRI), behavioral, and questionnaire data from the Michigan Longitudinal Study at four assessments spanning early (ages=10-13), middle (ages=14-17), and late (ages=18-21) adolescence, and early adulthood (ages=22-25). Activation parameter estimates for the primary contrast of interest (Successful Inhibitions (SI) on No-go trials > Go trials) were extracted for 11 Regions of Interest identified by a meta-analysis as active during

No-go vs. Go contrasts (Criaud & Boulinguez, 2013). We used activation during the SI vs. Go contrast because it is thought to reveal activation that is exclusive to the inhibitory process. Principal component analysis and confirmatory factor analysis were used to examine the factor structure of neural activation across ages 10 to 25. We then applied the diffusion decision model, a cognitive modeling approach, to behavioral GNG data in order to quantify distinct cognitive processes that underlie performance. Specifically, the diffusion decision model provides a more specific index of cognitive control (drift rate) than traditional response-time indices by accounting for construct-irrelevant influences on performance differences. Correlations between drift rate (i.e., cognitive control), brain activation from the SI vs. Go contrast, substance use, and social adaptation were examined.

Results: Results supported one factor of broad bilateral activation in prefrontal and parietal structures across the four waves spanning ages 10 to 25. However, test-retest reliability was poor (ICC = 0.20) and neural activity was unrelated to diffusion decision model parameters, substance use, and social adaptation. In contrast, faster drift rate (i.e., better cognitive control on the GNG) was associated with fewer drug problems and better school engagement.

Conclusion: This study was the first to examine the longitudinal factor structure of neural activation from the SI vs. Go contrast. While patterns of activation were consistent with what has been described in prior neuroimaging studies, poor reliability and lack of associations between neural activation, behavioral performance (drift rate), and clinical outcomes raises concerns about the utility of neural activation from the SI vs. Go contrast as a measure of cognitive control and its relevance to clinical outcomes in adolescence. Notably, the GNG task was not originally designed to be used during fMRI, and in a meta-analysis, Simmonds et. al (2008) suggest that treating Go and No-go trials as opposite contrasts in an fMRI design may lead to erroneous conclusions because both Go and No-go events involve response selection. Therefore, only examining activation on SI vs. Go contrasts is likely missing activation that is critical for task performance. It may be that cognitive control processes are better captured by neural activity during failed inhibition. Future research examining the construct validity of GNG task-related neural activation as a measure of cognitive control is warranted.

2-H-72 - Neurobiological correlates for reading and executive functions abilities in children with Rolandic Epilepsy

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Details

Rolandic Epilepsy (RE, currently termed self-limited epilepsy with centrotemporal spikes) has long been viewed as a benign epilepsy syndrome due to its self-resolving nature and responsiveness to common anti-seizure medications. This traditional view has been challenged over the past two decades in light of the high prevalence of mild cognitive deficits and behavioral problems among children with RE. These comorbidities may include attention deficits, mood disorders, and specific learning disorders, particularly reading and language impairments. Of note, while seizures in RE spontaneously resolve, comorbidities tend to persist into adulthood. This is the rationale behind the scientific focus on these comorbidities.

Reading is a complex cognitive process that involves both cognitive and linguistic skills. The required cognitive skills, commonly referred to as executive functions (EF), are necessary for the performance of goal-directed and complex activities. Children with RE have been repeatedly shown to have increased rates of reading difficulties as well as impaired EF. Yet, there are no data comparing reading difficulties in children with RE to children with dyslexia, the prototypic reading disorder. Moreover, no studies have focused on the possible link between RE, reading difficulties (RD), and impaired EF.

The current study aimed to characterize reading and EF profiles among Hebrew-speaking children with RE (n=9) vs those RD-only (n=18) and typically developing children (n=30) ages 8-15 years (matched for age, nonverbal IQ, and attention abilities) using behavioral and functional MRI resting state data (Inscapes-based resting state). Word, nonword, contextual reading, and reading comprehension abilities were assessed (using the Aleph-Taph battery), and EF abilities were compared across the three groups using Analysis of Variance (ANOVA). Functional connectivity within and between executive functions and attention networks (cingulo-opercular, frontoparietal, ventral, and dorsal attention networks) were generated from the resting-state data and associated with word-and contextual level as well as reading comprehension abilities.

Results demonstrated significantly lower word [F(2,60)=6.089, p=.004] and non-word [F(2,60)=8.940, p=.0] reading abilities in children with RD, followed by children with RE and typically developing children. However, lower contextual reading accuracy and comprehension [F(2,59)=9.048, p=.0], and visual attention scores (using the â€˜Diamon' task; F(2,59)=5.244, p=.008] were observed in those with RE, followed by RD and typically- developing children. Both EF networks and the dorsal attention network showed decreased within and between functional connectivity in those with RE compared to the two other reading groups, associated with decreased contextual reading ability, reading comprehension, and executive functions across the three groups (corrected for multiple comparisons, FDR<.05).

This study will be the first to systematically characterize the interaction between RE, reading difficulties, and EF. The fMRI data may improve the identification and classification of children with RE and reading difficulties. These RE-specific characteristics of reading difficulties may set the stage for applications using machine-learning models to identify reading impairments and propose tailored remedial interventions for children with RE.

2-H-73 - Examining dimensional attention performance as a predictor of neural activity during an inhibitory control task in children

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Details

Attention to dimensions, such as shape or color, has been identified as an aspect of attentional control that can guide cognitive processing. One aspect of cognitive processing that has not been explored in this regard is inhibitory control (IC). IC refers to the ability to suppress the processing of distractors and is predictive of academic achievement. One way to measure IC is with a visual search paradigm. In this task, children search for a target object among a set of distractors. This process requires attention

control to be able to choose the target feature while ignoring the distractors. Demands on IC can be manipulated by introducing a singleton item along the task irrelevant dimension. For example, in the additional singleton (AS) paradigm, when searching for a target shape, the search array can have homogeneously colored items or one of the distractors can be a unique color. In this case, the observer can use a dimensional attention (DA) filter to help inhibit attention from being captured by the task-irrelevant dimension. The goal of the current study is to understand how attention to dimensions predicts the neural and behavioral mechanisms of IC.

In the current study, 3.5- to 4.5- year olds will complete a modified version of the AS paradigm and two tasks assessing attention to dimensions: the Dimensional Change Card Sort (DCCS) task and the triad classification (TC) task while measuring fNIRS. The DCCS is a task in which children are told to sort cards by one dimension, e.g. color. After five trials, children are told to switch and sort by the opposite dimension, e.g. shape. The DCCS is a measure of flexible attention, or the ability to shift attention in order to meet task demands. Typically, in the DCCS, 3- year- olds fail to switch and continue to sort by the first dimension whereas 4-year-olds successfully switch and sort by opposite dimension.

Additionally, children will perform the triad classification task in which an experimenter shows children a reference object and two choice objects, instructing them to pick the choice object that goes best with the reference object. One of the choice objects, the identity choice, is maximally different from the reference object along one dimension but exactly the same along the other dimension. The other choice object, the holistic choice, does not match the reference object exactly but is overall more similar along both dimensions combined. The triad classification task is a measure of selective attention, which involves the ability to parse apart features of an object. Typically, younger children tend to choose the holistic object whereas older children tend to choose the identity object.

We expect to find that performance in the DCCS and TC tasks predicts performance and neural activation during the AS paradigm. Specifically, higher performance in the DCCS and TC tasks predict higher accuracy and lower reaction time during the AS task. Additionally, we hypothesize that performance during the DCCS and TC tasks will predict neural activation in the frontal and parietal cortex. Data collection for the current study is ongoing but almost complete, and therefore findings of the behavioral and neural results will be presented at the time of the conference.

2-H-74 - The Coordination of Proactive and Reactive Control Processes Across Development

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Details

Preschool children often engage cognitive control reactively, in the moment as needed; with development, children increasingly engage control proactively, in anticipation of needing it (Chatham et al., 2009). These developmental changes have been explained in terms of increases in the efficacy and capacity of children's proactive control. We propose and test an additional possibility: the *coordination* of reactive and proactive control may increase across development. Increased goal maintenance ahead of stimulus presentation (proactive control) should allow for decreased recruitment of goal activation in response to a stimulus (reactive control). For this efficient operation to occur,

proactive and reactive control mechanisms, which are behaviorally and neurally distinct, must coordinate (Czernochowski, 2014). Thus, increased proactive control may not always result in a matched decrease in reactive control, particularly in developmental populations new to engaging proactive control. We test whether the coordination between proactive and reactive control: 1) increases across development, and 2) relates to task performance.

As proactive and reactive control are temporal components of the same cognitive control operation, reaction time measures cannot differentiate these processes. ERP components can uncover fluctuations in proactive and reactive engagement within a single trial. The following proposed analyses will be completed prior to FLUX congress using collected ERP and reaction time data (published in Chevalier et al., 2020) from 29 six-year-old children, 30 nine-year-old children and 31 adult participants. Participants completed several conditions of a cued task-switching paradigm, where participants must sort an object by shape or color. We will use the reliable precue condition. In this condition, a cue presented ahead of the trial indicates whether the upcoming trial will require sorting the stimulus by color or shape. This preparation decreases reaction time. We will utilize one proactive ERP component, locked to the cue-onset: the posterior positivity (PP), as well as four reactive ERP components, locked to the target-onset: the P2, N2, P3 and pre-response negativity (PRN).

If proactive and reactive processes are coordinated across development, increased proactive control should be associated with decreased reactive control. We will test whether the proactive component amplitude predicts each reactive component amplitude across the three age groups using linear models. We hypothesize that the proactive component amplitude and age will interact in predicting the reactive component amplitudes. In adults and 9-year old children, but not 6-year old children, proactive control will significantly predict reactive control, providing evidence of efficient control coordination only in older children and adults.

We next look to uncover how the coordination of proactive and reactive processes relates to task performance. Greater engagement of proactive control predicts faster reaction times across development. If reactive control decreases proportionately with proactive control, then reactive control can be accounted for in the measure of proactive control. However, reactive control may provide additional relevant variance in reaction time if it is not well coordinated with proactive control. We will investigate this for each reactive ERP component using nested linear models and likelihood ratio tests. We hypothesize that adding the reactive component will not improve prediction of reaction time in adults and older children, but will in the youngest children, suggesting that children have reduced coordination between reactive and proactive processes that impacts their task performance.

These findings will shed light on whether a novel and important component of developing control is the coordination between proactive and reactive processes, which increases with development and relates to cognitive control performance.

I- Language

2-I-75 - Developmental trajectories of early word production and gestures through normative modeling

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Details

Normative modeling is a statistical approach to quantify how individuals vary from developmental expectations derived from a healthy population, and has been a fruitful technique for dissecting heterogeneity of functioning in individuals with complex brain disorders. In this study, we use the MacArthur-Bates Communicative Development Inventory (MB-CDI) to build normative models of word production for children 8- to 30- months old in order to predict heterogeneity in early language development and leverage deviance scores to characterize early language for children with agenesis of the corpus callosum (ACC). ACC is a congenital brain malformation defined by the complete or partial absence of the corpus callosum; it is still unclear how this malformation impacts language development specifically. Using deviation scores to describe individual differences from a normative sample has been shown to effectively parse population level heterogeneity for complex brain disorders, but to our knowledge, has not yet been applied to the heterogeneity and complexity of early language development generally (or for ACC). First, we trained and tested regression models on data from the Words and Gestures (WG) MB-CDI form, for both total production and total gestures. Our normative samples consisted of one external dataset (Marchman dataset from Stanford Wordbank, ages 8-18 months) with 2,932 children and a community sample (Phenoscreening dataset from University of Minnesota, ages 16-25 months) with 3,362 children. Poisson regressions for total production and Bayesian regressions for total gestures minimized root mean squared error and analysis of residuals from these regressions for the expected trends from 8-25 months produce high goodness of fit statistics. Next, we predict word production and gesture scores from our ACC sample (182 children) using the normative models, and calculate deviation scores (Z-scores) from the real and predicted values (ACC children below 25 percentile for production=14.3%, for gestures=31.1%; above 75 percentile for production=3.8%, for gestures=3.6%). This demonstrates the utility of normative modeling for documenting deviations for individuals with rare developmental disorders, rather than focusing on group-based generalizations. Further, we describe the utility of deviation scores when comparing measures with different scales, like production and total gestures, since data are transformed into a consistent reference frame relative to the normative trend. This work lays important groundwork for extending normative modeling to language delays in developmental disorders like ACC and autism spectrum disorders.

2-I-76 - Functional connectivity during passage listening predicts later reading ability in middle childhood

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Details

Children's early behavioral listening comprehension is highly predictive of their later reading abilities. However, less is known about the underlying neural mechanisms of these established behavioral relationships. To explore these associations, we collected fMRI data from 47 typically developing first-graders (age *M* = 7.5 years) and tracked their reading comprehension (RC) ability into third grade. During the fMRI session, children listened to 1) coherent narrative and expository passages and 2) matched,

scrambled phrases baselines. Compared to the baseline, the listening task elicited expected language comprehension network activity. Next, we investigated the various functional connectivity associations between the language network and other brain regions using a seed-to-voxel connectivity analysis. We were particularly interested in how language-related regions, identified by overlapping language atlas and task activity, were functionally connected to the rest of the brain. These regions included the left posterior superior temporal gyrus (pSTG) and the left inferior frontal gyrus (IFG). Activity in the left pSTG showed decreased functional connectivity with three default mode network (DMN) regions: the posterior cingulate cortex (PCC), the right angular gyrus (AG), and the right middle frontal gyrus. Interestingly, the associations predicted overlapping variance in children's later RC ability. The anticorrelation between left pSTG and PCC explained 10% of the variance in children's third-grade RC scores, and the anticorrelation between left pSTG and right AG explained 25% of the variance in their later RC scores. These models remained significant when controlling for first-grade RC ability and connectivity between these regions during the scrambled phrases baseline. We hypothesize that while listening to coherent speech, the way children's brains activate core comprehension processing regions and inhibit task-irrelevant implicates their later reading abilities. Additionally, we speculate that this functional relationship is likely to change as children gain more reading experience. Further analyses will elucidate these longitudinal relationships and how the modularity of these networks may further explain reading development.

2-I-77 - Children Know More Than You Think: An ERP Investigation of the Nature of Semantic Knowledge During Word Learning in Children

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Details

Learning a word is an incremental process, usually requiring many exposures to the word before one can demonstrate their knowledge of its semantic meaning. Yet, even before accurate demonstration of their semantic knowledge of a word, research suggests that one possesses some knowledge about the word. Electrophysiological studies of the N400 event-related potential (ERP) component, which reflects lexico-semantic processing, with both adults and children demonstrate that implicit semantic knowledge of novel words encountered earlier develops before participants behaviorally recognize the words as familiar. Also, several behavioral studies have found that when adults cannot correctly identify a wor's meaning after incidental exposure to it or a training phase, they consistently provide words with meanings that are within the same semantic category as the target word (e.g., providing *orange* for *apple*). However, it is unknown if children initially acquire semantic knowledge that is within the semantic category of the target wor's meaning like adults or if they use a different strategy and acquire inaccurate semantic knowledge that is out of the target wor's semantic category (e.g., claiming the meaning of *apple* to be *table*), as well as whether these types of semantic knowledge are differentiated electrophysiologically in children. The objective of this study is to fill these gaps in our knowledge, which holds implications for improving our understanding of how children learn new words and informing interventions for children with word learning difficulties.

Towards this aim, 69 right-handed, typically developing children aged 8 to 16 years completed a standardized language measure (i.e., the Clinical Evaluation of Language Fundamentals [CELF]; to assess general language ability) and participated in an incidental semantic identification task (ISLT). In the ISLT, behavioral and electroencephalography (EEG) data were collected while participants listened to 50 sentence triplets. All sentences in each triplet ended with the same nonsense word, which replaced a target noun that was also the same across the triplet. After each triplet, participants were asked to verbally provide a word with the same meaning as the nonsense word if they believe it had one. Incorrect responses were coded for whether they were within the same semantic category or out of the semantic category as the target word. We hypothesize that children will provide more within- than out-of-category responses and that the N400, derived from the EEG data, will reflect word learning (i.e., an attenuated mean amplitude for correct responses vs. incorrect responses) and capture differences in the semantic relationship between the incorrect responses and the target (i.e, attenuated mean amplitude for within-category responses vs. the out-of-category responses).

Analyses of the behavioral responses revealed that incorrect responses accounted for *M*=28.51% (*SD*=10.01%) of all responses and, as predicted, children provided more within- (*M* = 0.87, *SD*=0.18) than out-of-category responses (*M*=0.13, *SD*=0.18), *t*=-24.04, *p*<.000. The ERP analysis, to be completed by Flux, focuses on the N400 as it is sensitive to lexical-semantic differences in words and word learning in children using the above paradigm. Statistical analysis will follow protocols from previously published work, focusing on nine electrodes that are selected to cover a large area of the scalp and a 200 ms time window centered around the peak amplitude of N400 averaged across all participants since children often have later and/or different N400 latencies than adults. The mean amplitudes will then be subjected to a linear mixed-effect analysis with response type, age, CELF score, laterality, and anterior/posterior as independent variables. We will also consider the effects of age and general language ability on the N400. Findings from this study will provide valuable and unique insight into the word learning process.

J- Learning

2-J-78 - How adolescents generalize across rewarding experiences to learn and infer value

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Details

Adolescence provides a window of opportunity for learning. A key feature of adolescence is the rapid expansion of knowledge about the world. This growing knowledge provides a scaffold for generalizing any one particular experience to other similar experiences and allows individuals to integrate multiple separate memories to build an internal predictive model. However, while this process of learning and generalization has been extensively studied in adults, it remains unclear how generalization supports value-based inference during adolescence. From childhood to adulthood, connectivity between the striatum and distributed cortical regions strengthens, which may support the developmental emergence of flexible generalization of value. To test this, we designed a reward-based learning task that leveraged object categories as a form of general knowledge. Participants chose between pairs of objects for the

chance to receive a monetary reward. Objects were sampled from 33 distinct categories which were, on average, worth different amounts of reward (e.g., balloons = ~80Â¢, masks = ~20Â¢), allowing participants to learn the object category value. We tested whether individuals generalized category value to guide decisions when they were presented with novel objects from previously learned categories. To index explicit awareness of the category value structure, participants self-reported category values after learning. We examined age-related differences in 102 participants aged 10-25 years-old. Because retrieving and updating category knowledge relies on cortical systems that continue to mature during adolescence, we hypothesized that flexible category generalization would emerge with age. We found that 10â€“12 year-olds did not use category value to guide decision making. However, generalization increased with age, and older adolescents and adults were more likely to generalize category value. Surprisingly, although younger adolescents did apply category value to guide decision making, they still reported explicit awareness of the category values following the task. This reveals that younger participants learned category value but did not generalize this learning to guide decisions about novel choices. Together, these findings demonstrate that younger adolescents experience a knowledge-behavior gap: they can explicitly express value knowledge but don't apply it to guide value-based decision making. Ongoing work will reveal how ongoing brain development supports the emergence of flexible generalization.

2-J-79 - Intervention-driven changes in the Visual Word Form Area of struggling readers

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Details

Reading is a fundamental skill for academic success and is linked to many aspects of cognitive and social functioning. The ability to read fluently and comprehend written language depends on the development of specialized neural circuitry, including the selectivity of the Visual Word Form Area, or VWFA, for text (Cohen et al., 2002; Cohen & Dehaene, 2004). The VWFA is a region in left ventral temporal cortex (VTC) that plays a critical role in processing written words. It typically develops over time as individuals learn to read (Baker et al., 2007; Dehaene et al., 2010) and children with dyslexia and other reading struggles often lack a well-defined VWFA (Kubota et al., 2019).

The present study examines the impact of a reading intervention program on VWFA selectivity, size, and within-subject consistency. The study participants included 25 children (ages 8-13y) with a history of reading difficulties, who underwent an intensive 8-week reading intervention program that has previously been shown to improve reading skills in children with dyslexia (Donnely et al., 2019). Prior to the start of the intervention, and 4 months after its conclusion, participants were administered a battery of reading and cognitive measures to measure intervention-driven changes in reading ability. Additionally, participants completed a series of MRI scans including a functional localizer experiment targeting category selective regions of VTC (consisting of 4 runs of 4.5 minutes each). Data were preprocessed with fMRIprep (Esteban et al., 2017) and using Nilearn (Abraham et al., 2014), we fit a GLM to the data and calculated contrasts of text > other stimulus categories to define text-selective cortex. VWFA ROIs were defined on each participant's native surface for each timepoint.

To first determine the effect of the intervention on reading performance, we analyzed the behavioral assessments and found that after the intervention there was a notable enhancement in participant reading abilities. On average, participants scored 9 standard score points higher on the Woodcock-Johnson Basic Reading Skills composite index (ð›½ = 8.4, t = 15.3, p<2e-16). However, there was no noticeable progress in math skills, as indicated by the Woodcock-Johnson Math Facts Fluency standard score indicating that the intervention's impact was concentrated on improving reading. We then analyzed the functional data to determine if there were changes to the VWFA after the intervention. Prior to the intervention, many children lacked a text-selective region in visual cortex: 8/25 participants had no discernable VWFA. A chi-squared test revealed a significant difference in the proportion of emerging VWFAs after the intervention (Ï‡Â² = 6.6396, p=0.009974), with only 1 participant still missing a discernible ROI after the intervention. We also found that there was little spatial overlap between the VWFA before and after the intervention,, with a mean dice similarity coefficient of 0.288 (sd=0.266, se=0.053). We also performed a Mann Whitney U test to determine the difference in ROI size between timepoints and found that the VWFA increased significantly in size (*U*=169.0, *p*=0.005) from an average size of 150.92 vertices pre-intervention (range 10-739, sd=222.96) to 442.72 vertices post-intervention (range 14-2,808, sd=631.13). These results support findings from previous research (e.g., Kubota et al., 2019), which reveal a relationship between individual differences in reading ability and word selectivity in VTC. Here we extend this work by showing how an intensive reading intervention program can modify this architecture in children with dyslexia. In conclusion, this study demonstrates that an intensive reading intervention program can lead to significant improvements in reading abilities and the emergence and development of text-selective regions in VTC for children with dyslexia.

2-J-80 - The effects of novelty and uncertainty on exploratory behaviors following early life adversity

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Details

Background. Prior work has demonstrated that individuals with a history of early life adversity (ELA) exhibit decreased exploration in decision-making tasks. However, it remains unclear how two important but distinct characteristics of the environment, stimulus novelty and reward uncertainty, play a role in these patterns. Although often confounded in decision-making tasks, recent work suggests that these two components have unique effects on exploratory behaviors, underscoring the importance of decoupling these two motivators of behavior. The current study seeks to elucidate whether decreased exploration following ELA stems primarily from differences in novelty-seeking or uncertainty-avoidant behavior. This study is currently being designed, and data collection and analyses will be completed by the conference.

Methods. We plan to recruit a sample of 300 emerging adults (ages 18 to 25 years). Participants will complete a task that decomposes the unique effects of novelty and uncertainty in explore-exploit decision-making. On each trial, participants choose between two stimuli that vary in novelty and reward uncertainty, with the goal of learning which stimulus has the highest mean reward payout in order to obtain the most points. Participants will also complete the Childhood Trauma Questionnaire (CTQ), which includes subscales of abuse and neglect. We will first test whether the previously observed association in which greater ELA (indicated by total scores on the CTQ) is associated with attenuated exploration replicates in our sample. Building upon prior work, we will additionally investigate how novelty and

uncertainty of choice options, two components central to exploratory decision-making, relate to putative ELA-related differences in exploratory behaviors.

Analysis plan: Logistic regression. Using a multilevel logistic regression, we will model the probability that a participant chooses a given option on a given trial, with differences in expected value, reward uncertainty, and stimulus novelty between the two choice options for the trial as fixed effects in the model. Additionally, this model will test how these differences interact with ELA (total CTQ score) in predicting choice behavior.

Analysis plan: Computational modeling. We will fit a reinforcement learning model to examine how expected value, uncertainty, and novelty of a given option guide participant choice behavior by affecting the subjective utility of each choice option. The model will also include participant-specific free parameters for a novelty bias and uncertainty bias. Using linear regression, we will test whether novelty biases or uncertainty biases differ as a function of total CTQ scores.

Confirmatory hypothesis. In line with prior research, individuals with higher cumulative ELA (indicated by total CTQ score) will demonstrate lower exploration levels.

Exploratory hypothesis. We will test two competing possibilities: Attenuated exploration in individuals with a history of ELA could be driven by lower novelty-seeking behavior (indicated by the participant-specific novelty bias parameter) or by a greater aversion to reward uncertainty (indicated by the participant-specific uncertainty bias parameter).

Exploratory analysis. If the characteristics of the sample allow (i.e., if the distribution of abuse and neglect CTQ subscales across the sample are relatively normal and demonstrate variability in the levels of abuse versus neglect experienced), we will test whether the unique effects of novelty and reward uncertainty on exploration specifically differ based on the type of adversity experienced (i.e., abuse versus neglect).

General implications. Given the association between exploratory behaviors and mental health, this has implications for functioning in ELA-exposed individuals, who are at heightened risk for developing psychopathology.

2-J-81 - The Relationship between Autism Symptom Severity, Anxiety, and Stimming as a Coping Mechanism during a Socially-Mediated Math Activity

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Details

Background: Anxiety is a common emotion experienced by children with the autism phenotype.[1] In school-aged children, topics that require abstract reasoning, such as math, can be highly anxiety-provoking. This often leads to poor academic performance; in fact, 15-40% of autistic students have math difficulties.[2,3] Little is known about how to support students with the autism phenotype in general

education settings, yet there is an increasing number thereof.[5] Autistic self-advocates have identified self-stimulatory repetitive behavior, or stimming, as compensatory for anxiety.[4] More knowledge of the biological underpinnings of stimming and whether it confirms this compensatory role can help guide future educational supports.

Objectives: To evaluate if movement mitigates the relationship between autism symptom severity and math anxiety.

Methods: Data were collected as part of a study assessing differences in brain synchrony between children with and without autism and their parents. For the current analyses, participants were 46 children aged 7 12 years (M = 8.45, SD = 1.91) with (n = 28) and without (n = 18) autism. Movement energy analysis (MEA) data were calculated from video recordings of children completing a math flashcard game. To assess anxiety, children completed a self-report survey to indicate the degree of anxiety they experienced after completing a standardized math activity. Autism symptomatology was measured with the parent-report Autism Spectrum Quotient.

Results: Autism symptom severity significantly predicted both maximum MEA scores, B = 313.34, $p < .05$, 95% B_{Ca} [64.39, 649.92], and math anxiety, B = 0.02, $p = .05$, 95% B_{Ca} [0.00, 0.04]. Maximum MEA scores also significantly predicted math anxiety, B = $5.41e^{-05}$, $p < .001$, 95% B_{Ca}[$2.09e^{-05}$, $7.79e^{-05}$]. Maximum MEA scores fully mediated the relationship between autism symptom severity and math anxiety B = $4.12e^{-05}$, $p < .05$, 95% B_{Ca} [-0.01, 0.04].

Conclusions: While greater autism symptoms are linked to greater math anxiety, results showed that increased movement fully accounts and decreases this relationship. Since children are often encouraged to sit quietly in the classroom, understanding how movement and other psychophysiological characteristics may reduce anxiety can inform effective approaches for person-centered instruction. This understanding may be especially crucial for working with autistic children, many of whom may be especially reliant upon movement as a key mechanism for coping with anxiety.

2-J-82 - Interaction between childhood socioeconomic circumstances and brain development in elementary academic outcomes

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Details

Higher levels of parental socioeconomic status (SES), such as educational attainment, have been found to positively predict differences in children's brain development and academic outcomes. What remains elusive is the extent to which individual differences in children's brain development relate to academic outcomes at lower levels of parental SESâ€"that is, when structural resources are limited. Our study characterized volumetric brain correlates of academic outcomes in students (N = 340) from diverse SES backgrounds, who were enrolled in the study after first grade and returned for follow-ups annually for (up to) three years thereafter. At each visit, students were assessed for reading and arithmetic skills to collect academic scores, as well as underwent MR imaging to measure gray matter volume. Mediating analyses were conducted to evaluate which brain regions explained the associations between parental

SES and children's academic outcomes as a continuum. Moderation analyses were applied by testing the interaction term between parental SES and brain regions in predicting children's academic outcomes, thus parsing out the effects between lower versus higher levels of parental SES. Analyses also controlled for indices of students' neighborhood and school environments, first-grade IQ, and demographic information. Results showed that parental SES was positively related to volumetric differences in brain regions previously implicated in reading and arithmetic skills, which in turn predicted students' assessment scores. At lower levels of parental SES, regions previously implicated in attention and executive functions were revealed to positively associate with students' scores. Moreover, among these students at lower-SES levels, the interaction between regions implicated in attention/executive functions versus academic skills appeared to predict students' scores over time. Findings add to the growing literature on childhood socioeconomic circumstances, brain development, and academic outcomes.

K – Mechanisms (hormones, neurotransmitters, physiology)

2-K-83 - Sexually-Divergent Impact of Testosterone on Selective Attention in Youth

Jake Son [1], **Lucas Weyrich** [1], **Abraham Killanin** [2], **Giorgia Picci** [1], **Hannah Okelberry** [1], **Danielle Rice** [1], **Anna Coutant** [1], **Tony Wilson** [1]

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Details

Background: Childhood and adolescence are critical developmental periods for the emergence and refinement of cognitive control processes. While sexually-divergent trajectories of structural and functional neural changes have been well-documented during these periods, far less is understood about the role of hormones on the neural oscillatory dynamics underlying selective attention. In this study, we examine the impact of testosterone on spectrally-specific oscillatory changes using magnetoencephalography (MEG) in healthy youth.
Methods: MEG data were collected from 96 participants (ages 6-13, 44 female) during a Flanker task and were preprocessed and transformed into the time-frequency domain. Significant time-frequency windows (i.e., theta, alpha, gamma) were imaged using a beamformer and subtracted condition-wise (i.e., Incongruent Congruent) per participant. These flanker interference maps were subject to whole-brain correlations with testosterone (separately by sex) while controlling for the effect of age, prior to Fisher's z-transformation analyses.
Results: We observed novel testosterone-by-sex interactions for each spectral window ($p < .005$). In the theta band, the temporoparietal junction and the insula showed significant differences by sex that varied in direction. Sex differences were also found in the temporal and parietal cortices in the alpha band, as well as occipitotemporal cortices in the gamma band.
Conclusions: The association between testosterone levels and neural interference during a cognitive control task robustly differed by sex across a distributed network of regions known to be critical for selective attention and interference resolution. These findings contribute to extant literature by highlighting the potential role of hormonal cascades during puberty in sexually-divergent patterns of neurodevelopment.

2-K-84 - A multimodal investigation of sleep and anxiety in peri-pubertal adolescents

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Details

Objective

Anxiety disorders are prevalent in adolescence and are often preceded and exacerbated by poor subjective sleep health. However, disparate measures of sleep and anxiety, small sample sizes, and wide age ranges used in previous studies have made it difficult to reach a consensus on which aspects of sleep health are impaired in pediatric anxiety. While anxious youth consistently report low sleep satisfaction, objective measures often fail to capture sleep disturbances in pediatric samples. Sleep neurophysiology research has highlighted two important factors for restful, restorative sleep that may be impacted in anxiety: rapid-eye-movement (REM) sleep and spindles. As REM sleep plays a key role in emotional processing and is fragmented in adolescent depression, impaired REM may explain low sleep satisfaction in anxious youth. Sleep spindles are another important mediator of sleep-related functions that help diminish response to outside stimuli while sleeping. Low spindle activity is linked to worry and poor subjective sleep quality and may contribute to sleep disturbances in anxiety. Characterizing sleep health as youth enter puberty is an important next step for improving sleep and promoting healthy adolescent emotional development. We propose a multimodal, dimensional approach that assesses mental and sleep health across domains in a large sample of adolescents to answer open questions regarding the role of sleep health in adolescent anxiety.

Methods

Data are drawn from a sample of 200 adolescents (10-13y/o) who completed a larger study examining sleep and emotional memory in anxiety. To monitor their sleep, participants wore wrist actigraph watches and completed daily sleep diaries over a 2-week period. They also completed one night of polysomnography (PSG), the gold standard for assessing sleep neurophysiology, and the Children's Report of Sleep Patterns (CRSP) as a subjective measure of sleep health. Clinician-rated anxiety diagnosis was derived from the Anxiety and Related Disorders Interview Schedule (ADIS). Clinicians rated participants' anxiety severity over the past week via the Pediatric Anxiety Rating Scale (PARS). Participants and parents reported on participants' anxiety over the past 3 months via the Screen for Child Anxiety Related Disorders (SCARED). A composite anxiety score across measures (binary ADIS anxiety diagnosis, PARS-6, child SCARED, parent SCARED) was estimated using principal components analysis (PCA) to capture a dimensional measure of anxiety severity that considers accounts from multiple sources. Data collection and PCA are completed; the following Aims are planned.

Aim 1: Determine associations between anxiety and subjective sleep health in early adolescence. Hypothesis: Anxious youth will report high levels of sleep disturbances on the CRSP.

Aim 2: Determine associations between anxiety and actigraphy sleep metrics and daily diaries over a 2-week period. Hypotheses: Anxious youth will report sleep disruptions, but actigraphy-derived metrics of

sleep efficiency will not relate to anxiety. Anxiety may show weak associations with actigraphy-derived number of arousals, but the association between self-reported nightly arousals and anxiety will be stronger than with actigraphy. Diary estimates will correlate with actigraphy estimates, but this effect will be reduced in anxious youth.

Aim 3: Determine associations between anxiety and sleep architecture assessed via PSG. Hypotheses: At the macro-architecture level, anxious youth will show less REM sleep, more REM fragmentation, and lower sleep efficiency. At the microarchitecture level, anxious youth will show decreased spindle activity which will correspond to lower daily diary sleep quality ratings the morning after PSG.

Exploratory Aim: Post-hoc clustering analysis will be conducted on the combined sleep metrics to identify sleep health profiles across objective and subjective domains and their associations with anxiety in early adolescence.

L- Memory

2-L-85 - The development of functional memory networks connected to the hippocampus

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Details

Decades of research has focused on the role of the hippocampus (HPC) in memory formation, and its' role in episodic memory. Along with the HPC, memory functions may also be slow developing, with episodic development continuing through at least middle-childhood (Ghetti and Bunge, 2012). While hippocampal development is one explanation for these changes, the brain does not develop in isolation; age-related changes in broader memory networks may also undergo dramatic changes. Recent work in adults revealed long-term memory networks that are functionally connected to the HPC including a Medial Temporal Network (MTN) and Default Mode Network (DMN) (Ritchey et al,. 2015; Barnett et al., 2021). These networks and their functions are still being explored, but critically, have not yet been tested in the developing brain.

In adults, the MTN and DMN can be further subdivided into regions that are thought to serve related, but dissociable memory functions. The MTN is comprised of medial temporal regions and precuneus that connect strongly to posterior HPC and is thought to bridge communication between visual perception regions, the DMN and the HPC. The DMN can be subdivided into Posterior Medial (PM), Anterior Temporal (AT), and Medial Prefrontal (MP) networks. The PM network supports episodic functions with broad connections to HPC, whereas the AT network (connected to anterior HPC) supports item-level memory and relational binding (Ritchey et al., 2015). Given that these networks connect to the slow-developing HPC, and the differing developmental trajectories of item-level and episodic memory, investigation of these memory networks may reveal maturity differences corresponding with the development of the HPC and memory behaviors.

To this end, we aim to conduct a pre-registered study investigating the development of these cortico-hippocampal networks using a publicly available fMRI movie-watching dataset spanning toddlers (3-4 yrs, n = 32), early childhood (5-7 yrs, n = 55), middle childhood (8-12 yrs, n = 31) and adults (18-39 yrs, n

= 32) (Richardson et al., 2018). We predict these networks will generally be slow developing given evidence of protracted hippocampal and prefrontal cortex development into adolescence. That being said, we predict some sub-networks will develop earlier than others. Given literature showing general posterior to anterior developmental gradients of networks across the brain, it may be that more posterior subnetworks like the MTN and PM sub-network of the DMN develop earlier than the AT and MP networks that include regions such as the medial prefrontal cortex that mature through adolescence (Shaw et al., 2008). Alternatively, in a competing memory-centric hypothesis, the PM network may instead develop *later* than the AT network given the PM network's association with slow-developing episodic functions compared to the AT network's role in item memory and relational binding, which may be well-developed even in toddlers (Richmond et al., 2015).

To test these competing hypotheses, we plan to conduct functional connectivity analyses in developmental and adult samples. First, to determine when these regions reach adult-like maturation, we will use a region of interest approach using the network of regions identified by a recent functional neuroimaging study in adults (Barnett et al., 2021), initially treating age continuously. However, we do not know if these parcellations will necessarily be present in this developmental sample, so we will also re-run the parcellation in age-brackets (defined above). We will identify networks in using a Louvian community detection algorithm (approach described in Barnett et al., 2021). After identifying any differences between group parcellations, we will conduct continuous age regressions for each parcellation using generalized additive models. Characterizing the development of these networks, will inform the development of key memory behaviors.

2-L-86 - Different levels of videogaming in children are associated with different neurocognitive outcomes

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Details

Objective: While most research linked videogaming to adverse outcomes in children, findings have been divided with respect to videogaming association with cognitive skills and mental health. In addition, the underlying neurobiological mechanism, if any, remains unknown. Here, we compared mental health and cognitive measures as well as BOLD signal in large samples of mild and heavy videogamers (VG) to non-videogamers (NVG) during a working memory task using task-based fMRI, in a large dataset of 9- and 10-years old children from the Adolescent Brain Cognitive Development study.

Methods: Participants are administered a screen time survey asking how much time children 'Play video games on a computer, console, phone or other device (Xbox, PlayStation, iPad)?â€. Videogaming hours were self-report for a typical weekday and a typical weekend day, from which videogaming hours/week were derived for each child. Outcomes of interest included mental health scores from the Child Behavior Checklist (CBCL), cognitive from the NIH ToolboxÂ® cognition battery, behavioral performance measures on the N-back task (as measured by '). These outcomes were assessed and compared with linear mixed models across NVG (0 h/week of videogaming), mild VG (1-3 h/day videogaming), and heavy VG (3+ h/day videogaming). In addition, cortical BOLD signal during the N-back fMRI task was compared across the three groups using non-parametric permutations, and FDR-corrected results at $p<0.05$ are reported.

Results: Mild VG (N=638; videogaming =11â^“5 h/week) were the best performers on the NIH toolbox cognitive tasks compared to NVG (N=1128) and heavy VG (N=679; videogaming =25â^“7 h/week). In addition, in line with the literature, the CBCL behavioral and mental health scores were higher in VG, particularly attention problems, depression, aggressive behavior and ADHD scores in heavy VG compared to both NVG and mild VG, leaving open the possibility that mild VG may be on a trajectory to show larger effects with time and more exposure to videogaming. Interestingly, mild VG only had higher thought problems and ADHD scores than NVG, and lower symptom scores than heavy VG for most measures. They also had the highest IQ scores and performed significantly better on Flanker and pattern recognition tests compared to NVG, while both mild and NVG performed equally better on list and card sorting tests than heavy VG. Mild VG and heavy VG performed significantly better (as measured by ‘) and showed higher neural activation on the 2-back vs. fixation contrast of the N-back task compared to NVG in bilateral Precuneus and the right precentral gyrus.

Videogaming is associated with enhanced performance on the N-back task, coupled with higher neural activation in cortical brain regions playing a critical role in working memory and visuospatial attention. In addition, in line with the Goldilocks hypothesis, the findings suggest that a moderate amount of videogaming may offer important cognitive benefits with dramatically less detrimental associations with mental health measures.

2-L-88 - Exploring relations between child age, hippocampal structure and spatial reorientation performance

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Details

Spatial reorientation is a crucial aspect of spatial cognition that allows an individual to situate themselves within their external environment after being lost or disoriented (Julian et al., 2018). The hippocampus is a medial temporal lobe structure that is part of a broader neural substrate supporting spatial cognition (Burgess et al., 2002). In adults, an extensive neural substrate, including the hippocampus, supports spatial reorientation. However, little is known about the neurobiological development of spatial reorientation. Significant development in the hippocampus and spatial cognition occurs between the ages of four- and six-years-old. Previous studies have implicated total hippocampal volume and age as predictors of individual differences in spatial reorientation task accuracy, but their specific contributions have not been directly compared. The current study aims to characterize how age and individual differences in hippocampal volume correlate with children’s performance on a spatial reorientation task.

Thirty typically-developing four- to six-year-old children (*M*=5.7 years, *SD*=.88; 16 boys) completed an age-appropriate spatial reorientation task, and a T1- and T2-weighted structural MRI protocol. During this visit, the parents completed a demographic survey.

After controlling for sex and the mother’s level of education, multiple regression analyses revealed that older children were significantly more accurate on the spatial reorientation task (r = 0.54). Total

hippocampal volume did not predict spatial reorientation task accuracy controlling for the same covariates (r = -0.16). These findings suggest that age, rather than total hippocampal volume, may aid children in recovering their sense of direction when lost.

Keywords: *spatial reorientation*, *development of spatial cognition*, *neurobiology of spatial cognition*, *structural magnetic response imaging*

2-L-89 - Anxiety, Memory Bias, and Social Support during Adolescence

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Details

During adolescence, onset rates of social anxiety peak just as peer feedback increases in its frequency and salience. Socially anxious adolescents have greater engagement in a broad network of brain regions implicated in threat and salience processing during peer feedback including amygdala, insula, medial prefrontal cortex, and ventral striatum. However, prominent theories suggest that negative memory biases for social experiences may also contribute to social anxiety symptoms. Few studies have tested this relation outside of unverifiable autobiographical events. Our lab recently developed the Recall After Feedback Task (RAFT) that overcomes this problem by exposing participants to positive and negative purported peer feedback prior to probing their recall for this feedback. Using this task, we demonstrated that more severe symptoms of social anxiety were associated with a bias towards recalling peer feedback as more negative than positive. However, it is plausible that perceived social support, which buffers against negative affect and anxiety during adverse experiences, may mitigate this relation. To test this, adolescents (N=36) completed the RAFT while undergoing fMRI. Forthcoming analyses will determine the extent to which perceived social support moderates the relation between negative memory bias and anxiety. We will also assess the extent to which brain function during encoding of social feedback influences associations between social support, memory bias, and anxiety. Regions of interest will include structures implicated in threat and salience (e.g., amygdala, insula, medial prefrontal cortex, and ventral striatum) as well as memory-related processes (e.g., hippocampus). Findings will help determine if social support is a protective factor in mitigating expressions of anxiety in adolescents who exhibit a negativity bias.

2-L-90 - Multimodal Analysis of Neural Signals Related to Source Memory in Young Children

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Details

Episodic memory plays a vital role in cognitive development, enabling individuals to encode, store, and retrieve information for future use, as well as facilitating neural connectivity and brain development.

The emergence of source memory is an important milestone during memory development. Decades of research have explored neural correlates of source memory using Electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). However, connections between findings from the two approaches, particularly during development, remain unclear. The goal of this project is to identify similarities and differences between neural correlates of source memory from an existing EEG and fMRI dataset collected from a sample of children aged 4 to 8 years. Specifically, we will conduct source localization of task-relevant event-related potentials (ERPs), to identify projected EEG sources that overlap with previously-identified regions of fMRI activations. The project utilizes an existing dataset described in previous publications from our lab (redacted for review). The dataset includes participants' EEG-recorded and fMRI-recorded brain activity during the same source memory task (different stimuli used for the two modalities), and a structural MRI image of each participant. Both EEG and fMRI data have been preprocessed as described in our previous publications. We identified the late slow wave (LSW) component to have significant conditional differences between subsequent source memory correct vs. source memory incorrect trials. We also identified 7 brain regions showing differences in BOLD signal to subsequent source memory correct vs. source memory incorrect trials.

For this project, age-specific brain templates were applied to guide brain extraction and segmentation. EEG electrode locations were re-estimated for each participant using 14 manually-marked anatomical landmarks. The anaylses to be completed for this project include 1) the realignment of LSW peaks for each participant to facilitate accurate source localization, 2) A general linear model to identify significant predictor channels of the task performance, to determine the EEG channels that will to be included in the source localization analysis, and 3) source localization of LSW peaks in individual head space for each participant. Identified cortical sources of LSW signals will be compared to existing fMRI results from this dataset to identify anatomical similarities and differences. This project has the potential to bring together developmental literature on EEG and fMRI in order to better understand the neural sources underlying source memory in young children. While few multimodal neuroimaging studies have been conducted in young children, this project will demonstrate the potential of combining multimodal measures in this age group to better understand memory development, paving the way for future developmental research.

M- Methods

2-M-91 - A New and Public Resource to Advance Understanding of and ADHD and ASD

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Details

INTRODUCTION: Obtaining MRI data in children, particularly those with neurodevelopmental disorders, has historically been challenging. These methodological challenges contribute to the limited understanding of neurobiology in neurodevelopmental disorders such as ADHD and ASD. Notable gaps remain in existing datasets, despite great efforts to collect phenotypic and MRI data in these clinical

populations. One gap relates to the development of precision functional mapping (PFM) datasets in clinical samples where >1hr of fMRI data is collected for individual mapping. The Subpopulations in ADHD and ASD study (Subpop) conducts extensive data collection on individual participants by creating a PFM dataset that is first of its kind. The goal of this dataset is to address the current gap and pitfalls of pre-existing datasets in the field of pediatric neurodevelopmental research. Researchers will be granted the opportunity to not only conduct critical analyses, but also answer complex questions the field has yet to address regarding behavioral and cognitive differences between children with and without these neurodevelopmental disorders.

METHODS: At the University of Minnesota and Washington University St. Louis, 9 and 10-year-olds are enrolled into the Subpop study. This cohort (N = 240) will be comprised of youth with ADHD, ASD, and age-matched controls. The Subpop study collects behavioral phenotyping data, a saliva sample, T1 and T2 structural MRI data, and multi-band multi-echo (MBME) resting state fMRI data. Eligible participants complete up to 7 study visits made up of 3 cognitive/clinical visits and 4 scanning sessions. The protocol calls for parent and child clinical interviews, parent and teacher surveys, parent and child self-report measures, surveys about other biological siblings and parent, as well as multiple cognitive testing sessions for the child. Families complete a minimum of 40 questionnaires and the child completes 6 different cognitive tests. Additionally, participants are completing the 4 scanning sessions, and for an average child 108 minutes of data are retained when using a stringent motion censoring threshold (FD < 0.2mm). Assessed domains include but are not limited to memory, executive function, social communication, peer relations, sleep habits, stress, personality, and symptomatology of 26 different clinical diagnoses. Lastly, all participants are evaluated by two senior clinicians to assess comorbidities, symptoms, and diagnostic accuracy of pre-existing conditions.

PRELIMINARY CONCLUSION: As more fields move towards a data-sharing model to improve the validity of research findings, the Subpopulations in ADHD and ASD dataset will prove to be an invaluable resource to researchers and aims to improve the understanding of neurodevelopment and brain behavior relationships. This enriched and individual-specific dataset will provide the opportunity for precision functional mapping and transdiagnostic subtyping, thus allowing researchers to better understand functional connectivity as it relates to the symptoms of the target disorders. We will present the specifics of our data collection and what researchers can expect to access when the data resource are made publicly available. By establishing and maintaining this dataset, we aim to improve the diagnostic accuracy, etiological understanding, and care-management of children and families affected by these disorders.

2-M-92 - Reports of the death of brain-behavior associations have been greatly exaggerated

Carolina Makowski [1], **Timothy Brown** [1], **Weiqi Zhao** [1], **Donald Hagler** [1], **Hugh Garavan** [2], **Tom Nichols** [3], **Terry Jernigan** [1], **Anders Dale** [1]

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Details

Magnetic resonance imaging (MRI) has been a popular and useful non-invasive method to map patterns of brain structure and function to complex human traits. A more ambitious challenge is to define features of the developing brain that predict cognitive, social, or emotional traits, and thus uncover

opportunities to improve behavioral outcomes. Recently published observations in a sample of thousands of children cast doubt upon these prospects, particularly for prediction of cognitive traits from resting state functional MRI (fMRI), which seems to account for little behavioral variability. Here we compare the sample sizes required to detect reproducible brain-behavior associations across imaging modalities using both univariate and multivariate methods. We demonstrate that by applying multivariate methods to high-dimensional brain imaging data, we can capture lower dimensional patterns of structural/functional brain architecture that correlate sufficiently robustly with cognitive phenotypes to be reproducible with only 42 individuals for working memory-related fMRI, and between ~50-75 for structural/diffusion MRI. Power is further enhanced when empirically modeling the task fMRI time series data, with only 36 individuals required. Dimensionality reduction of empirically-modeled task fMRI data also allowed us to obtain a finite number of separable spatio-temporal components predictive of general cognition, which yielded larger effect sizes than any individual univariate association and more interpretable patterns of brain-behavior associations (e.g., dorsolateral-prefrontal and parietal activation linked to cognitive performance). These results point to an important role for neuroimaging in translational neurodevelopmental research and showcase the ability to measure meaningful and reproducible brain-behavior associations without the need for thousands of individuals.

2-M-93 - Using Low-field MRI to Improve Accessibility of Neuroimaging Measures in Developmental Samples

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Details

Objective: Low-field strength MRI scanners offer increased portability, decreased cost, and better accessibility compared to the current 'gold-standardâ€ in neuroimaging, but produce noisier, lower-resolution images. Recently, researchers have used deep learning to generate super-resolution images sufficient for automated brain volume segmentation of low-field scans of adults, but these results have not been demonstrated in youth. For low-field imaging to be used routinely in community settings, we must first demonstrate feasibility in a community sample of youth.

Method: In 28 youths (9-26 years), we obtained T1- and T2-weighted structural images from a 3T scanner and a Swoop Hyperfine 0.064T scanner. We applied the SynthSR neural network to co-registered low-field images to synthesize super-resolution MP-RAGE images, and then used FreeSurfer to segment the synthesized and 3T images. We examined the correlation between respective cortical and subcortical measures derived from the two methodologies.

Results: Global cortical surface area and intracranial volume measurements strongly correlated across methodologies (total surface area: r=0.84, p=1.6e-8; total intracranial volume: r=0.68, p=4.2e-5). Average cortical thickness did not significantly correlate (r=.24, p=0.21), reflecting large variations in the correlation of regional thickness measures (r range: -0.01-0.88). Other regional measures showed more consistent relationships: surface area (mean r=0.661), cortical volume (mean r=0.57), and subcortical volume (mean r=0.63).

Conclusions: We show promising preliminary evidence for using low-field MRI in youths. In the future, we plan to test the ability to accurately calculate neuroimaging summary scores with low-field MRI scans, as these measures demonstrate promise for future use in clinical settings. Low-field MRI is one way to ensure that we measure these scores in underserved communities.

2-M-94 - Reducing the Need for General Anesthesia in Children Undergoing Neuroimaging by Preparation and Motion Correction

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Details

Study Objective:

At Copenhagen University Hospital (Rigshospitalet) virtually all children under the age of 8-10 years routinely have magnetic resonance (MR) scans performed in general anesthesia (GA). Results from Denmark and abroad show that it, in many instances, is possible to scan children from the age of 3-4 years without the need for sedation or GA by appropriate preparation [1,2,3]. Rigshospitalet is a tertiary referral center for rare and complex pediatric diseases, therefore, requirements for image quality are very high, and only a small degree of residual motion is acceptable. Although complications directly related to GA are rare [4], there is an increasing concern about the potential neurotoxic effects of repeated GA [5]. Additionally, logistic and resource challenges are associated with using GA [2].

This prospective study aims to demonstrate that high-quality diagnostic images can be obtained in young children by MR scan preparation in combination with motion correction, thereby avoiding the use of GA.

Methods:

We want to test the clinical efficacy of a new approach to imaging children that undergo MRI scans for diagnostic purposes, including

1. preparation with a mobile device application (open source, code available on https://github.com/melanieganz/MoCoProject) and mock scanner training,
2. distraction of the children via pre-chosen movies during the MR scan, and
3. introducing a novel markerless motion tracking device that can register children's movements during image acquisition and prospective motion correction of the MR sequences [6].

The inclusion criteria for our study were pediatric patients aged 4 to 10 years referred for an electively scheduled clinical cerebral MR scan in GA. Exclusion criteria were unstable medical conditions

interfering with the safety of the MR scan, non-fluent in Danish, no pronounced visual or auditory impairments, and no major physical or developmental challenges that interfere with participation in the experimental protocol.

The motion tracking, training, and preparation procedures are systematically evaluated to identify the best procedure for imaging children of different ages and different levels of functioning. Anxiety levels were assessed using the State-Trait Anxiety Inventory Questionary for children (STAI-C) [7] at home (trait), before and after mock scanner training, and again before and after the real MR scan (state).

Results:

As of April 24th, 2023, 44 children (age at enrollment: 6.90 Â± 2.04 years, sex: 21 F/23 M) have been enrolled in the prospective study with a wide variety of clinical indications (genetic syndromes, epilepsy, CNS tumors, assessment for cochlear implantation as well as early puberty and headache). Of the 44 children, 11 are scheduled, and 33 have already undergone the training and been MR scanned. Of the 33 children, 31 successfully completed the MR scan, and the clinical neuroradiologists approved the quality of the scan for clinical diagnosis a 94% success rate.

We await study completion before analyzing the STAI-C questionnaire data and evaluating the impact of prospective motion correction.

Conclusions:

Our preliminary results show the value of preparation and training for reducing the need for GA in pediatric patients undergoing MR scans. Using preparation via a mobile phone app and an additional session in a mock scanner, we can reduce the rate of GA by 94%. We expect to conclude data acquisition by early fall 2023 if the current inclusion rate continues.

References:

1. Runge, European Journal of Radiology 2018;107:183-7.

2. TÃ¶rnqvist, Journal of Child Health Care 2015;19(3):359-69.

3. de Bie, European Journal of Pediatrics. 2010 Sep 1;169(9):1079-85.

4. Cravero, Anesthesia & Analgesia 2009;108:795-804.

5. Stratmann, Anesthesia & Analgesia 2011;113:1170-9.

6. Frost, Magnetic resonance in medicine 2019;82(1):126-44

7. Spielberger, Lushene Consulting Psychologists Press 1970.

2-M-95 - Using Deep Learning Cortical Surface Reconstruction Methods on Infants: a Preliminary Study

Timothy Hendrickson [1], **Eric Feczko** [1], **Lucille Moore** [1], **Martin Styner** [2], **Omid Kardan** [3], **Taylor Chamberlain** [4], **Brad Bower** [5], **Sally Stoyell** [1], **Sooyeon Sung** [6], **Monica Rosenberg** [7], **Christopher Smyser** [8], **Alice Graham** [9], **Jed Elison** [1], **Damien Fair** [1]

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Details

Introduction: 3D shape reconstruction using deep learning techniques is a burgeoning field. More recently, these techniques have been applied to the field of neuroscience, specifically to reconstruct cortical surfaces from volumetric 3D brain MRIs. Reconstructing cortical surfaces is an important step in handling brain MRI data as it is fairly well established that analyzing cortical data on a 2D surface is beneficial [1â€“5]. While deep learning cortical reconstruction techniques have been applied to adult MRIs, to our knowledge it has not been applied to infants. Here, we trained a model on infants from the Baby Connectome Project (BCP) [6] using CorticalFlow++[7] to automatically reconstruct cortical surfaces from 3D volumetric MRIs.

Methods: CorticalFlow++ was trained on 63 participants 46 within the training set, 8 in validation, and 8 in testing set from the BCP study. Model training required the 3D anatomical MRIs and the cortical surfaces produced from FreeSurfer [8â€“10] which were treated as the pseudo ground truth surfaces.

Results: Once the model was trained, the model was used to perform prediction on 8 test set participants. The predicted surfaces left (LH) and right (RH) pial surfaces and LH and RH white matter surfaces were compared to the pseudo ground truth Freesurfer surfaces to evaluate the model. Using 90% Hausdorff distance, it was revealed that all predicted surfaces were comparatively close to the pseudo ground-truth surfaces RH white: (Î¼ = 34.5, ïƒ = 3.82); LH white: (Î¼ = 33.05, ïƒ = 3.67), RH pial (Î¼ = 38.46, ïƒ = 4.10), LH pial (Î¼ = 37.18, ïƒ = 3.80).

Conclusions: These preliminary results reveal that the trained model does well at predicting all surfaces, although it does slightly worse at predicting pial than white surfaces. Subsequent project steps will involve incorporating data augmentation using SynthSeg [11] to improve model performance and generalizability.

References

1. Anticevic, A. *et al.* Comparing surface-based and volume-based analyses of functional neuroimaging data in patients with schizophrenia. *Neuroimage* **41**, 835â€“848 (2008).

2. Fischl, B. *et al.* Cortical folding patterns and predicting cytoarchitecture. *Cereb. Cortex* **18**, 1973â€“1980 (2008).

3. Frost, M. A. & Goebel, R. Measuring structuralâ€“functional correspondence: Spatial variability of specialised brain regions after macro-anatomical alignment. *Neuroimage* **59**, 1369â€“1381 (2012).

4. Tucholka, A., Fritsch, V., Poline, J.-B. & Thirion, B. An empirical comparison of surface-based and volume-based group studies in neuroimaging. *Neuroimage* **63**, 1443â€“1453 (2012).

5. Van Essen, D. C., Glasser, M. F., Dierker, D. L., Harwell, J. & Coalson, T. Parcellations and hemispheric asymmetries of human cerebral cortex analyzed on surface-based atlases. *Cereb. Cortex* **22**, 2241â€“2262 (2012).

6. Howell, B. R. *et al.* The UNC/UMN Baby Connectome Project (BCP): An overview of the study design and protocol development. *Neuroimage* **185**, 891â€“905 (2019).

7. Cruz, R. S. *et al.* CorticalFlow^++: Boosting Cortical Surface Reconstruction accuracy, regularity, and interoperability. *arXiv [eess.IV]* (2022).

8. Dale, A. M., Fischl, B. & Sereno, M. I. Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage* **9**, 179â€“194 (1999).

9. Fischl, B., Liu, A. & Dale, A. M. Automated manifold surgery: constructing geometrically accurate and topologically correct models of the human cerebral cortex. *IEEE Trans. Med. Imaging* **20**, 70â€“80 (2001).

10. Fischl, B., Sereno, M. I. & Dale, A. M. Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. *Neuroimage* **9**, 195â€“207 (1999).

11. Billot, B. *et al.* SynthSeg: Domain randomisation for segmentation of brain scans of any contrast and resolution. *arXiv [eess.IV]* (2021).

2-M-96 - Updating the restriction spectrum imaging model for the ABCD study

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Details

Diffusion-weighted magnetic resonance imaging (dMRI) has been established as the go-to technique for non-invasive measurements sensitive to in-vivo brain tissue microstructure. Numerous models have been developed to provide a biophysical interpretation of the diffusion-weighted signal. A common approach is to represent the total diffusion signal as a sum of signals from different cellular compartments, weighted by their respective volume fractions. The signal from each compartment can be represented as a function of the apparent diffusion coefficients for each compartment. Out of necessity, to ensure algorithmic stability, many models fix the compartment apparent diffusion coefficients (ADCs), and variation in the diffusion signal is interpreted as a variation in the tissue compartment volume fractions.

The restriction spectrum imaging (RSI) model has been used in the Adolescent Brain and Cognitive Development (ABCD) study to quantify cerebral microstructural changes in the developing brain and is included in every public data release. RSI employs spherical deconvolution to reconstruct an orientation distribution function for each tissue compartment. As implemented in the ABCD study, RSI includes restricted, hindered and free water compartments. The hindered and restricted compartments are modeled as fourth order spherical harmonic (SH) functions, and the free water compartment is

modelled using zeroth order SH functions. Compartment ADCs, the number of tissue compartments, and the maximum SH order for each compartment were set from previous studies but not optimized for studying the adolescent brain. Therefore, in this study we intend to (i) optimize the RSI model for studying microstructural alterations during adolescence by estimating optimal compartment ADCs directly from the ABCD study data, and (ii) to determine the best compartment configuration for the ABCD data via model comparison. This will determine the RSI model to be used in future ABCD data releases.

This study will include baseline and two-year follow up dMRI scans from the ABCD study. We will test eight different model configurations of three or four tissue compartments and vary the maximum spherical harmonics order of each compartment. To determine the optimal compartment ADCs for each model, a global fitting procedure will be implemented across all voxels within a brain mask that includes cortical and subcortical grey matter, white matter and cerebrospinal fluid, for each scan. Model fitting will be carried out using simplex search method in MATLAB R2020a to minimize the mean squared error between the observed and model-predicted diffusion signal, averaged over all voxels. Estimated ADCs will then be averaged across scans to define optimal ADCs for each model. To our knowledge this will be the first time that ADCs have been fit directly from the data for a diffusion model of brain tissue microstructure in an adolescent population. The eight different models will be re-fitted for each scan using these optimal values and the Akaike information criterion (AIC) will be calculated per scan and averaged across scans to determine the quality of each model. The AIC will be used to rank the models and select the most appropriate one for the ABCD data. Additionally, we will investigate whether updates to the RSI model result in changes to the derived scalar indices released with the ABCD tabulated data such as the restricted normalized isotropic (RNI), restricted normalized directional (RND), and free water normalized isotropic (FNI) diffusion measures. We will also investigate whether there are age-related changes in ADC values within the ABCD study cohort.

This study will define the RSI model for future releases of ABCD data.

2-M-97 - Building a clinically feasible risk calculator for psychopathology in adolescence: a machine learning approach

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Details

Introduction: Youth in the U.S. are facing a mental health crisis, with rates of suicidal behaviors increasing sharply over the past decade (Ivey-Stephenson et al., 2020), along with a shortage of providers equipped to handle the patient load. Effective prevention of mental health problems in youth is imperative and requires a systematic method to identify those at risk. A plethora of studies have used one domain of information such as demographics, questionnaires, genomics, or neuroimaging to predict risk for youth psychopathology. However, as etiologies of mental illness are multifaceted and arise due to a host of interacting risk factors, predictions may be more robust if we integrate data from across disciplinary silos. Further, current studies offer limited clinical utility, as the evaluation of the most valuable predictors for psychopathology is often based on model performance alone and does not consider the cost involved in collecting the diagnostic. Settings such as primary care visits or inpatient

hospitalizations offer youth the most points of contact with the healthcare system and provide a fruitful opportunity to implement a screening tool for psychopathology; but, there is minimal capacity for expensive diagnostics such as genomics and neuroimaging, particularly in low-resource contexts. Thus, clinical feasibility must be considered in addition to model performance when evaluating which measures are most helpful in identifying youth at risk for psychopathology.

Objective: Here, we employ machine learning on multimodal, longitudinal data from the ABCD Study to predict internalizing and externalizing symptoms two years later, using both model performance and an estimation of relative cost to evaluate the predictive value of measures.

Methods: We leverage data from ~9k youth in the ABCD Study. Multimodal information at baseline (age 9-10) will be used to predict psychopathology risk status at the 2-year follow-up; CBCL T-scores greater than 93rd percentile are labeled 'clinicalâ€', between 80th and 92nd percentile are labeled 'sub-clinicalâ€', and otherwise labeled 'minimalâ€ risk. Internalizing and externalizing subscales are predicted separately. Predictors are entered sequentially according to increasing cost involved in collection, as follows: 1) socio-demographics; 2) anthropometrics available on an electronic health record; 3) geo-coded information about the chil's socioeconomic, educational, and environmental conditions; 4) environmental experiences including parental mental health, prenatal exposures, family, school, peers, and traumatic events; 5) lifestyle factors about sleep, religion and afterschool activities; 6) neurocognition and 7) structural and resting-state functional MRI measures. We plan to iteratively incorporate each layer of information and run machine learning models (random forest, XGBoost, and regularized regression) to calculate the predictive performance gained beyond the combined performance of the cheaper diagnostics used in previous iterations. We also plan to employ feature importance to identify the most powerful predictors within each layer. Analyses are currently underway; we plan to present preliminary results from the random forest model at Flux Congress.

Hypotheses: Given the pervasive impact of childhood adversity on mental health (McLaughlin et al., 2020), adding exposures related to trauma and family & peer environments may provide the most predictive benefit from both a cost and model performance perspective. Given the small effect sizes for associations between neuroimaging measures and psychopathology (Marek and Tervo-Clemmens et al., 2022), we hypothesize that neuroimaging will be of minimal additive value.

Implications: We hope that this study will help to identify the most optimal and cost-effective predictors for identifying children at risk for mental illness, and ultimately contribute to the prevention of youth psychopathology.

N- Networks

2-N-98 - Development of Functional Systems In 0-2 year-olds

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Details

Objective: The brain is organized into different systems that serve distinct functions in healthy adults, and are often used for dimensionality reduction in functional connectivity (FC) studies to understand brain-behavior associations. To conduct such brain-behavior research, the system models used to partition the brain should fit well to actual system-level divisions in the data. However, at the earliest stages of post-natal development, adult models of brain systems may not be appropriate. Several groups, ours included, have developed functional atlases with age-specific delineation of brain systems, but no prior research has benchmarked the improvement, if any, these system parcellations provide as models for infant brain organization compared to their adult counterparts. Here, we assess the confidence of each spatial location belonging to its assigned system(Yeo et al. 2011) based on infant FC at 0-2 years old to measure the goodness of fit of the different adult and infant system parcellations.

Method: We used the vertex-wise FC in 32k fsLR space from infants and neonates scanned during natural sleep from the Baby Connectome Project (BCP, 8-29 months grouped in 5 bins, Howell et al. 2019) and Early Life Adversity, Biological Embedding (eLABE, gestational age 38-45 weeks) datasets. Results from the Washu120 young adult dataset (Gordon et al. 2016) were also included as a comparison to the infants and neonates. We considered various systems-level parcellations developed from the adult (19-32 years, Laumann et al. 2015), infant (8-26 months, Kardan et al. 2022) and neonate (gestational age 38-45 weeks, Sylvester et al. 2022) FC . We used the silhouette index (SI; Rousseeuw 1987) measure to quantify the confidence of each spatial location belonging to its assigned system. The SI at each vertex i compares the mean intra-cluster distance (a_i) and the mean nearest-cluster distance (b_i): $SI_i = (b_i â€“ a_i) / \max(a_i, b_i)$. In our case, the distances were measured as 1-Pearson's correlation between functional connectivity maps from seed vertices and the clusters were the systems. The resulting SI lies between -1 and 1 and a high SI indicates that the vertex is well-matched to its assigned system compared to other systems. A high mean SI indicates that the data have been well-clustered.

Result: First, we found that neonate, infant, and adult FC were all best represented by the system parcellation it is defined in (mean SI~0.2) and not by the system parcellation from other age groups (mean SI~0). Second, we found that the confidence for adult system assignments (mean SI) increased across ages from 9 to 25 months. Third, we found that the mean SI varied greatly across systems with three major patterns of development: 1) visual, motor, retrosplenial, salience, dorsal and ventral attention systems were adult-like (mean SI>0) by 1 year and some of the systems can be even more segregated from other systems (higher mean SI) than their Washu120 adult counterparts; 2) the default, parietal memory, and frontoparietal association systems were rapidly developing from one to two years after birth, but still less segregated (lower mean SI) than their Washu120 adult counterparts; 3) the cingulo-opercular and auditory systems were the slowest to mature and remained far from adult-like (mean SI<0) in organization by 2 years old. Lastly, we showed that core regions previously reported to have a high consensus of adult systems across individuals (Dworetsky et al. 2021) highly overlap with the regions with SI>0 to adult systems in the neonate and infant data (~0.70-0.75 in overlap coefficient across two datasets).

Conclusion: We found that resting-state system organization can be very different across newborn, infancy, and adulthood stages. We also observed a diversity in developmental trajectory of different resting-state systems from 0 to 2 years old and identified stable system 'coresâ€ which had similar

system-organization throughout the lifespan.

2-N-99 - Estimation of Brain Connectivity Networks and Covariate Effects in Pediatric Traumatic Brain Injury

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Details

Objective: Pediatric Traumatic Brain Injury (TBI) is particularly concerning because it can disrupt the typical course of brain development. Severity of TBI predicts disrupted brain development; however, emerging evidence suggests that other characteristics, such as sex and age at injury, may also moderate outcomes following TBI. Few investigations of pediatric TBI target age and sex effects on brain connectivity even though the neurological disruption resulting from TBI is characterized as a disorder of brain connectivity. The present study investigates age and sex effects on resting state functional connectivity (rsfmri) in children age 8-15 years with history of mild-severe TBI (n = 70, 12.54 years, 39% female) and an aged matched healthy comparison group (HC, n = 50, 12.13 years, 36% female).

Method: Heterogeneity is a known characteristic of rsfMRI from children and in patients following TBI. This presentation will provide insights for classification of brain connectivity in the first year following pediatric TBI using an analytical approach for estimating functional networks that accounts for heterogeneity. By accounting for heterogeneity, our approach is more sensitive to age, sex, and injury effects on rsfmri networks. Furthermore, we rely on a hierarchical model to learn functional connectivity relations for each group of subjects and the dependence of the connection strength on covariate values. We use a sparse model to identify key connections within each group and to select a subset of edges with strengths that depend on covariate values (i.e., age and sex). In this presentation, connectograms will illustrate group level network characteristics (i.e., group-level edges), with arcs between regions denoting that the group-level function is present and influenced by the given covariate. Additional covariate results will be plotted relative to subject-level edge strength estimates illustrating an inverted U shape developmental pattern.

Results: Our modeling results highlight effective connectivity relations within each group (TBI vs. HC) and how the magnitude of certain dependencies varies based on sex or age. Examining the networks further, we evaluated whether specific edge strengths were affected by covariates of age and sex. From this, we see that both age and sex have an influence on the edge strength function for both HC and TBI groups, with more edges in the HC group compared to the TBI group. Whereas fewer edges were evident relative to HC, in the TBI group age, and to a lesser extent sex, selectively influenced edges of the left putamen. This finding converges with previous reports of frontal-striatal (including putamen and caudate) network disruption following pediatric TBI. Current findings elucidate the functional implication of striatal injury and characterize how patient characteristics, in this case age or sex, might strengthen or attenuate impact of injury on striatal brain networks.

At a more granular level, we see that the model does well in capturing different functional shapes relative to covariate data, such that edge strengths change as a function of each covariate. For example,

in the TBI group, we observe stronger effective connectivity between left triangular part of inferior frontal gyrus and left inferior temporal gyrus for males compared to females. With regard to effects of age, developmental profiles showing inverted U-shaped function were found but differed between HC and TBI groups. Broadly, the trends of the estimated effective connectivities with respect to age change (i.e., peak) at around 11 years for HC group; whereas the trends change at around 13 years for TBI group.

Conclusion: This study implemented a recently-developed statistical technique to advance our understanding of pediatric TBI. Results linking disordered functional connectivity with the patient characteristics of age at injury and sex offer clinically relevant insight for predicting long-term outcome following TBI.

2-N-100 - Resting State Fronto-Amygdala Network Density Associated with a Parent-Focused Intervention for Childhood Anxiety

Kelley Gunther [1], **Daniel Petrie** [2], **Elizabeth Kitt** [1], **Alexis Broussard** [1], **Sadie Zacharek** [3], **Cristina Nardini** [4], **Grace Hommel** [5], **Alyssa Martino** [5], **Tess Anderson** [5], **Hannah Spencer** [6], **Paola Odriozola** [1, 7], **Carla Marin** [5], **Wendy Silverman** [5], **Eli Lebowitz** [5], **Dylan Gee** [1]

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Details

Functional connections between the amygdala and prefrontal cortex during rest play a central role in a chil's regulation of anxious behaviors (Liu et al., 2015). In this study, we draw participants from a randomized controlled trial examining the efficacy of a parent-focused anxiety intervention designed to decrease family accommodation (Supportive Parenting for Anxious Childhood Emotions; SPACE). Family accommodation, where parents and other family members change their behaviors in efforts to lessen their chil's anxiety, is common in pediatric anxiety disorders (Lebowitz et al., 2013). The SPACE intervention leverages the notion that aspects of a chil's environment, such as family and parental behaviors, are critical in the etiology and maintenance of anxiety. Family members may provide external regulation for their child or filter their chil's experienced environment. Targeting these behaviors through SPACE has proven to be an effective alternate treatment for pediatric anxiety (Lebowitz et al., 2019), with promise for children who have not had success with other interventions. However, much remains unknown about mechanisms supporting the efficacy of SPACE.The current study aims to test whether the SPACE intervention modulates patterns of resting state functional connectivity.

Parents and their children (6-12 years with a primary diagnosis of anxiety) were randomly assigned to either SPACE, cognitive behavioral therapy (CBT), or a control parenting intervention (parental education support; PES) across one of two separate waves of data collection. Children completed a resting state fMRI scan before and after they/their parents participated in the intervention. Resting state data were preprocessed using fMRIprep 20.2.1. Group Iterative Multiple Model Estimation (GIMME) was used to construct person-specific networks between regions of interest (ROIs) from both the pre- and post-intervention resting state connectivity data (Gates et al., 2017). ROIs were selected as defined by the Harvard-Oxford atlas, including the amygdala, frontal medial cortex, frontal orbital cortex, and frontal

pole.GIMME is unique in that it assesses contemporaneous and lagged relations, as well as autoregressive paths, in network mapping. Considering lagged relations establishes Granger causality as compared to traditional correlation approaches to neuroimaging data (Gates & Molenaar, 2012). GIMME may present orthogonally to traditional correlation approaches, offering a different perspective on network connectivity (Gunther et al., 2022).

We were interested in how the interaction between intervention and change in symptoms may relate to changes in network density. To capture network density we counted the number of edges in each chil's network map, where more edges indicated greater network density. Anxiety symptoms pre- and post-intervention were measured using the clinician-administered Pediatric Anxiety Rating Scale. We tested the interaction between residual change in anxiety symptoms and intervention on residual change in edges. Study wave and child age were entered as covariates, and a Poisson regression was used to account for the count nature of the network density variable.

We found a significant interaction between residual change in symptoms and intervention, $b = 0.39$, $p = .047$. Probing this interaction revealed that youth in the SPACE condition had an inverse relation between residual change in symptoms and residual change in edge count. That is, for youth whose parents engaged in the SPACE intervention, a greater than predicted decrease in anxiety was associated with greater than predicted edges post-intervention. Slopes were not significant for CBT or PES. Taken together, these findings suggest that the SPACE intervention may modulate density of fronto-amygdala connectivity along with symptom reduction in a way that is unique from other treatments.

2-N-101 - Characterizing Default Mode Network Connectivity Profiles Among U.S. Adolescents and Associations Between Sleep Duration, Internalizing, and Externalizing Problems: Findings from ABCD Study

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Details

The Default Mode Network (DMN) is a large-scale functional brain network that includes the precuneus, posterior cingulate, medial prefrontal, and inferior parietal cortices. The DMN undergoes significant changes throughout late childhood and adolescence, matched by underlying structural and functional brain development. Although developmental science has documented normative adolescent brain development trajectories, the focus on average change may obscure inter-individual differences and intra-individual changes in brain development. Indeed, the connectivity between adolescents' DMN and other brain networks varies. Adolescents are at risk for sleep and psychiatric problems and that variation in the DMN may account for this risk. The current study used Latent Profile Analysis (LPA) to identify patterns of DMN network connectivity based on multiple indicators (within the DMN and between the DMN and fronto-parietal, salience, ventral attention, cingulo-opercular, cingulo-parietal, and dorsal attention networks) in a large national prospective sample of adolescents. Then, we tested the brain network connectivity profiles' predictive utility of socioemotional adjustment two years later.

Data were used from Adolescent Brain & Cognitive Development Study, including baseline (49.3% female; M_{age}= 9.51, SD=.50) and two-year follow-up (M_{age} =11.94, SD=.65). The racial-ethnic composition

was 61.8% European American, 7.0% African American, 18.7% Latino(a), 2.7% Asian/Pacific Islander, and 9.7% Other. Echoplanar functional neuroimaging data were collected using 3T MRI scanners with a 32-channel head coil. A sample of 9,130 participants remained after quality control. Resting-state connectivity was calculated within and between networks using Pearson correlation based on the Gordon parcellation scheme. Sleep duration, efficiency, latency, and wake minutes at a two-year follow-up were measured using Fitbit Charge HR 2 devices. Internalizing problems were measured using the Child Behavior Checklist at a two-year follow-up.

Analyses were performed in *Mplus* 8.2. LPA was used to determine adolescents' resting-state profiles at baseline. The determination of the optimal class solution was based on Akaike's Information Criterion (AIC), Bayesian Information Criterion (BIC) and entropy values. Next, we used the BCH approach to examine the prospective links among profile membership (baseline) and each outcome at two-year follow-up. A full information maximum likelihood algorithm was used to estimate missing data.

A 4-class solution was chosen based on the AIC, BIC and entropy values. The largest profile is the *Low within-DMN connectivity* group (*N*=4346;48.52%). The second largest profile (*N*=4030; 44.99%) was the *average* subgroup. The third profile (*N*=364; 4.06%) was hyper connectivity. The smallest profile (*N*=217; 2.43%) was the high within-DMN and low DMN-Cinguo-opercular connectivity group. *The low within-DMN connectivity* group had the lowest sleep duration and *Hyper connectivity* class had the highest sleep duration. *High within-DMN, low DMN-cingulo-opercular* group had the lowest wake minutes and *hyper connectivity* group had the highest wake minutes. *High within-DMN, low DMN-cingulo-opercular* group has the highest externalizing problems and *average* group have the lowest externalizing problems.

Our results highlight the implications of using these rsFC patterns to better identify at-risk adolescents and monitor the effectiveness of responses to existing treatments for sleep and psychiatric disorders.

2-N-102 - Functional network segregation and integration along the sensorimotor-association axis in adolescence

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Details

Introduction: Functional brain network organization balances segregation, high local within-system connectivity that supports specialized functions, and integration, high global between-system connectivity that supports flexible communication. Segregation supports specialized cognitive functioning, is impacted by adverse experiences, and may be perturbed in psychopathology. During development, functional networks tend to segregate to confer specialized functions. One potential spatiotemporal pattern along which functional network segregation might develop is the sensorimotor-association (S-A) axis. The S-A axis spans from unimodal sensorimotor to transmodal association regions, capturing the hierarchical organization of diverse biological properties (Sydnor et al., 2021). Here, we investigate how the remodeling of functional network connectivity proceeds along the S-A axis.

Methods: We leveraged a sample of 683 adolescents (388 female, 295 male, 8-22 years old) from the Philadelphia Neurodevelopmental Cohort who underwent resting-state functional MRI (rs-fMRI) at 3T. Scans were preprocessed using fMRIPrep (version 20.2.3) and eXtensible Connectivity Pipeline (XCP) Engine (Ciric et al., 2018), correcting for head motion, global physiological and tissue-based signal, and other motion artifacts. BOLD signal time series were extracted from 400 regions and partitioned into a 17-system parcellation (Yeo et al., 2011). Functional connectivity was calculated using product-moment correlations and the resulting matrices represented a graph. We calculated clustering coefficient (to index segregation) and participation coefficient (integration) per parcel and averaged them by network. We quantified age effects by comparing nested (with age) generalized additive models (GAM) to null models (without age), as in prior work (Pines et al., 2022). Model covariates included sex, head motion, and average global functional connectivity. We then examined the association between each region's age effect and its rank along the S-A axis using spin-based permutation tests.

Results: Global age effects (whole-brain averaged) showed a decrease in participation coefficient ($\hat{I}"R^2_{adj}$=-0.019, p=0.001) and increase in clustering coefficient ($\hat{I}"R^2_{adj}$=0.021, p<0.001) with age. We found strongest decreases in participation coefficient in middle axis networks such as dorsal attention (DAN), ventral attention (VAN), frontoparietal (FPN), and default mode (DMN) (DAN B: $\hat{I}"R^2_{adj}$=-0.036; VAN A: $\hat{I}"R^2_{adj}$=-0.033; VAN B: $\hat{I}"R^2_{adj}$=-0.024; DMN A: $\hat{I}"R^2_{adj}$=-0.017; FPN B: $\hat{I}"R^2_{adj}$=-0.017; *all* p_{FDR}<=0.001). Additionally, we found highest increases in clustering coefficient in some of the same networks (DAN B: $\hat{I}"R^2_{adj}$=0.034; VAN A: $\hat{I}"R^2_{adj}$=0.032; FPN A: $\hat{I}"R^2_{adj}$=0.028; DMN A: $\hat{I}"R^2_{adj}$=0.026; DMN B: $\hat{I}"R^2_{adj}$=0.023; *all* p_{FDR}<0.001). Models relating parcel-wise age effects to hierarchical position along the S-A axis showed peak segregation in the middle of the axis. Specifically, we observed a convex spline for age-related changes in clustering coefficient, with middle S-A axis regions showing the greatest increase in segregation and regions at the poles showing the least (p_{spin}<0.001). We observed a concave spline for participation coefficient with strongest decreases in integration with age in middle axis regions and less strong age effects at the poles (p_{spin}<0.001).

Discussion: We found that segregation increased in middle S-A axis networks, consistent with previous results. One interpretation is that these regions undergo protracted development during a critical period of substantial cognitive and affective demands. Our results lay the foundation for further investigation of how the balance of segregation and integration develops, and how network remodeling may support the maturation of functional network organization.

2-N-103 - Brain network organization underlying urgency in children with ADHD and effects of methylphenidate

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Details

Background: Children with Attention-Deficit/Hyperactivity Disorder (ADHD) often exhibit deficits in emotion regulation. More specifically, relative to unaffected children, children with ADHD are more likely to experience emotions more intensely, react more impulsively to events, and demonstrate a lower capacity to regulate their emotions. These behavioral characteristics appear similar to Cyders and Smith's (2008) theoretical conceptualization of urgency, which proposes that under heightened emotional states, children are more likely to engage in ill-considered or rash actions than at other times. Therefore, children with ADHD may be more likely to exhibit urgency due to a combination of difficulties with emotion regulation and impulsivity. Although urgency is thought to emerge from variations in levels of dopamine and serotonin in the fronto-striatal-limbic pathway, there remains a paucity of literature examining how functional brain network organization underlies urgency in children with ADHD. Here, we apply advanced network neuroscience techniques to examine the relation between brain network organization and urgency in children with ADHD. Additionally, given that methylphenidate is a first-line treatment for ADHD, and has been shown to reduce deficits in emotion regulation, we also seek to examine how methylphenidate may affect brain network organization underlying urgency in children with ADHD.

Methods: Twenty-six medication-naÃ¯ve children with ADHD between the ages of eight and 12 years (*Mean* age=9.69 years, SD age=1.15 years; 14 males, 12 females) participated in a double-blind, placebo-controlled, crossover trial with short-acting methylphenidate (0.3mg/kg; rounded up to the nearest 5 mg). Children completed two separate functional magnetic resonance imaging resting-state scans and go-no-go tasks (one on placebo and one on methylphenidate). Their parents completed the UPPS-P Impulsive Behavior Scale, a measure of a parent's perception of their chil's urgency. Functional connectivity was estimated between pairs of brain regions using a whole-brain atlas, and then network membership of each brain region was defined. Graph theory metrics of participation coefficient and within-module degree were calculated on the network level to characterize the integration and segregation of networks with respect to the rest of the brain and how they differed following the administration of methylphenidate. Urgency was calculated by aggregating items on the positive urgency and negative urgency scales. Mean scale scores were used in analyses.

Results: On placebo, higher levels of urgency were associated with reduced participation coefficient (integration) of the salience network during the resting-state scan (beta=-.47, SE=.21, t=-2.27, p=.03) and increased participation coefficient (integration) of the reward network during the go-no-go task (beta=.45, SE=.2, t=2.31, p=.02). No significant associations between urgency and brain networks were observed following the administration of methylphenidate.

Discussion: These findings suggest that the integration of the salience network with other brain networks at rest, and the integration of the reward network with other brain networks during the go-no-go task, are involved in urgency in children with ADHD. Given both the salience and reward networks include nodes implicated in the fronto-striatal-limbic pathway, it may be the case that the integration of the salience network (including nodes primarily in prefrontal and striatal regions) is associated with urgency at rest due to limited task demands, whereas integration of the reward network (including nodes primarily in limbic regions) is associated with urgency during tasks demanding inhibitory control. Together, these findings suggest that brain network organization underlying urgency in children with ADHD may change and reconfigure based on task demands.

2-N-104 - Gerrymandered brain networks in ADHD reveal atypical network topography is associated with disorder severity.

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Details

BACKGROUND: ADHD is a multifaceted neurodevelopmental disorder with both genetic and neurological risk factors. The variation in functional topography produces challenges, but also a potential insight into investigating neural mechanisms underlying the disorder. Capturing functional topographic variation in neural networks is essential to draw accurate conclusions with regard to individual connectivity, thereby allowing investigators to characterize how cortical real estate is associated with each network. This variation in functional topography may be the result of ADHD severity or may be the result of increased genetic risk for ADHD. Examining the relative amount of cortical surface area and compactness of each neural network may indicate how the brain allocates computational resources in affected systems. We explored whether increased ADHD severity and/or increased genetic risk for ADHD in children is associated with changes in network topography, specifically network surface area and compactness.

METHODS: We processed the resting state functional data from 489 children (n=195 typically developing and 294 with ADHD) from the Oregon ADHD-1000 dataset, and 6000 typically-developing children from the Adolescent Brain Cognitive Development Study (ABCD) using the abcd-hcp-pipeline. Only participants with high-quality data (at least 10 minutes of low-motion resting state data (frame displacement <0.2?mm) were used to calculate functional connectivity. Using whole brain functional connectivity data, we applied a neural network mapping algorithm, called template matching to identify individual-specific networks. We then quantified the amount of total surface area and Polsby-Popper compactness,(where $PP(n)= 4ï€A(n)/P(n)^2$, where A(n) is the area of the network and P(n) is the length of the perimeter) of each network in MNI space using each individual's own cortical surface mesh. In addition, common single nucleotide polymorphisms (SNPs) for ADHD were used to calculate polygenic risk scores (PGRS). Using multiple linear regression, with covariates for age, sex, and head motion, we tested whether variation in topography was associated with ADHD severity or genetic risk using polygenic risk scores using separate models. To explore how network proportion shifts with ADHD severity, we split the data into quintiles.

RESULTS: We found that variability in network topography was associated with ADHD severity. We observed an increase in the surface area of the salience network between the lowest quintile and the highest quintile of ADHD composite scores in typically developing children (8%), which was substantially larger in our enriched sample (22%). We also observed a 1-3% decrease in the default mode network size compared to a 13% decrease in our enriched sample. Additionally, we found compactness of the visual network was significantly associated with ADHD severity. We found 6 networks where surface area significantly predicted PGRS in the ADHD cohort, 2 of which replicated in ABCD, including the cingulo-opercular and the lateral somatomotor networks.

CONCLUSION: ADHD-associated dIfferences in network surface area suggests a potential measure of differences in large scale functional allocation such that the default mode occupies a smaller proportion of cortical real estate while the salience network and somatomotor occupy a larger proportion in children that are affected by ADHD. Furthermore, this suggests that network compactness, which may reflect efficiency of communication, is associated with ADHD severity. Together this highlights a complex interrelationship between associated genetic risk factors and ADHD symptoms on functional topography.

2-N-105 - Structural connectivity and working memory within cognitive networks in children with and without ADHD

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Details

Background: A prominent theory of attention-deficit/hyperactivity disorder (ADHD) is that the symptoms emerge from dysfunctional connections between brain regions. Functional studies have shown dysfunctional connectivity within and across networks including the default mode (DMN), fronto-parietal (FPN), and ventral attention (VAN) network. Current literature also demonstrates that cortical brain regions engaged during working memory (WM), an executive function that is frequently impaired in children with ADHD, overlap with these three networks. However, limited work has been done to probe the relationship between WM and the underlying structural connections for these networks relative to children with ADHD. To this avail, this study investigates the structural connectivity (SC) of these three networks and their relationship to WM performance in children with and without ADHD. We hypothesized that children with ADHD would have poorer WM performance in comparison to typically developing (TD) children. We also hypothesized that children with ADHD would have greater within-network SC of the DMN, FPN and VAN, whereas TD children would have greater between-network SC of these networks. Finally, we expected to find that poorer WM was associated with lower between-network and higher within-network SC for the three networks of interest.

Methods: We collected diffusion-weighted images (DWI) from medication-naÃ¯ve children with ADHD (n = 28, mean age = 9.8 years) and TD children (n=23, mean age = 10.3 years) between the ages of 8 and 12 years old. FSL 6.0.3 was used to perform eddy-currents corrections, account for susceptibility distortions, and interpolate outlier data. Remaining outliers were removed with DTIPrep 1.2.10. Only participants with greater than 75% of acquired gradients were included in the analyses. Mrtrix 3.0.3 was used to estimate white matter fiber orientation distributions and to generate streamlines from spherical regions of interest (ROIs) based on the functional parcellation of a whole brain atlas (Seitzman et al., 2020). For each participant, a 187 x 187 matrix of streamline counts between pairs of ROIs was used to calculate two graph metrics for each network: within-module degree (WD) to measure within-network SC and participant coefficient (PC) to measure between-network SC. Graph metrics were calculated with Brain Connectivity Toolbox in MATLAB. To evaluate our hypotheses, we first used a two-sample t-test to compare WM performance (digit span) between the two groups. Second, we used a two-sample t-test to compare graph metrics between groups. Lastly, we performed two linear regressions (one for each graph metric, WD and PC). For each, the independent variables were the corresponding metric for each

network (ex: WD for DMN, FPN, and VAN) and the dependent variable was working memory performance.

Results & Conclusions: We found no significant differences in WM performance when comparing children with and without ADHD. There was also no significant difference between groups when comparing graph metrics (WD or PC) for DMN, FPN, or VAN. However, when the groups were combined the linear regression revealed that PC for VAN predicted WM performance (beta=.483, t=2.78, p=0.008), such that reduced PC was associated with poorer WM performance across all participants. Therefore, these results suggest that the integration of the structural connections of VAN with other cortical networks is important for working memory performance; however, this may not be specific to symptomatology of ADHD. These results also provide structural underpinnings that support current functional connectivity literature.

2-N-106 - The spatiotemporal dynamics of EEG microstate networks during three to six months of infancy

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Details

EEG microstates are brief (~80-100 ms) periods of quasi-stable spatial configurations of neural activity on a rapidly evolving time-scale (Lehman et al., 1987). Microstate analysis is an emerging method for investigating the instantaneous global brain networks and the functional organization of the dynamic brain (Michel & Koenig, 2018), particularly during the early developmental stages of human infants (Brown & Garstein, 2023). In a recent study, Gui et al. (2021) observed four microstates in infancy that corresponded with social attention and later potential emergence of ASD, suggesting that EEG microstates can be a powerful tool to predict functional brain dynamics and later developmental trajectories. The present study will examine EEG microstates at the first 3- and 6- months of age in the resting-state condition. We hypothesize that these infants would demonstrate distinct microstates comparable to those identified in adults and we expect to draw parallels with the fMRI resting-state networks.

High-density EEG data were acquired from 3-month-old (N=257) and 6-month-old (data collection in progress, current N=250+) infants using Magstim EGI 128 channel system as part of an ongoing longitudinal study (KHULA) in Cape Town, South Africa. The infants were placed in a dimly lit room on the caregivers' laps where they silently held a toy/ watched bubbles or books placed in front of them. All data from the 3-month-old infants have been pre-processed using the Harvard Automated Processing Pipeline for EEG (HAPPE) (Gabard-Durnam et al., 2018). Data were acquired at a sampling frequency of 1000 Hz and 2000 ms long segments were extracted from the 3 min long recording sessions. Participant datasets that retained 15 or more segments were selected, making a total of 242 usable 3-month-old participants' data.

We propose to conduct microstate analyses on the pre-processed EEG resting state/baseline data for both the age groups. First, we will compute the Global Field Power (GFP) across each age group to investigate the natural resting microstate fluctuations over time. Next, using a more recent development in microstate analysis known as Atomize and Agglomerate Hierarchical Clustering (Murray et al., 2008), we will simultaneously extract the topographies at all GFP peaks within a given age group and categorize them into small classes based on their topographic similarities using a modified K-means algorithm (Pascual-Marqui et al., 1995). The goodness of fit will be determined using the General Explained Variance (GEV) and/or the cross-validation (CV) criterion, the least representative cluster will be identified, atomized and the members will be reassigned to the most similar clusters. Based on this classification, the microstate topographies will be placed back into a sequential order to determine the amount of time spent in each of the microstate. Finally, we will statistically compare these patterns across each time period (3-, and 6-months), which till date has not been reported. Additionally, we plan to implement these microstate features from the current EEGLAB microstate toolbox (Poulsen et al., 2018) into our HAPPE software with parameters customized exclusively for infant EEG data.

2-N-107 - The effects of methylphenidate on brain organization underlying attention in stimulant-naïve children with ADHD.

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Details

ADHD is characterized by fluctuations in attention and heightened reward sensitivity. Stimulants, such as methylphenidate, improve these symptoms in many children with ADHD. However, little is known about how methylphenidate changes the large-scale brain organization that underlies these behaviors. Studies of dynamic brain organization, which capture changes in network organization on the order of seconds, may be particularly useful for understanding how methylphenidate changes attention and reward sensitivity since these processes also change over seconds. This pre-registration will use data from a medication challenge study in children with ADHD to examine the effect of methylphenidate on dynamic brain organization.

We scanned stimulant-naÃ¯ve children with ADHD (8-12y, N=34) on and off a single dose of methylphenidate. In the scanner, participants completed two attention-demanding tasks: standard and rewarded versions of a go/no-go task. Timecourses of activity will be extracted from a whole brain 300 ROI atlas making up 14 functional brain networks. To estimate dynamic functional connectivity, we will use dynamic conditional correlation to estimate pairwise correlations between all ROIs at each data acquisition timepoint (i.e., every two seconds). For both tasks, we will use multilayer networks to model the community structure of the brain at each timepoint. We will calculate flexibility, which measures the number of changes in community affiliation across the task, separately for each task and for each region.

Then, we will compare flexibility on and off methylphenidate for each task, and further compare methylphenidate-driven changes in flexibility between the regular and rewarded go/no-go tasks.

We predict that methylphenidate will increase flexibility of the default mode, cognitive control, and attention networks, indicating that on methylphenidate these networks will show more reconfiguration across the task. Since both reward sensitivity and attention are expected to improve with methylphenidate, we also predict that the change in flexibility will be greater during the rewarded go/no-go task as compared to the standard go/no-go task. This work will contribute information about the impact of methylphenidate on brain network dynamics and thus inform models of the neural basis of stimulant action, which is critical for predicting treatment outcomes.

P – Rewards/Motivation

2-P-108 - Growing up fast and slow: wild mice present an opportunity to hold age constant and study adolescent brain and behavioral development on two different life history trajectories

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Details

A wild species of mouse, *Mus (M.) spicilegus*, presents an exciting model to study adolescent brain development and risk-taking behavior because it shows different dispersal life history trajectory depending on season/photoperiod of birth. *M. spicilegus* born in Autumn delay dispersal until spring, while *M. spicilegus* born in Spring/Summer disperse quickly within the first 2-3 months of life. We find this useful as a species in which to study adolescent brain and behavioral development because we can hold chronological age constant but compare mice not motivated to disperse vs. motivated to disperse depending on photoperiod.

Our initial data show postnatal 60-70 day old *M. spicilegus* born on a Short day (SD) 10h:14h light:dark photoperiod have lower weights and reduced novel object investigation compared to Long day (LD) 12h:12h reared mice (Cryns et al., 2022) of the same age. These data confirm we can induce differences in developmental life history trajectory profiles using photoperiod in the lab environment in this wild species. This sets the stage for more in depth analysis of the brain.

At Flux, we will present our upcoming plans to use *in vivo* and *ex vivo* imaging to monitor dopamine system development and the pruning of cortical dendritic spines in *M. spicilegus* reared on SD and LD photoperiods. In particular, we plan to study exploratory behavior while imaging dopamine release in the tail of the striatum (TS) which has recently been reported to regulate approach and retreat behavior in response to novel objects (Menegas et al 2018; Akiti et al. 2022). We posit that the maturation of inputs to TS and the release of dopamine in TS may play a critical role in regulating and promoting different behavioral dispersal strategies, exploratory, and risk-taking behavior in animals across development. We further predict that SD photoperiod will delay spine pruning in the frontal cortices relative to LD photoperiod (at postnatal day 60 SD>LD spine density). We speculate this delay in pruning

in SD mice will occur to enable frontal cortex spine pruning to coincide with learning encountered during delayed dispersal.

These data will be impactful because they will help to inform what is and is not delayed when key behavioral aspects of adolescence like dispersal are delayed. This will help isolate requisite timing and possible function of key features of adolescent brain development.

2-P-109 - Characterizing striatal dopamine-related neurophysiology in rewarded response inhibition in youth at risk for problematic substance use

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Details

Little is known about the relationship between the neurodevelopment of dopamine (DA) systems and substance use behavior. Differences in response inhibition and striatal reward sensitivity have been shown in adolescents with increased substance use vulnerability (Tervo-Clemmens et al., 2017, 2020), and we have recently shown that striatal tissue iron, reflecting DA availability (Larsen et al., 2020), contributes to frontostriatal development (Parr et al., 2021) and to individual differences in rewarded response inhibition in adolescence, with stronger effects of rewards in individuals with *high* tissue iron relative to *low* iron (Parr et al., 2022). We will leverage this template to understand the role of striatal neurophysiology in rewarded response inhibition in adolescents at risk for problematic substance use.

The National Consortium on Alcohol and NeuroDevelopment in Adolescence (NCANDA) study combines neuroimaging with assessments of executive function and substance use in a large, multisite, longitudinal cohort (ages 12-21 at baseline). Indices of striatal tissue iron were obtained via time averaged and normalized T2* weighted images (nT2*w) for the Duke and Pittsburgh sites (300 participants (55% F), up to 5 visits; 1152 sessions). Executive function was assessed using the anti-saccade task (reward and neutral conditions). Linear mixed effects models investigated relationships between nT2*w, anti-saccade, and binge drinking (Hasler et al., 2022).

In confirmation of prior studies (Peterson et al., 2018), nT2*w indices of DA-related striatal neurophysiology increased throughout adolescence into adulthood (B = .09, t =2.70, p =.007). Preliminary results suggest that adolescents with *high* nT2*w endorsed higher levels of binge-drinking relative to *low* (B = -.42, t =-2.39, p =.02). Anti-saccade performance improved across adolescence (B = .38, t =8.45, p <.001) and was modulated by rewards (B = .25, t =6.04, p <.001; reward M =.81, SE =.008; neutral M =.76, SE =.009), and binge drinking was associated with enhanced rewarded anti-saccade performance (B = .35, t =1.94, p =.05; binge drinking M =.88, SE =.01; non- M =.78, SE =.01), potentially reflecting increased reward sensitivity.

We provide novel *in vivo* evidence that individual differences in DA-related neurophysiology may support increased reward sensitivity, which may contribute to higher incidences in binge-drinking. Future work

will examine longitudinal relationships between neurobiological factors and deviations from normative development that predict substance use into adulthood.

2-P-110 - Neural and Clinical Predictors of Adolescent Development of Pleasure Sensitivity and Cognitive Control

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Details

Adolescence is characterized by rapid neurodevelopment of reward systems and less slower development of cognitive control. While this development serves adaptive functions, individual differences in physical and social reward functioning and cognitive control are associated with several key outcomes including depression and early substance use problems. While developmental trajectories of adolescent reward and control functioning have been frequently examined, less is known about factors that may predict individual differences in the development of reward functioning and cognitive control. Identifying factors related to the development of reward and control functioning may have implications for identifying risk factors and intervention targets for various clinical outcomes. Here, we conducted preregistered analyses to examine prospective associations between several effective connectivity and clinical features early in adolescence and the longitudinal trajectories of reward functioning and cognitive control. We used a diverse community sample of 205 adolescents, aged 9-14 at baseline, that were assessed every 9 months for 3 years. Longitudinal outcomes included measures of physical and social pleasure sensitivity, as well as inhibitory control. Effective connectivity was estimated with Group Iterative Multiple Model Estimation (GIMME), providing person-specific directional connectivity networks for each participant. We specifically tested longitudinal associations with baseline network degree strengths of a subcortical reward hub and cortical cognitive control hub. We also examined adolescent depression and family history of major depressive disorder and substance use disorder, each assessed at baseline. Results showed a decreasing trajectory of physical pleasure sensitivity but increases in inhibitory control across adolescence. Moreover, higher control network strength and child depression were each associated with lower social pleasure sensitivity, and child depression was also associated with lower inhibitory control scores. Finally, we found a significant interaction such that individuals with higher control network strength showed steeper decreases in physical pleasure sensitivity over time, while individuals with lower than average control network strength showed small increases in pleasure sensitivity over time. Overall, results suggest that higher control network strength early in adolescence is associated with lower pleasure sensitivity between adolescents and decreases in pleasure sensitivity across adolescent development. This finding warrants further study in larger samples if decreased reward development across adolescence may serve as an indirect pathway between early adolescent control network functioning and later outcomes such as depression and substance use.

2-P-111 - Sex differences in reward processing pathways between prenatal maternal mood and later depression risk: A latent profile approach

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Details

Introduction: Prenatal maternal mood has been shown to increase offspring's risk for depression; however, the exact cognitive mechanisms are not fully elucidated. A candidate pathway for the development of depressive symptoms relates to impaired reward processing. Specifically, adolescents with high familial risk of depression and those with depression demonstrate decreased reward seeking. Decreased reward seeking has been postulated as a risk endophenotype for depression, particularly in women, and may explain the phenomenon of anhedonia in depression. However, no studies have examined sex differences in the association between prenatal maternal mood and reward processing behaviour during early school age in non-clinical populations.

Methods: Data were from 1194 mother-child dyads in a prospective cohort in Singapore. Household income, maternal education, and prenatal maternal mood were obtained at 26-28 weeks' gestation. Mothers completed the Edinburgh Postnatal Depression Scale (EPDS) and State-Trait Anxiety Inventory (STAI), for which a prenatal general maternal mood factor was generated. Child variables included sex and gestational age. The CANTAB Cambridge Gambling Task (CGT) measured reward-directed behavioural responses at 8.5 years (n=439) while self-reported depressive symptoms were assessed using the Child Depression Inventory (CDI) at age 10 (n=736). Latent profile analysis using the CGT was conducted to understand profile groups related to reward processing. Path analysis models examined the associations between prenatal maternal mood, latent profile probabilities and symptoms on the CDI by sex, while adjusting for household income, maternal education, and gestational age. Lastly, a mediation path analysis examined whether the association between prenatal maternal mood and later depression was mediated by individual differences in reward processing.

Results: In our cohort, no significant differences in family characteristics were found between boys and girls (all $p>0.05$). Latent profile analysis of the 8.5-year CGT demonstrated a four-profile solution (AIC=16954.12, Entropy=0.952), consisting of Risk Averse, Slow Processing, High Risk-taking, and Typical Performing. Boys showed significantly higher class probabilities in 'High Risk-Takingâ€ group, while girls were more likely to belong in 'Risk Averseâ€ and 'Slow Processingâ€ groups (all $p<0.05$). In boys, a path model with mediation analysis showed positive associations between prenatal negative mood factor and increased class probability in 'High Risk-takingâ€ (ÃŸ=0.18, 95%CI: 0.04, 0.32, $p=0.009$), as well as 'High Risk-takingâ€ and depressive symptoms (ÃŸ=0.27, 95%CI: 0.13, 0.41, $p<0.001$). Both prenatal negative mood factor (Mediator 1) and class probability in 'High Risk-takingâ€ (Mediator 2) provided a full mediation path in a double serial manner between the relation between lower household income and increased depressive symptoms at age 10 in boys (Direct: ÃŸ=-0.27, 95%CI: -0.41, -0.13; Indirect: -0.10, 95% CI: -0.20, 0.01; AIC=12918.38, CFI=0.99, RMSEA=0.032). In girls, increased class probability of 'Slow Processingâ€ was associated with higher depressive symptoms in girls (ÃŸ=0.16, 95% CI: 0.004, 0.32, $p=0.045$); however, no mediation was found.

Conclusion: Our study shows sex-differentiated relations between reward processing on CGT and depressive symptoms in school-age children, suggesting different cognitive manifestations of depression for boys and girls. While decision-making processes on the CGT do not mediate the relation between prenatal maternal mood and later depression among females in our cohort, increased risk-taking was found to be a mediator that explained increased depression risk associated with prenatal mood among males. This supports mother's mental health during pregnancy as a leverage point for intervention.

2-P-112 - Examination of Adolescent Person-Specific Neural Networks Implicated in Reward Processing and Internalizing Symptoms

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Details

Reward processing, a central construct in emotion processing and cognitive functioning, has been implicated in internalizing disorders, such as depression and anxiety. Three neural subsystem networks - each reflecting the intercommunication among constituent brain regions - play a role in reward processing: 1) The control subsystem is implicated in regulatory roles for cognitive functioning, as well as reward-based planning and error monitoring. 2) The approach subsystem is involved in reward prediction and anticipation. 3) The salience subsystem is central to coding affective values to rewards and outcomes. These subsystems interact closely with each other and functional connectivity within and between these subsystems have been related to both depression and anxiety symptoms.

Despite the plethora of research on neural mechanisms implicated in anxiety and depression, less is known about the role of neural reward subsystems in relation to internalizing symptoms. Additionally, most existing studies linking neural mechanisms of reward processing and internalizing symptoms employ mean-based approaches in estimation of functional connectivity, which may not accurately reflect individual variability in brain networks. Therefore, the current project examined how reward processing neural networks estimated using a person-specific functional connectivity mapping technique relate to internalizing symptoms in adolescents.

A total of 167 adolescents aged 15 to 17 years from the Future of Families and Child Wellbeing Study, a population-based longitudinal cohort study, with substantial representation of marginalized youths, were included in the analyses. Data collection had been completed prior to analysis.

A latent factor of internalizing symptoms was created from multimodal measures of depression and anxiety, including parent and child reports on clinical interviews and questionnaires. Functional neuroimaging data collected during the Monetary Incentive Delay task were extracted from 12 *a priori* regions of interest (ROIs), which were each linked to specific subsystems of reward processing (i.e., control, approach, salience). Person-specific functional networks among these reward subsystem ROIs were then estimated using Group Iteration Multiple Model Estimation (GIMME). Network measures, including density, path strength, and node centrality, were computed for each individual subsystem. These network measures were then used to predict internalizing symptoms using multiple regressions.

Results showed that density of the control subsystem network was uniquely related to internalizing symptoms in adolescents (r = .17, p = .029), such that adolescents with more densely connected control subsystem were higher in internalizing symptoms. This relationship remained after adjusting for additional covariates, including age, gender, pubertal development, race, income, and framewise displacement ($\hat{I}^2$ = .15, p = .044). There were no significant associations between approach or salience subsystems and internalizing symptoms. Our findings suggest differential mechanisms between specific reward processing neural subsystems relating to internalizing. Specifically, these findings highlight functional connectivity among regions that are salient for regulatory control and error detection during reward processing is associated with youth internalizing symptoms. Further analyses investigating the role of other functional networks is underway, and combined with the current study, could contribute to a better understanding of neural functional connectivity relating to internalizing disorders.

2-P-113 - Ventral striatum reactivity to positive social stimuli mitigates the longitudinal effect of parental depression on youth's depression and risk taking

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Details

It is well documented that exposure to parental depression could lead to children's increased internalizing and externalizing problems, in part due to impaired parenting quality, such as harsh practices or lack of responsiveness to children's needs (Goodman et al., 2011, 2020). Exposure to parental depression may be especially detrimental for adolescents who face increased challenges in behavioral regulation and emotion reactivity during this transition period of development (Casey et al., 2019). However, past neuroimaging studies suggested that reward sensitivity may have the capacity to buffer the detrimental influences of adverse social contexts on one's adjustment (e.g., Dennison et al., 2016; Holz, 2020). Given that adolescence is a period when reward sensitivity peaks, reactivity in ventral striatum (VS), a core brain region in the neural reward system, may act as a protective neurobiological factor for adolescents exposed to parental depression to build resilience (Telzer, 2016).

Building on this line of research, the current study aims to examine (1) whether parental depression may predict youth's increased depression and risk taking over time, and (2) whether individual differences in VS activity to social stimuli (i.e., human faces with emotional expressions) may moderate the longitudinal effect of parental depression. Specifically, this study mainly focused on positive social stimuli (e.g., happy faces) because it signals social reward (Bhanji & Delgado, 2014). It is possible that VS activity to social reward may play a buffering role, such that the effects of parental depression on youth's depression and risk taking are smaller among youth with high (vs. low) VS activity to positive social stimuli.

The current study employed assessments from the ongoing Adolescent Brain Cognitive Development (ABCD) study at baseline (W1) and two-year follow-up (W2). In total, 7932 youth (Mean age = 9.96 years

at W1, SD = 7.52; 49% females) and their parents (89% females) were included in the current analyses. Parents reported on their own depression at W1 and their youth's depression and risk-taking behaviors at both waves. Youth's VS reactivity to positive and negative social stimuli (i.e., happy and fearful faces) during the Emotional n-Back Task was obtained at baseline. Youth were nested in family and site. All analyses adjusted for youth's age, gender, and ethnicity, parents' gender, educational attainment, and marital status.

Results showed that parental depression predicted youth's increased depression (Î² = .12, $p < .001$) and risk-taking behavior (Î² = .07, $p < .001$) two years later, controlling for youth's baseline functioning and demographic covariates. More importantly, youth's VS activity to positive social stimuli moderated the longitudinal effects of parents' depression on youth's depression (Î² = -.03, $p = .04$) and risk taking (Î² = -.04, $p = .005$) over time. Simple slopes analyses suggested that the effect of parental depression on youth's depression was smaller for youth who showed high VS activity toward positive social stimuli ($B = .55$, $SE = .13$, $p < .001$) than youth with low VS activity ($B = .86$, $SE = .13$, $p < .001$). Similarly, the detrimental effect of parental depression on youth's risk taking was smaller for youth who showed high VS activity toward positive social stimuli ($B = .13$, $SE = .08$, $p = .11$) than youth with low VS activity ($B = .42$, $SE = .09$, $p < .001$). Whereas VS activity to negative social stimuli did not significantly moderate the longitudinal effect of parental depression (Î²s = -.03, *ps* >.18).

In line with prior research, the current findings indicate that parental depression is a risk factor that increases the likelihood of adolescents' depression and risky behaviors over time. More importantly, the findings highlight the adaptive role of ventral striatum reactivity to positive social stimuli in protecting youth from maladjustment under adverse family contexts (i.e., high parental depression).

2-P-114 - Sensitivity to reward as a buffer against negative mental health consequences of pandemic-related stress: a preregistered analysis in the Human Connectome Project in Development

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Details

Background:

Exposure to stress, both in the forms of individual stressors and community stressors (McLaughlin et al, 2022), is one of the most powerful predictors of the development of psychopathology in children and adolescents. The COVID-19 pandemic has introduced many stressors to youth including loss of loved ones, threat of illness, and loss of structure and routine. Greater exposure to stressors during the pandemic has been associated with increases in psychopathology in youth, even when controlling for pre-pandemic symptoms (Rosen et al., 2021; Varma et al., 2021; Vindegaard & Benros, 2020). Understanding factors that promote resilience in the face of stressors from the pandemic is of critical importance. Previous work demonstrates that sensitivity to reward buffers against the development of

psychopathology in instances of severe stressors including maltreatment (Dennison et al., 2016; Kasparek et al., 2020).

Present study:

In this preregistered analysis, we hypothesize that neural sensitivity to reward prior to the pandemic will serve as a buffer against the negative mental health consequences of stress that occurred as a result of the COVID-19 pandemic. To test this hypothesis, we will utilize longitudinal data collected as part of the Human Connectome Project- Development (HCP-D) in individuals spanning ages 9-17 years.

Time Point 1 Measures (pre-pandemic):

We will analyze sensitivity to reward using fMRI BOLD response to reward (using the GUESSING task modeled off of Delgado et al., 2000) at Time 1 of data collection (pre-pandemic). We will measure reward sensitivity using increased activity in the ventral striatum, dorsal striatum, and ventral medial prefrontal cortex for wins as compared to losses (Somerville et al., 2018).

Time Point 2 Measures (during the pandemic):

Youths were contacted during the pandemic (October 2021-January 2022; n = 332) and we assessed pandemic-related stressors including, for example, if they lost a loved one, if their parent was a frontline worker, and if they experienced difficulty doing school work remotely. We also assessed mental health using the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997).

Analyses:

We will first investigate whether COVID-related stressors are associated with increasing internalizing and externalizing psychopathology during the pandemic. Next, we will examine whether there is a main effect of neural reward sensitivity on mental health during the pandemic. Finally, we will separately test whether neural sensitivity to reward moderate the association between pandemic-related stress and psychopathology symptoms. All analyses will control for pre-pandemic symptoms, age, and sex. We predict that individuals who have a higher sensitivity to reward will be protected against the negative mental health outcomes of high levels of pandemic-related stressors. If our hypotheses are supported, this will add to the growing body of literature that cites reward sensitivity as a potential target for intervention.

2-P-115 - A multi-sample evaluation of the measurement structure and function of the modified monetary incentive delay task in adolescents.

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Details

Background: Interpreting the neural response elicited during task functional magnetic resonance imaging (fMRI) remains a challenge in neurodevelopmental research. The monetary incentive delay (MID) task is a popular fMRI reward processing task that is extensively used to probe motivational processing of monetary cues. Despite being the most widely used task, the measurement properties of the MID task with regard to fMRI signals have not yet been evaluated using modern psychometric tools.

Objective: In this Registered Report (Stage 1 in-principal acceptance at *Developmental Cognitive Neuroscience* [osf.io/f9u3w]), we evaluate multiple measurement properties of neural estimates from fMRI during the anticipation phase from the MID task through analysis of data obtained from three independent adolescent samples (N ~108, N ~ 150, N ~ 1000) that completed similarly designed MID tasks.

Methods: We examine psychometrics of six anticipatory contrast measures: Big Gain versus Neutral, Big Gain & Small Gain versus Neutral, Big Gain versus Big Loss, Big Loss versus Neutral, Big & Small Loss versus Neutral and Big Loss versus Big Gain; and four task-relevant brain regions from the Harvard-Oxford atlas: Bilateral Nucleus Accumbens and Bilateral Insular Cortex. In **Aim 1a** we use confirmatory (restricted) factor (CFA) to evaluate whether six anticipation task contrast measures for four regions of interest (ROIs) reflect the hypothesized latent factors, approach and avoidance. The hypothesis is that the contrasts across the four hypothesized regions (e.g., NAcc and AI) load onto two factors, approach and avoidance, and the same structure is present in each adolescent sample. In **Aim 1b**, an exploratory structural equation model (ESEM) is used to discover the presence of non-zero cross-loadings across brain regions. In **Aim 2**, exploratory (unrestricted) factor (EFA) is used to evaluate the structure of the measures using a data-driven approach across the three samples. Here, no specific hypotheses are forwarded. Rather EFA of data for each study are obtained separately and then compared qualitatively and quantitatively. In **Aim 3**, we consider the effects of pubertal development on factor structure and evaluate whether measurement properties of the MID stabilize as with pubertal maturity. Specifically, Local SEM (sliding window) is used to examine how the factor loadings change across the self-reported pubertal developmental scale in the ABCD study. Due to the unclear evidence how pubertal development may impact the measurement properties of the MID task, no *a priori* hypotheses are specified.

Implications: This study empirically tests whether the hypothesized dimensional structure of the MID task actually manifests in empirical data. The multi-group invariance analyses indicate whether and to what extent the psychometrics properties of the MID support comparison of results across samples and studies. This information will be essential for developmental cognitive neurosciences using these measures in individual-differences research.

Q – Socioemotional processing

2-Q-116 - Identifying Functional Connectivity Mediators of the Age-Related Changes in Negative Affective Experience Across Adolescence

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Details

Research shows that among healthy adolescents, there is a downward shift in emotional experience in the direction of more frequent negative and less frequent positive states. While this increase in negative emotional experience, or *negative affect*, is thought to be developmentally normative, sustained increases in negative affect during developmental years can result in an increased risk for the development of psychopathology that often persists into adulthood. Importantly, within global increases in negative affect, specific forms of negative affect are found to show distinct age-related changes across development, each with unique affect-functional outcome relationships. While the age-related changes in emotional processing across adolescence are documented and confer tangible, long-term health risks, the neurodevelopmental underpinnings of these changes are poorly understood. Evidence primarily from adult and clinical populations reveals that functional connectivity within and between intrinsic brain networks, or networks with coherent spontaneous activity at rest, dynamically interact to give rise to a wide range of emotional experiences. However, while brain networks are shown to undergo connectivity changes across the adolescent transition period, little work has examined resting-state correlates of negative affect in healthy adolescent samples, with existing studies limited by small sample sizes. In the current study, we aim to explore whether connectivity within and between key resting-state networks mediates the observed age-related changes in different forms of negative affect across adolescence. We acquired a sample of 650 participants aged 8-17 years as part of the Human Connectome Project in Development (HCP-D), a large-scale cross-sectional and longitudinal study of brain connectivity in youth, for analysis. We focus our analysis on four well-established resting-state networks that have been shown to support cognitive and emotional processing: the default mode network, frontoparietal network, cingulo-opercular network, and dorsal attention network. Networks will be extracted using the Cole-Anticevic Brain Network Parcellation scheme to allow for the inclusion of cortical-subcortical circuitry that may be relevant for understanding adolescent emotional experiences. To identify specific resting-state mediators, we plan to conduct a multiple mediation analysis with age as the independent variable, three forms of negative affect that showed age-related changes (sadness, general anxiety, and evaluative anxiety) as dependent variables, and within and between-network connectivity strength for the four identified resting-state networks as mediator variables. For networks that emerge as significant mediators, we plan to conduct secondary mediation analyses to determine which region-to-region connectivity metrics explain the most variance in mediating the age-affect relationship. Given the non-linear age-related changes in negative affect, the age paths will be modeled nonlinearly. We expect that each type of negative affective experience involves the participation of all four core distributed brain networks, and thus each network partially contributes to the age-related changes in negative affect. However, we predict that different network *profiles* (i.e., the relative degree of connectivity strength within and between networks and patterns of specific region-to-region connectivity) will emerge as distinct mediators for each negative affect type. Our results will highlight the intrinsic connectivity patterns that contribute to changes in different forms of negative affect across adolescence, offering a mechanistic account that will help elucidate neurodevelopmental processes underlying affective experience. Ultimately, we hope our findings serve to refine affective neuroscience theories and offer a deeper characterization of the rapid and complex emotional and neural changes that occur during this dynamic phase of life.

2-Q-117 - Computational modeling of social feedback processing reveals differential impression updating across development

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Details

As individuals enter adolescence, they must navigate an entirely new social landscape that includes the near constant signaling of social inclusion and shifting social bonds. To ensure social belonging, adolescents must use these signals to flexibly update future social behavior. At the same time, this phase of development is a time of hypersensitivity to peer rejection, including intensified emotional and stress responses. Therefore, the way that this feedback is used to inform one's social standing may be subject to biases that differ with age. I have previously shown that--despite equivalent experiences of peer acceptance and rejection--adolescents internalize peer rejection and diminish self-views, whereas adults elevate self-views and devalue the peers who reject them. Here, I examine the computational and neural indices that explain these age-related differences in how peer feedback differentially guides impression updating of the self and others. In the present study, 84 participants (aged 10-23) completed a reciprocal social evaluation task during fMRI to assess how peer acceptance and rejection modulate underlying neurocognitive processes that support the integration of peer feedback. Given its role in feedback-based learning, I hypothesized that differential neural functioning of the corticostriatal circuit would explain these age-related differences. In particular, I hypothesized that adolescents will preferentially upweight learning from rejection to inform self-views, while adults will boost self-views by upweighting acceptance, and these learning signals will be reflected in the striatum and medial prefrontal cortex. I ran a classic reinforcement model with a 2-learning rate design (i.e., independent learning rates for positive and negative feedback) that allowed for testing of asymmetries in learning from acceptance and rejection across age. Findings indicated that compared to adults, adolescents had a higher learning rate for both positive and negative feedback, where they showed greater responsivity to feedback in informing their subsequent predictions. Adults on the other hand, updated their predictions based on a longer history of trials. Meanwhile, those who experienced a task-induced drop in self-views, which tended to be early adolescents, were more responsive to negative feedback and less responsive to positive feedback, whereas those who experienced a task-induced boost in self-views, which tended to be adults, showed the opposite pattern. And finally, when examining the association between learning rates and evaluation-induced neural activation, we found that those who showed increased medial prefrontal activation to acceptance vs. rejection, who also tended to be boosters, were also less responsive to negative feedback. Future analyses will further explore age-related differences using advanced computational analyses, including adaptive Bayesian inference modeling, to explore differential model fit. These findings will enhance our understanding of the developmental differences in learning from social evaluation by characterizing latent moment-to-moment neural responses using computational modeling approaches.

2-Q-118 - Characterizing amygdala nuclei resting-state connectivity with cortex as a function of age in adolescence: a high-field longitudinal investigation

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Details

Adolescence represents a period of marked affective and cognitive development, supported in part by the neural refinements of fronto-amygdala regions and their connectivity during a time when GABAergic and glutamatergic indices of critical period plasticity are occurring in frontal cortex. Alterations in this circuitry are implicated across several major psychopathological disorders, which typically emerge

during adolescence. Initial studies have found developmental changes in large parts of the amygdala and prefrontal cortex. However, the amygdala has several nuclei that have unique function and connectivity whose maturation *in vivo* in humans has not yet been investigated. Here, we characterize at the amygdalar nuclei level, developmental changes in connectivity, its association with glutamatergic changes in PFC, and how these are associated with internalizing/externalizing phenotypes. We collected 7 Tesla resting-state fMRI data in 164 healthy participants ages 10-30, scanned 1-3 times for a total of 219 scans to characterize fronto-amygdala resting-state functional connectivity development. Amygdala nuclei were segmented using subject-specific anatomical definitions from FreeSurfer. Internalizing and externalizing phenotypes were assessed using youth and adult self-reports (YSR/ASR). We found that functional connectivity between the rostral anterior cingulate cortex (rACC) and lateral nucleus (LN) (F = 8.82, Bonferroni p = .011) and between the ventral ACC (vACC) and corticoamygdaloid transition area (CAT) (F = 9.52, Bonferroni p = .005) increased with age. Further, after controlling for age effects, we found that stronger CAT vACC rsFC was associated with greater internalizing (F = 4.11, p = .018) and externalizing (F = 3.61, p = .029) phenotypes in healthy participants. These results suggest that amygdala connectivity with ACC uniquely strengthens through adolescence, which in turn may support the establishment into adulthood of cognitive influences over affective function.

2-Q-119 - Social touch during feeding predicts infants' BOLD response in immature neural pathways

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Details

Social touch is nonsexual, pleasurable, affective touch that conveys social information and aids in the formation of social bonds. In infancy, feeding is a unique opportunity for parent-child bonding, due to the significant amount of social and operational touch. Gentle, affectionate touch (such as soft caresses or strokes) during breastfeeding has been shown to be neuroprotective in infant development, although the neurological mechanisms have yet to be explored. In adults, c-tactile afferents encode the emotional valence of touch through contralateral projections in the spinal cord, which traverse through the thalamus and into the insular cortex. Similarly, tactile sensory information is encoded via  afferents, which travel ipsilaterally into the medulla, traverse contralaterally, continue to the thalamus and then to the somatosensory cortex. However, infants display both ipsilateral and contralateral neural responses during touch, which may be reflective of immature neural profiles that rely on callosal connections. Around three months of age, callosal pruning occurs, making the thalamo-cortical pathways more salient. Thus, our research aims to assess how external environmental factors, like gentle touch during feeding, may influence the salience and lateralization of social tactile processing. We hypothesize that infants who experience more gentle touch during feeding will show a greater BOLD response to social compared to non-social touch in the thalamus, somatosensory cortex, insula, and medulla. To assess this question, nine full-term infants under five months of age underwent a five-minute feeding paradigm where parents were instructed to feed the infant as they would at home. These videos were later behaviorally coded to measure the total duration of gentle touch during the feeding. Afterwards, infants were rocked to sleep and underwent functional magnetic resonance imaging (fMRI). During the fMRI, infants were gently stroked with a paintbrush on their left leg to simulate both social (paintbrush on skin) and non-social (paintbrush strokes with plastic placed between paintbrush and the skin) touch.

Second-level analyses for the main effect of social compared to non-social touch showed greater BOLD response in the left occipital cortex, left somatosensory cortex, left and right supramarginal gyrus, right frontal pole, right precuneus cortex, right and left precentral gyrus, right medial prefrontal gyrus, right and left superior parietal lobe, right central opercular cortex, right and left superior frontal gyrus, right planum temporale, right medial and inferior frontal gyrus, right occipital fusiform gyrus, right temporal fusiform cortex, right and left middle temporal gyrus, and left occipital pole. A general linear model was then used to predict whole-brain BOLD response from the total duration of gentle touch during feeding. Gentle touch positively predicted BOLD response in the right brainstem. These results indicate that infants globally process social touch in neural regions similar to adults. However, the lack of contra-lateralization of the neurological responses to social tactile stimuli may be indicative of immature neural pathways that may be ascending through callosal connections. Additionally, studies in adults have shown spatial representation of touch discrimination within the brainstem and midbrain regions. Perhaps gentle touch aids in the development of discriminatory pathways early in life. Future work will need to take a longitudinal approach to measure the trajectory of change from processing via callosal connections to thalamo-cortical connections.

2-Q-120 - The influence of parental validation on anterior insular activity among adolescents during real-time fMRI dyadic neurofeedback

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Details

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Submission Theme: Socioemotional Processing

Objectives: Parenting behaviors such as emotional validation can influence adolescent neurocircuitry and emotion regulation (ER), and interventions targeting these behaviors may therefore promote healthy socioemotional development. Our research team has adapted real-time functional magnetic resonance imaging (fMRI) neurofeedback for the parent-adolescent relationship, such that the parent views the neurofeedback signal during an interaction with their child (dyadic neurofeedback, DNF; Kerr et al., 2022). Parents are instructed to attempt to downregulate activity in their adolescent's right anterior insular cortex (aIC), represented by a moving bar on a computer screen, while discussing an emotional situation with their adolescent. The current study seeks to examine parenting behaviors that correlate with the downregulation of an adolescent's aIC. More specifically, we seek to examine how the presence of validating and invalidating parental statements influence adolescent aIC activation during DNF. We hypothesize that 1) increased validation will be associated with reduced aIC activation and 2) increased invalidation will be associated with increased aIC activation.

Methods: Data will be utilized from an ongoing randomized clinical trial of DNF (target *n* = 70 dyads; youth ages 14-16 years; control group completes the same task without DNF). During the scan, the parent sits in the control room and communicates with the teen via active noise-canceling microphones and headphones (OptoAcoustics Ltd.). Audio recordings of parental statements during the scan are transcribed and coded for validating and invalidating statements using the Validating and Invalidating Behavior Coding Scales (VIBCS; Schneider & Fruzetti, 2002). Validation (for example, 'It makes sense that you'd feel that wayâ€) and invalidation (for example, telling the adolescent how they *should* feel) are coded separately for each scanning run on a 1-7 scale. Mean right aIC activity during the â€˜listen' blocks of the task (i.e., when the adolescent is listening to their parent speak) will be calculated for each scanning run to account for training effects in the neurofeedback group across the course of the scan (five 6-minute runs total).

Analysis Plan: R statistical software will be used for data analysis. Linear mixed-effects models will predict aIC activity from validation and invalidation with youth gender and age as covariates and random effects for scanning run and participant. Preliminary analyses of pilot data (*n* = 8 dyads; all female) using a median split (high validation *M*=4.60; *SD*=0.37; low validation *M*=3.50; *SD*=0.87) indicate that parents expressing higher validation have more success in lowering their daughters' aIC activity (Cohen's *d* = 1.58).

Significance: The evidence from this study may have the potential to inform parenting strategies that contribute to ER development. Knowledge of communication strategies associated with adaptive ER and the downregulation of the aIC might also have implications in the mental health field. Furthermore, this study can inform future studies on the use of validation to promote ER and aIC downregulation.

2-Q-121 - A common neural response to experiencing and regulating infant and adult affect in postnatal mothers

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Details

The transition to parenthood requires developing caregiving behaviors in order to sensitively respond to infants' needs. A crucial caregiving skill is parents' ability to identify their infant's emotions and regulate their own emotional response. Perinatal neuroimaging research has identified consistent patterns of neural activation in mothers in response to infant stimuli that are interpreted as socioemotional processing to meet the demands of parenting an infant. However, no prior research has tested whether mothers' neural responses to their infant's affect are the same as those involved in emotional experience and regulation in other contexts. We employed conjunction analyses to clarify which components of mothers' neural response to their infant's affect are shared with passively viewing and labeling adult affective faces (tasks designed to elicit emotional response and implicit emotion

regulation, respectively) in a sample of 24 low-income mothers at three months postnatal. Our results support a common neural response to viewing infant and adult affect in affective processing regions (ventrolateral prefrontal cortex, orbitofrontal cortex, amygdala, thalamus, and hippocampus), but no areas of common response to viewing infant affect and implicitly regulating adult affect. In a post-hoc analysis, we found that endorsed use of explicit emotion regulation strategiesâ€"positive reappraisal, rumination, and self-blameâ€"in response to their infant's negative affect was associated with activation changes in the medial prefrontal cortex and dorsolateral prefrontal cortex that were in part consistent with prior literature outside the perinatal context. This project is an important step toward understanding emotional experience and regulation in the parenting context.

2-Q-122 - Adolescents' perceptions of parenting behaviors mediate the association between maternal childhood abuse and maltreatment and adolescent behavioral problems

Kendall Parks [1], **Jessica Uy** [1], **Jessica Buthmann** [1], **Ian Gotlib** [1]

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Details

Exposure to childhood maltreatment (CM) increases risk for psychiatric disorders, suicidal ideation, and other maladaptive outcomes across the lifespan, including during the transition to parenthood. Mothers who experienced CM are more likely to experience poorer mental health and engage in maladaptive parenting behaviors. Indeed, maladaptive parenting behaviors, such as hostile, intrusive, and abusive practices, may increase the risk that their adolescent offspring develop psychopathology, potentially perpetuating cycles of maltreatment across generations. In order to reduce the risk of maltreatment and psychopathology across generations, it is critical that we gain a more comprehensive understanding the dynamics of maladaptive parent-adolescent relationships. Unfortunately, it is not yet clear precisely how maternal CM leads to difficulties in adolescents' functioning. Maternal CM may itself not be pathognomonic of adolescent difficulties; rather, adolescents' subjective perceptions of the sequelae of their mothers' CM (i.e., their parenting behaviors) may be important in this context. In this study we compared mothers' and adolescents' perceptions of the mothers' parenting behaviors as mediators of the association of maternal CM with adolescent behavioral problems.

Our sample included 97 mother-adolescent dyads who are participating in an ongoing longitudinal study of the effects of early life stress on psychopathology (mean adolescent age=15.46 years +/-1.05; 41M/56F). Mothers reported on their own experience of CM before the age of 18 years using the Childhood Trauma Questionnaire (CTQ), a 28-item measure of CM history that has 5 subscales: physical abuse, physical neglect, emotional abuse, emotional neglect, and sexual abuse; we also aggregated subscales to yield total abuse and total neglect scores. Mothers' parenting behaviors were assessed using the Parental Psychological Control (PPC) questionnaire, completed by both the mothers (Parent PPC) and the adolescents (PPC-CP). Finally, mothers completed the Child Behavior Checklist (CBCL), a 120-item questionnaire assessing offsprings' behavioral difficulties that yields scores for internalizing, externalizing, and total problems. We tested whether maternal CM is related to adolescent difficulties and whether PPC scores mediate these associations.

For males, both CBCL internalizing problems and CBCL total problems were positively associated with maternal physical abuse (r=0.5, p<0.001; r=0.45, p=0.003), emotional abuse (r=0.32, p=0.04; r=0.41,

p=0.008), total abuse (r=0.44, *p*=0.004; r=0.47, *p*=0.002), and total childhood trauma (r=0.36, *p*=0.02; r=0.4, *p*=0.009); however, these direct effects were not mediated by either parent or adolescent perceptions of maternal parenting. In the full sample, PPC-CP significantly mediated the association of maternal emotional abuse with CBCL total problems (indirect effect=0.28, SE=0.15, 95% CI: [0.05, 0.62]).

In this study, we found that, for males, maternal history of trauma and abuse were related to adolescents' internalizing and total problems. In the full sample, adolescents' perceptions of their mothers' parenting behaviors significantly mediated the association of maternal emotional abuse with adolescents' total problems. These results underscore the importance of mothers' early childhood experiences in affecting their adolescents' psychological functioning; further, they suggest that parent training for mothers, and/or reframing adolescents' perceptions of their mothers' parenting behaviors, may reduce adolescents' risk of experiencing psychological difficulties.

2-Q-123 - Detecting the M170 face response using optically pumped magnetometers in young children and adults

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Details

Background: There is a paucity of neuroimaging studies in early development due to the challenges surrounding recording neural responses in infants and toddlers. Optically pumped magnetometers (OPMs), a new â€˜wearable' magnetoencephalography (MEG) technology (e.g., Boto et al., 2018; Hill et al., 2022), offers substantial advances in signal strength, data quality and tolerance of movement compared to traditional cryogenic MEG. Thus, OPMs have tremendous value for recording brain responses in very young children. Little research has investigated the early neural underpinnings of face processing in young children, particularly the emergence of the source localized M170 evoked faces response, and whether this response reflects similar face-sensitive mechanisms as in adults. The current study is the first to establish the characteristic M170 face response using OPMs in 3- and 4-year-old children and adults.

Methods: We recorded evoked fields to emotional faces in 9 children (3-to-4 years; Mage ï,±SD = 4.1 ï,±0.8 years; 3 males) and 21 adults (Mage ï,±SD = 32.54 ï,±11.61 years;11 males) with 40 dual-axis OPM zero-field magnetometers (forming an 80 channel MEG system (Cerca Magnetics Limited, UK)). Data were epoched (-500 to 1000ms) relative to faces onset, and band-pass filtered between 2-40Hz. The data were co-registered, using EinScan (Shining 3D, China) to transform the coordinates of a 2mm grid in MNI space to the participants' head position and source activity was estimated using a LCMV beamformer. For each participant, the percentage change from baseline was calculated, and the voxel within the left and right fusiform gyri with the maximum change from baseline was identified; the timeseries were then extracted to determine peak amplitudes and latencies. The whole-brain percentage change in power relative to baseline was also plotted for the M170 time window in children (150-230ms) and in adults (120-180ms).

Results: The adults showed the characteristic face-sensitive M170 response in the bilateral fusiform gyri. We observed a larger evoked response in the right fusiform, with a peak amplitude of 21.3nAm

(SD=25.6) and latency of 171ms (SD=17.7). The left fusiform showed a peak amplitude of 14.9nAm (SD=18.2) and latency of 172ms (SD=40.3) to faces. Children also demonstrated an M170 response to faces in the bilateral fusiform gyri. For the right fusiform, a peak amplitude of 16.4nAm (SD=12.9) and peak latency of 169ms (SD=16.7) was seen. For the left fusiform, the peak amplitude was 14.0nAm (SD=7.7) and latency was 180ms (SD=16.2). There were no significant main effects for hemisphere, group, nor group-by-hemisphere interactions. In adults, the mean percent change in source power from baseline showed a significant increase in power in bilateral frontal and temporal areas, including the bilateral fusiform gyrus, which was larger in the right hemisphere (pcorr <0.05). In children, the percentage change in power to faces was not significantly different from baseline, however visual inspection of mean power showed recruitment of left temporal areas, including the fusiform and bilateral frontal areas.

Discussion: This is the first study to examine face-sensitive responses in young children and adults using OPMs, and to demonstrate the feasibility of this modality to record and detect reliable MEG data recordings in 3- and 4-year-old children. Using this new technology, we replicated the well-established M170 response to emotional faces for the first time in 3-and 4-year-olds, reflecting surprisingly similar face processing components to adults at this age. Data collection in children is ongoing; however, these preliminary findings validate the use of OPMs in young children and will provide greater insight into the early developmental trajectory of face processing.

2-Q-124 - Relationships between gut metabolites, socio-emotional brain processing, and behavior in youth with autism

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Details

Objective

A growing body of research indicates that gut-brain-behavior relationships may modulate symptomatology in autism spectrum disorder (ASD). Specifically, levels of tryptophan and glutamate pathway metabolites have been shown to be different in ASD than typically developing (TD) people, and may modulate symptomatology. The tryptophan pathway includes serotonin, involved in neural modulation of socio-emotional processing, and kynurenine, known to potentially lead to neurotoxicity. Additionally, methylglutamate has been associated with clinical symptoms of ASD. However, there is a limited number of human studies on this topic, with almost no studies using brain imaging, behavioral, and gut metabolite data from a single group of children. Here, we explore tryptophan and glutamate metabolite levels, as well as behavior and neural activity during an fMRI task where TD and ASD youth watched videos of other people making facial expressions and/or hand actions a task known to elicit differential brain activation in ASD youth.

Methods

38 TD (mean age=11.91 years; 19 males) and 40 autistic (mean age=12.26 years; 29 males) children (age range: 8-17) completed an fMRI task where they viewed videos of other people making facial expressions and hand actions. They also provided a stool sample for metabolomic analysis and completed behavioral measures (e.g., diet, antibiotic history, gastrointestinal (GI) symptoms, birth history, Developmental Neuropsychological Assessment-II [NEPSY-II], and the Social Responsiveness Scale-2 (SRS-2). ASD participants additionally completed the Autism Diagnosis Observation Schedule (ADOS-2). Brain regions of interests (ROIs) were chosen based on group differences in activation (TD>ASD) and prior literature. Functional activity in the ROIs (6mm sphere centered on peak voxel) were then extracted during tasks to run general linear models and correlations with behavioral data and centered log transformed tryptophan and glutamate metabolite concentrations, adjusted for medication usage. Model covariates included age, gender, IQ, and body mass index.

Results

As compared to the TD group, the ASD group displayed significantly lower kynurenate levels (tryptophan pathway; p=0.02, FDR) and showed behavioral differences in GI symptoms, NEPSY ToM and affect recognition subscales, and SRS social skills (p<0.01). Consistent with prior fMRI studies, when viewing others' facial expressions and/or bodily actions, ASD youth, as compared to TD youth, showed decreased brain activity in the bilateral inferior frontal gyrus, pars opercularis (IFGop), right dorso-anterior insula, and left mid-cingulate cortex; and greater activity in the right ventro-anterior insula (all *p*s<0.01, SVC). For behavioral-brain correlations, in the ASD group, decreased activity in the right IFGop during processing of others' facial expressions was significantly correlated with increased autism severity, as measured by the ADOS comparison score (R=-0.54, p<.05). Importantly, across groups, a tryptophan pathway metabolite (anthranilate), and a glutamate metabolite (methylglutamate), were positively associated with brain activity in the right IFGop during viewing others' facial expressions and/or bodily actions (p<0.05, FDR). Tryptamine, another tryptophan metabolite, showed a similar relationship in the right IFGop, right fusiform face are (FFA), and mid-cingulate that neared significance (p<.06, FDR).

Conclusion

Our results support the hypothesis that tryptophan metabolites and glutamate metabolites may be related to brain differences commonly observed in autism (IFGop hypoactivity during socio-emotional processing), which in turn relate to autism severity.This is the first study to explore the relationships between brain, socio-emotional processing, and gut metabolites in autistic and TD children, and highlights the complex interplay between these factors.

2-Q-125 - The moderating role of parental trauma history on the association between adolescent externalizing symptoms and emotion regulation-related amygdala activation

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Details

Introduction: Adolescence is a sensitive developmental period for emotion regulation and the emergence of psychopathology, including externalizing spectrum disorders. Previous fMRI work has linked youth externalizing symptoms to hypo-activation of the amygdala during emotion regulation tasks. Given that parents play a prominent role in the development of emotion regulation skills, it is likely that parent factors may influence neural circuitry of emotion regulation and psychopathology. Specifically, parents' trauma exposure has been linked to the transmission of risk for psychopathology to their children at least partially through influencing youths' emotion regulation capacity.

Objective: The goal of the present study was to assess whether the links between youth externalizing symptoms and emotion regulation-related amygdala activation vary as a function of parent's history of interpersonal violence.

Methods: Participants were 91 adolescent-parent dyads (youth: M/SD_{age}= 12.24/.95; 52.7% female; 92% biological mothers. Parents completed an interview of their own trauma history and measure of their chil's psychopathology. Approximately half (59.3%) of parents reported at least one instance of interpersonal violence. Adolescents completed an fMRI emotion regulation task that required youth to either regulate or react (focus factor) to negative or neutral trials (valence factor). Analyses examined whether parent trauma history moderated the effect of youth externalizing symptoms and amygdala activation to the focus demands and stimuli valence of the fMRI task, after accounting for youth age, biological sex, and handedness, and internalizing symptoms. Hypotheses were tested using repeated measures GLM in SPSS.

Results: There was no significant 4-way (externalizing x parent trauma x focus x valence) interaction. However, there was a significant interaction between parental trauma, youth externalizing symptoms, and amygdala activation in relation to the Focus contrast (F = 5.706, p = .019). Probing of the interaction revealed significant group differences in relation to the 'Reactâ€ condition. Specifically, among youth whose parents did have a trauma history, externalizing symptoms were *negatively associated* with amygdala activation during React trials, regardless of stimuli valence. However, among youth whose parents had no trauma history, externalizing symptoms were *unrelated* to amygdala activation during React trials. No significant differences were observed in relation to the 'Regulateâ€ trials.
Discussion: Existing literature has found that youth externalizing symptoms are associated with hypo-activation of amygdala during emotion regulation tasks. However, the role of parenting factors in these associations has been relatively understudied. We found that the link between youth externalizing symptoms and emotion regulation-related amygdala activation varied as a function of parental trauma history. This finding suggests that parent-level factors play an important role in the neural circuitry supporting emotion regulation among early adolescents with externalizing symptoms. Specifically, parents' own experiences of trauma may influence emotional reactivity, but not reappraisal, among adolescents with externalizing symptoms. Future research is needed to replicate and extend these findings in order to further conceptual models of adolescent emotion regulation.

2-Q-126 - Connectome-based modeling predicts childhood socio-emotional development

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Details

OBJECTIVE: Socio-emotional development, a process through which children learn skills to build meaningful social relationships and successfully express and manage emotions, is critical to future well-being. Throughout childhood, changes in brain structure and function, particularly in the prefrontal cortex, support socio-emotional development. The purpose of this study was to investigate the neural systems that contribute to individual differences in socio-emotional development during childhood. METHODS: Independent cohorts of children aged 4-11 and adults aged 25-30 underwent fMRI while passively viewing a high valence, action-oriented movie clip from *Finding Nemo* and the engaging, nonsocial *Inscapes* film. Two years later, children aged 8-13 completed self-report questionnaires to assess socio-emotional development. Bootstrap exploratory graph analysis, a dimensionality reduction method from network psychometrics, was employed to estimate distinct latent communities from questionnaire data. As a feature reduction step, inter-subject correlation analysis identified brain regions that were consistently evoked during *Finding Nemo* in contrast to *Inscapes* in adults. Then, functional connectivity between the synchronous brain regions was calculated for all children. Connectome-based predictive modeling, a machine learning method that is sensitive to individual variability in functional connectivity patterns, was implemented to predict scores on the latent socio-emotional development communities. RESULTS: Internalizing and sociability latent communities were estimated from self-report questionnaires. Higher scores on the internalizing community were associated with more symptoms of anxiety and depression and more perceived loneliness, while higher scores on the sociability community were associated with more skills essential for initiating and maintaining effective relationships, including empathy and engagement. We found that functional connectivity models predicted scores on the sociability community with significant accuracy and scores on the internalizing community with accuracy approaching significance. While functional connectivity in the sociability connectome existed between regions distributed throughout the entire brain, more functional connectivity between orbitofrontal cortex regions of the prefrontal cortex emerged as particularly predictive of higher levels of sociability. CONCLUSIONS: In summary, we demonstrated that individual differences in functional connectivity patterns predicted variability in scores on a sociability latent community identified from self-report questionnaires of childhood socio-emotional development. Previous work indicates that stable patterns of functional connectivity between hubs within the prefrontal cortex are established between childhood and adolescence. Additionally, the orbitofrontal cortex is a brain region involved in learning, predicting, and making decisions about emotional and reward-related behaviors. Together, this evidence suggests that children with higher levels of sociability may have more mature brain connectivity profiles such that socio-emotional content is more intrinsically rewarding. These results have implications for our basic understanding of the neural systems underlying individual differences in childhood socio-emotional development, which may be informative of health outcomes and quality of life through adolescence and adulthood.

2-Q-127 - Exposure to threat adversity and amygdala-prefrontal connectivity during emotion regulation: Exploring the role of emotional clarity

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Details

Background: Poor emotion regulation is a transdiagnostic feature of psychopathology in adolescence (Beauchaine, 2015). Connectivity between the amygdala and prefrontal (PFC) regions (e.g., vmPFC, dlPFC) is hypothesized to support emotion regulation (Silvers et al., 2014), and disruptions to the normative development of this connectivity is likely to contribute to risk for psychopathology (Jenness et al., 2021). Prior research demonstrates that exposure to threat during childhood is associated with difficulty understanding and identifying emotions (*emotional clarity*, Luke & Banerjee, 2013; Westbook & Berenbaum, 2016) and poor self-reported emotion regulation (Gruhn & Compass, 2020). However, it is unclear to what extent threat impacts amygdala-PFC connectivity, or the extent to which emotional clarity may moderate this association, as low clarity predicts more emotion dysregulation and decreased amygdala-PFC connectivity (Faulkner et al., 2020; Pandey, Saxena, & Dubey, 2011). **Objective:** The goal of this preregistered project (https://osf.io/jse65/) was to test the hypotheses that (1) greater childhood threat exposure would be associated with lesser amygdala-vmPFC/dlPFC connectivity during a well-established emotion regulation task, and that (2) higher emotional clarity would buffer against the effect of threat on amygdala-vmPFC/dlPFC. **Methods:** 138 adolescents assigned female sex at birth (ages 9-17) completed a standard fMRI emotion regulation task (e.g., Ochsner et al., 2004; Silvers et al., 2012). Emotional clarity was measured using the poor awareness subscale from the Emotion Expression Scale for Children. Childhood threat exposure was computed as a cumulative risk score of sexual, physical, and emotional abuse based on youth self-report on the Children's Coping Strategies Questionnaire, the Childhood Trauma Questionnaire, the Peer Victimization Questionnaire, and MINIâ€¯International Neuropsychiatricâ€¯Interview as well as parent report on items from the Parenting Styles and Dimensions Questionnaire and the Stress and Adversity Inventory Screener. **Analytic Strategy:** We will conduct generalized psychophysiological interactions for emotion regulation trials (Negative Decrease > Negative Look) as an index of task-based amygdala-PFC connectivity. Functional and structural MRI data have been preprocessed using *fMRIPrep*, but we have not yet conducted connectivity analyses. Using hierarchical regressions, we will then look at the main effects of and interaction between childhood threat exposure and emotional clarity on amygdala-PFC connectivity. Analyses will control for age, race/ethnicity, and other dimensions of adversity (i.e., deprivation). Additionally, we will explore associations between threat exposure and mean framewise displacement. If there is a significant association, mean motion will be entered into functional connectivity models as covariates of non-interest. **Significance:** Results from this analysis may yield insight into the neural and psychological mechanisms linking early life adversity and emotional development, as well as mechanisms that support emotional resilience. Understanding these mechanisms is crucial for identifying interventions to mitigate risk.

2-Q-128 - Childhood violence exposure and neural mechanism of emotion generalization and differentiation

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Details

Emotion categories are complex, multimodal representations of experiences with shared features, which are distributed across the brain. The formation and updating of emotion categories across development requires generalizing across and differentiating between diverse multimodal experiences under a single categorical umbrella, a process that likely relies heavily on the hippocampus and default mode network. Because emotion concepts are complex and distributed across the brain, successful identification of neural activity patterns that differentiate between discrete emotions has only been achieved consistently through multivariate techniques, including representational similarity analysis (RSA). Greater representational dissimilarity of neural responses to emotions in these brain regions thus may reflect greater emotion differentiation. Exposure to repeated, unpredictable violence in childhood may limit the developing brain's ability to generalize across and differentiate between diverse multimodal experiences and develop coherent emotion categories. This study investigates mechanisms of emotion generalization and differentiation in the adolescent brain and how they are influenced by childhood violence exposure. It will test the following hypotheses: 1) Engaging in emotion labelling will be associated with greater activation in ventrolateral prefrontal cortex, dorsomedial prefrontal cortex, and temporoparietal junction, and reduced activation in the amygdala compared to passive viewing of affective stimuli. 2) Behavioral measures of emotion differentiation will correspond with multivoxel representational similarity in brain regions activated during emotion labelling. 3) (exploratory nondirectional hypothesis) Childhood violence exposure will be associated with differences in multivoxel representational similarity in brain regions activated during emotion labelling. The sample for this study is 70 adolescents aged 13-18 years, over half of whom have some exposure to violence. A composite measure of violence exposure variety, severity, and frequency was based on adolescent and parent-report on multiple scales. In the scanner, participants viewed short emotionally evocative video clips and were instructed to either label their emotions while watching the videos or to attend to the number of people in the video. To test hypothesis 1, the univariate contrast of BOLD activation when labelling emotions vs counting people will be used to identify brain regions activated by emotion labelling. Within each of the regions involved in emotion labelling, representational similarity analysis will be used to compare each participant's pattern of neural activity in response to every video to the pattern of neural activity in response to every other video. Outside of the scanner, participants view the same set of emotionally evocative videos used in the emotion labeling task. Participants move a sliding bar to indicate how much they feel each of five emotion words while looking at the video**:** angry, disgusted, scared, sad, and upset. To test hypothesis 2, the rank correlation (Kendall's tau-a) between the representational dissimilarity matrices of the voxel-wise patterns within each neural region across the stimuli will be computed for each region in each subject and then correlated with the behavioral representational dissimilarity matrix. A significant positive correlation would suggest that neural activity in that region encoded subjective emotional appraisals. Finally, we will compute mean representational similarity for each region for each subject. To test hypothesis 3, we will examine the association between childhood violence exposure and representational similarity within each region. Results of this investigation will illuminate the neural mechanisms underlying how adolescents generalize across and differentiate between emotion categories as well as how early experiences may contribute to individual differences in these processes.

2-Q-129 - Examining the impact of early family adversity on neural mechanisms underlying emotion processing in first-time fathers

Genesis Flores [1], **Darby Saxbe** [1], **Sarah Stoycos** [1]

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Details

Previous research suggests that individuals with a history of family adversity exhibit atypical emotion recognition and neural activation in response to emotional face stimuli. In particular, family adversity exposure has been linked to faster and more accurate recognition of negatively-valenced and threat-related emotional faces, as well as altered activation in corticolimbic regions, including the amygdala and prefrontal cortices. These findings have significant implications for expectant and new parents whose abilities to perceive and appropriately respond to others' emotional cues play a critical role in sensitive and motivated caregiving. The present study will examine whether early family adversity exposure impacts fathers' postpartum neural responses to emotional facial expressions and explicit recognition of emotional faces in a sample of 35 first-time fathers. Fathers completed the Risky Families Questionnaire, a retrospective report of abuse, neglect, and conflict in the family environment that may have occurred prior to age 18, prenatally. Fathers returned at about 6 months postpartum and underwent a standardized implicit face emotion functional neuroimaging (fMRI) task and a forced-choice behavioral emotion recognition task. Based on prior research, we hypothesize that fathers reporting greater experiences of early family adversity will demonstrate faster and more accurate recognition of negatively-valenced emotional faces, accompanied by increased corticolimbic neural response. fMRI data will be preprocessed and analyzed according to the general linear model in FSL. Whole brain analyses and a priori hypothesized region of interest analyses on corticolimbic regions will be conducted to examine overall neural response to distress cues. Parameter estimates from activated regions will be converted into percent signal change and extracted using Featquery. Behavioral explicit emotion recognition task data will be analyzed using an unbiased hit rate (Hu; Wagner, 1993) and raw accuracy (H) analyses. We will examine the association between early family adversity, percent signal change, and explicit emotion recognition using bivariate correlations and multiple linear regression. â€‹â€‹To our knowledge, the proposed analyses will be the first to examine associations between early family adversity, emotional face recognition, and neural processing in first-time fathers. Findings are expected to broaden our current understanding of how early life experiences impact the transition to fatherhood and to potentially contribute to later development of prevention and interventions aimed at promoting healthy adjustment to fathering.

2-Q-130 - The impact of early life adversity on neural reward processing in early childhood

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Details

Background: Early life adversity (ELA), defined as childhood experiences that require significant adaptation, predicts adverse psychiatric outcomes across the lifespan such as increased symptom severity, chronicity, and risk for suicidality. Dysfunction in neural reward systems may represent a mechanistic pathway linking ELA to psychiatric illnesses. However, few studies have examined the impact of ELA on aberrant neural reactivity in early childhood prior to critical windows of risk for psychopathology onset.

Probing the critical period when the detrimental impact of ELA on neuroaffective reactivity may first emerge is essential to tailoring early preventive interventions for high-risk, ELA-exposed youth to alter risk sequelae for psychopathology. Previous studies of ELA and reward processing have focused primarily on adolescent and adult samples, limiting the generalizability of previous findings to young children.

Emerging research emphasizes differential impacts of ELA subconstructs, which can be grouped into experiences of deprivation (i.e., absence of expected environmental stimulation) and threat (i.e., threat to safety). Preliminary evidence suggests that deprivation is more closely related to reward systems dysfunction; however, prior research in this area has been limited by small sample sizes due to the cost-prohibitive nature of functional magnetic resonance imaging (fMRI), which also demonstrates low tolerability for young children.

Objective: The proposed study seeks to replicate and extend findings regarding relations between ELA and reward processing to an early childhood sample using reliable, developmentally-sensitive neurophysiological tools.

Method: Recruitment is currently ongoing to sample 120 risk-enhanced 5-6 year old children from inner-city Chicago. Half the sample has been specifically recruited for a maternal history of depression. Children complete a validated monetary reward task while electroencephalogram is recorded. Electrocortical response following gain and loss trials on the EEG reward task will be averaged 350-450 ms following gain and loss feedback. Mothers complete self-report questionnaires probing various ELA subconstructs (e.g., food insecurity, trauma exposure, socioeconomic status), and residential addresses are acquired for neighborhood geocoding of violence and deprivation exposure.

Analyses: ELA measures will be standardized and combined to create an index of ELA, which will be further divided into subconstructs of ELA, threat and deprivation. The RewP residual will index reward responsiveness, calculated by regressing mean activity during win trials onto loss trials. Linear regressions will be run with the ELA composite as the independent variable and reward response (RewP Residual) as the dependent variable. Separate models with be run to examine the two subconstructs of ELA, threat and deprivation, as independent variables, controlling for the other subconstruct. Child gender and maternal history of MDD will be added as covariates.

Hypotheses: Greater exposure to ELA will predict blunted RewP (Hyp 1a). Deprivation will significantly predict reduced RewP, controlling for threat (Hyp 1b).

As data collection and preprocessing is ongoing and nearly 60% of the proposed sample has been recruited, it is feasible to complete the proposed analyses utilizing the majority, if not all, of the sample prior to Flux 2023. Data collection is anticipated to be complete at the end of summer 2023, and pre-processing is ongoing. Analyses and interpretation will be completed in early fall of 2023 in preparation for Flux.

2-Q-131 - Neural Correlates of Emotion Reactivity and Regulation in Excitability and Irritability: Implications in ADHD

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Details

Emotion dysregulationâ€”defined as a reduced ability to modify one's emotional response to a provocative internal or external stimulus in a manner adaptive to meeting one's goalsâ€”is increasingly recognized as a core symptom of attention deficit hyperactivity disorder (ADHD). It interferes with an individual's quality of life, social interactions, and relationships. To date, research on emotion dysregulation in ADHD has largely been limited to irritability (negative affect), overlooking the potential role of excitability (positive affect), and the relationship between ADHD and activations in emotion related regions, such as the reward system and amygdala, has been mixed. Moreover, the distinction between the underlying neural correlates of excitability, irritability, and ADHD symptoms remains unexplored, although each could be a separable target for intervention. To address this knowledge gap, we aim to investigate the neural basis of excitability and irritability using validated fMRI and behavioral protocols during an emotion reactivity and regulation task in a population of 8- to 14-year-old children enriched for emotion dysregulation and ADHD (n=50) recruited and characterized as part of a larger NIMH-funded study, including a planned interim analysis of the first 20 participants. Our goal is to determine the relationship between irritability, excitability, and ADHD symptoms with behavioral and neural correlates of emotion regulation and generation, with particular focus on the positive affect (reward)-related regions of the brain. We hypothesize that: (i) Study participants will be able to appropriately regulate their emotional response to positive- and negative-valance images as measured both directly (subjective reporting) and indirectly (using response time as a proxy); (ii) During emotion generation, both excitability and irritability will correspond to activation in general emotion related regions of the brain (i.e., amygdala), but only excitability will predict increased activity in positive emotion (reward) regions (i.e., ventral striatum); and (iii) When regulating their emotional responses, greater excitability, irritability, and ADHD symptom burden will correspond to less effective emotion regulation as assessed by change in subjective report and lower activation in the emotional control regions of the brain (i.e., dorsolateral prefrontal cortex, inferior frontal gyrus, anterior insula). With regards to behavioral data, our task successfully evoked both positive and negative emotions, and participants demonstrated an ability to regulate the intensity of their emotional response to positively- and negatively- valanced images using the technique provided. Moreover, we found our measure of excitability, or dysregulation in positive affect, corresponded to both how intensely the participants experience the positive scenes and their change in emotion rating with regulation, which suggests excitability may be indexing children who have more intense positive emotional experiences. No such relationships were found for irritability with either positive or negatively emotional evocative stimuli. Neuroimaging analyses are ongoing to (i) assess the effect of excitability on positive affect (reward)-related regions; (ii) determine whether both excitability and irritability correspond to activation in general emotion regulation regions; and (iii) determine whether greater excitability, irritability, and ADHD symptom burden correspond to lower activation in emotional control regions. Improving our understanding of the neural basis of excitability and irritability may help clarify some of the disparate neuroimaging findings with regards to emotion processing in ADHD and provide potential biomarkers for emotion dysregulation, affording novel avenues for targeted interventions for children with ADHD and emotion dysregulation.

2-Q-132 - The impact of prenatal drug exposure on neural correlates subserving the processing of negative emotional stimuli

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Details

Introduction

Prenatal drug use is self-reported in ~10% of pregnant women in the US (England et al., 2020). The prevalence of prenatal drug exposure (PDE) and its serious ramifications highlight the urgency for understanding how PDE impacts long-term development of offspring. Although accumulating evidence suggests that PDE is linked to increased risks for adverse neurocognitive and socio-emotional outcomes in adolescence (Buckingham-Howes et al., 2013), particularly in the domains of emotional and behavioral regulation, the underlying neural mechanisms remain unclear. The current study aims to investigate whether PDE is linked to altered neural response to negative emotional stimuli in adolescents.

Methods

Participants

The data are drawn from a longitudinal study following a cohort of drug-using women and their infants, along with a community comparison (CC) group of caregiver-child dyads, to investigate the effects of PDE on adolescent development (Riggins et al., 2012). The PDE and CC groups were well-matched for socioeconomic status, race, and mother's age during first pregnancy. The current study sample includes 39 adolescents (N_{PDE} = 17, M_{age} = 18.22, 58.8% female; N_{CC} = 22, M_{age} = 17.11, 59.1% female).

Experimental Design

fMRI data were collected during an event-related emotion source memory paradigm task, consisting of an encoding and retrieval phase (Erk et al., 2005). The emotional picture stimuli consisted of 44 negative and 44 neutral pictures from the International Affective Picture System (IAPS; Lang et al., 1999). This study focuses on the encoding phase, which had two periods: rating the emotion of the pictures and binding a neutral target (i.e., colorful line drawings) to the picture. During each trial, a picture was first presented for 2.5s and participants rated its emotional valence (i.e., neutral = 1, negative = 2); the rating period was repeated if no-response was made the first time. Then, a neutral target was placed on top of the picture for 3s (for binding of the target item and picture). Fixation crosses were jittered for 1-5s between the rating and binding periods. Intertrial intervals were also jittered for 1~5s.

Image Acquisition

Neuroimaging data were collected on a 3.0T Trio scanner with a 12-channel head coil (Siemens AG, Erlangen, Germany). Structural imaging consisted of a whole-brain oblique axial T1-weighted scan

(MPRAGE; voxel size = 1.0 Ã— 1.0 Ã— 1.0 mm; TR = 1900 ms; TE = 3.51ms). Whole-brain functional images were acquired using a gradient-echo, echo-planar sequence (36 oblique interleaved slices; voxel size = 3.43 x 3.43 x 4 mm; TR = 2s; TE = 27ms).

Analytic Approach

fMRI data pre-preprocessing and subject-level analyses will be performed using AFNI (Analysis of Functional Neuro-Imaging; Cox, 1996). Pre-processing steps include skullstripping, coregistration of functional data to anatomical volumes and the MNI template, slice timing correction, smoothing, and motion correction. First-level analyses will employ a general linear model with the time course of negative and neutral pictures during the rating and binding periods as predictors. For adolescents who have repeated rating periods, the no-response periods will be entered as an additional regressor. Six nuisance regressors will be included to account for motion. Participants with more than 25% TRs censored will be excluded from subsequent group-level analyses. Region of interest (ROI) analyses comparing reactivity to negative versus neutral stimuli for the PDE and CC groups will be conducted using the left and right amygdala as seed regions in R. Exploratory whole-brain analysis will examine if the PDE and CC group exhibit differential neural responses to negative emotional stimuli. All models will include age and sex as covariates. We aim to finish data pre-processing and analysis by Flux 2023.

Poster Session 3

Saturday, September 9, 2023

A- Attention

3-A-1 - Neural Signature of Social Encoding

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Details

In any situation, infants are presented with more information than they can learn about at once. Cues such as object familiarity and social partner behavior can help infants prioritize what to attend to in order to learn efficiently. How infants use objects and social cues to guide initial learning, and how that initial learning influences future attention and expectations are key topics in the literature on cognitive development. Social cues such as joint attention cues have been shown to enhance learning, operationalized as infant object encoding. Recent work has shown that infants encode objects better (i.e. subsequently attend more to novel objects) not only following 1st party experiences of joint attention (JA) cues but also after observing JA cues between two other people (Thiele et al., 2021). We are investigating if enhanced learning in the context of JA is supported by the same or different neural mechanisms as learning that occurs in the absence of JA. Are specific regions of the prefrontal cortex more active during episodes of JA to an object (whether the infant is involved in the JA or merely observing it)? Are there regions in which activation is predictive of object encoding, and if so are they the same or different depending on JA context?

Results from an online behavioral pilot including 50 infants (M_{age}=10.1) replicated the finding that when an object is presented in the context of JA, infants *do* subsequently look longer to novel objects, compared to infants' novelty preference in trials without JA ($F(1) = 5.17$, $p = .02$). We are currently collecting behavioral and prefrontal cortex fNIRS data from fifty 9.0- to 12.0-month-old infants (N=30 collected). We plan to complete data collection by the time of the conference. We will examine the relationship between activation in the lateral prefrontal cortex (LPFC) during object encoding and infants' subsequent novelty preference, given that activation in the LPFC has been associated with successful encoding (e.g. Turk-Browne et al., 2009). To test if LPFC activation predicts infants' novelty preferences, we will model trial-by-trial novelty preferences as a function of mean trial activation during encoding in each hemisphere of LPFC (as well as MPFC as a control region), trial type (JA+ or JA-), and region x trial type interactions, as well as participant age and random effects. Main effects of LPFC activation on novelty preference in one or both hemispheres, in the absence of interactions with trial type, would suggest that similar neural mechanisms support encoding in contexts with and without JA. A region x trial type interaction would suggest, instead, that mechanisms may differ across these contexts.

3-A-2 - The development of joint attention during parent-infant book-reading: a dual head-mounted eye-tracking study

Julia Farrell [1], **Jamie Newland** [1], **Alexia Brown** [1], **Valeria Burgos-Villanueva** [1], **Andreas Keil** [1], **Lisa Scott** [1]

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Details

Joint attention (JA) is a crucial developmental milestone that emerges in the first year of life and is essential for both language and socio-emotional development (Mundy & Newell, 2007; Yu et al., 2019). However, the factors that support the development of JA across contexts are not well understood. The current study examined the development of JA during parent-infant naturalistic book-reading in 6- and 9-month-old infants and their caregivers. Dual eye-tracking (Positive Science, LLC) was used to measure parent and infant visual attention during a 5-minute book-reading task. The number and duration of instances of joint attention to the book, as well as parents' gestures and extratextual speech, were coded frame by frame using DataVyu. To date, data from 40 dyads have been collected and data from 12 dyads have been coded and pre-processed. All 40 dyads will be coded and analyzed for this presentation. Preliminary analyses of these 12 dyads suggest that JA to the book decreases with age, with 6-month parent-infant dyads exhibiting a longer duration of joint attention (M = 132305 ms, SD = 60519 ms) than 9-month dyads (M = 63498 ms, SD = 27918 ms), $t(10) = 2.529$, $p < 0.05$. Additionally, parents' increased use of gestures is negatively correlated with joint attention (r = -0.33), while extratextual speech had mixed effects on JA. Parents who spoke more often had more instances of JA with their infant ($r = 0.36$), but parents with a longer extratextual speech duration had less total JA with their infant ($r = -0.26$). These results provide preliminary insights into the nature of early JA during book-reading, highlighting the importance of context in understanding parent-infant interactions. Notably, patterns of JA vary according to an infant's age and are shaped by the multimodal behaviors that co-occur with JA, specifically parent gestures and extratextual speech. The present investigation aims to uncover the factors that support JA during shared book-reading between 6 and 9 months of age. These factors may be useful for future intervention or prevention programs aimed at fostering infant learning from parent-infant interactions.

B – Brain connectivity

3-B-3 - The lion sleeps tonight, but do you? The moderating effect of sleep on the link between functional connectivity and youth behavioral problems

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Details

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Insular-prefrontal cortex connectivity plays a crucial role in emotional regulation, and altered connectivity is associated with the development of psychopathology across the lifespan. Sleep is an essential bioregulatory mechanism during child development, and inadequate sleep has been linked to neural connectivity and youth behavioral problems. However, less is known about how sleep moderates the association between resting-state functional connectivity and adolescent behavioral problems. The biological sensitivity to context model suggests that individuals vary in their susceptibility to stressors,

such that individuals who are more susceptible will react more strongly to both negative and positive environments, which in turn can promote either risk or resilience to stress. Therefore, in this study we investigate sleep as a biological sensitivity context in the association between functional connectivity and behavioral problems in adolescents. We hypothesize that poor sleep will exacerbate the association between insular-prefrontal cortex connectivity and behavioral outcomes in adolescents, particularly internalizing and externalizing problems. Participants were recruited from rural Georgia (N = 145, mean age = 12.9, 52% female) and data were collected over 18 months. Sleep duration, sleep duration variability, sleep midpoint, and sleep midpoint variability were recorded using actigraphy watches at baseline. Resting-state functional connectivity between the anterior insula (AI) and medial frontal gyrus (MFG) was obtained using fMRI, and internalizing and externalizing problems were assessed using the CBCL at both baseline and follow-up. Demographic covariates including age, sex, race, and income were controlled in all analyses. Analyses were performed in Mplus 7.4. Structural equation modeling using maximum likelihood estimation was used in all modeling procedures. Significant interactions were found between all sleep areas and functional connectivity on internalizing and externalizing problems. Specifically, among those who had low sleep duration, adolescents who also had high AI-MFG connectivity showed significantly reduced externalizing problems compared to those with low connectivity ($\hat{I}^2$ = .54, p<.01). Similarly, among adolescents who had low AI-MFG connectivity, internalizing problems were greatly reduced compared to those with high connectivity when also paired with high sleep midpoint ($\hat{I}^2$ = .29, p<.05), high sleep midpoint variability ($\hat{I}^2$ = .44, p<.01), and high sleep duration variability ($\hat{I}^2$ = .88, p<.001). The interaction between functional connectivity and sleep duration and midpoint on behavioral outcomes was largely ipsilateral (left to left, right to right). In contrast, the interaction between functional connectivity and the variability of these constructs (sleep duration variability and midpoint variability) on internalizing problems were largely contralateral (left to right, right to left). Furthermore, functional connectivity between the left MFG to the right and left insula was shown to follow a biological sensitivity to context model. In poor sleep, behavioral problems are reduced in participants with low AI-MFG connectivity; conversely, in the context of adequate sleep, behavioral problems are reduced in individuals with high AI-MFG connectivity. Our results highlight sleep as a promising prevention and intervention target to enhance youth wellbeing.

3-B-4 - Relations between stress and obsessive-compulsive symptoms vary as a function of somatomotor-putamen resting state connectivity during adolescence

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Details

Obsessive-compulsive symptoms (OCS) are common during adolescence; however, most do not meet diagnostic criteria for obsessive-compulsive disorder (OCD). Despite this, OCS during adolescence is associated with comorbid psychopathologies and behavioral problems like depression and suicidal ideation. Two factors that may be associated with promoting or exacerbating OCS are stress and hyperactivity in motor and subcortical brain circuits. Studies have generally found that increased stress is associated with more OCS symptoms. Additionally, resting state fMRI studies have found that somatomotor-subcortical connectivity is elevated in OCD compared to healthy controls. Despite the theoretical and empirical overlap of these constructs, they are often studied independently, and no such studies exist in adolescent samples. Thus, the current study examined resting state connectivity

between the somatomotor network and the putamen, stress, and their interaction on changes in OCS from approximately 10 to 13 years of age. Participants were drawn from the ABCD study 4.0 release (*n* = 5170). This release had resting state fMRI data for two time points (Baseline and 2-year follow up), and measures of stress and OCS at three time points (Baseline, 1-year follow up, and 2-year follow up). Multilevel modeling was used to account for nesting in the data and to assess the trajectories of OCS in this age range. We found that stress moderated the association between somatomotor network-putamen connectivity and OCS ($\hat{I}^2$ = 0.47, *S.E.* = 0.14, *p* = 0.001). Participants with higher stress than their mean across the three time points and stronger connectivity between the somatomotor network and the putamen had the most OCS. This finding remained significant after controlling for their average stress-levels and whether they met the clinical threshold for OCD at any time point. This finding suggests that stress and hyperactivity within habit related circuitry may contribute to increased OCS during early adolescence. Future studies using ABCD study data should assess whether these trends continue throughout the adolescent period.

3-B-5 - Does maximising connectome-based identifiability improve connectome-based phenotype prediction in developing youths?

Jivesh Ramduny [1], **Clare Kelly** [1], **Robert Whelan** [1], **Tamara Vanderwal** [2], **Yihe Weng** [1]

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Details

Individual differences in functional connectivity (FC), which are unique and stable like a “fingerprint”, have been shown to predict individual differences in behaviour. In prior work, we identified pre/post-processing factors that improved connectome fingerprint-based identification and reduced the number of participants excluded from analyses due to excessive motion. Here, we build on this by assessing whether the same factors can boost the robustness of brain-behaviour relationships. We assess whether factors including (1) the dimensionality of parcellation schemes, (2) inclusion of cortical vs. subcortical regions, and (3) motion exclusion strategies improve the predictive power of connectome-based predictive modelling (CPM) for brain-behaviour relationships for age, psychopathology [CBCL], and intelligence [FSIQ].

Participants with structural and two resting-state MRI scans were obtained from the Healthy Brain Network (N=540; 6-21 years). Standard data preprocessing was performed with a 36-parameter model including the global signal. Participants with RMS framewise displacement (rmsFD) > 0.20 mm were excluded. For each participant, the fMRI data were parcelled to construct two 268x268 FC matrices.

Using functional connectome fingerprinting, we computed the similarity between each participant’s REST1 FC matrix and all REST2 FC matrices using Pearson’s R. Similarity scores were ranked, and fingerprint accuracy was computed by assigning a score of 1 if their REST2 FC matrix was ranked first and 0 otherwise. CPM was performed to predict linear associations between FC and the behavioural phenotypes. Age, sex, and rmsFD were covariates, and 95% of the significantly positively (POS) and negatively (NEG) correlated edges ($p < 0.01$) were selected across a 10-fold cross validation over 100 iterations.

To improve the baseline connectome-based fingerprinting for predicting individual differences in behaviour, we first used a frontoparietal network mask followed by finer cortical and whole-brain parcellation schemes. We then applied scrubbing to estimate the FC matrices of the participants based on their least motion-corrupted timepoints whose rmsFD < 0.20 mm. We performed bagging to bootstrap subsets of the participants' least contaminated timepoints with replacement over 500 iterations and compute their FC matrices. The CPM-based predictions were externally validated using a sample of typically developing controls from the Autism Brain Imaging Data Exchange [ABIDE] (N=435; 6-57 years).

The baseline HBN-derived fingerprint ID accuracy was 78%. Baseline CPM-derived brain-behaviour relationships were predictive of age (POS: $R = 0.61$, $p < 0.001$; NEG: $R = 0.58$, $p < 0.001$), CBCL (POS: $R = 0.16$, $p = 0.019$), and FSIQ (POS: $R = 0.16$, $p = 0.027$). The ID accuracies improved up to 87% when cortical and whole-brain parcellations were employed at higher resolutions (e.g., ~500 parcels). In contrast to previous work with adult populations, fingerprint identification decreased when the analyses were restricted to the frontoparietal networks, and when head motion strategies were applied. While the relationships between the observed and predicted phenotypes were maintained across parcellation schemes and motion mitigation strategies, scrubbing preserved the CPM-derived CBCL associations. Further, whole-brain parcellations and motion strategies maintained the CPM-derived FSIQ relationships. The CPM-based predictions were also generalisable in the ABIDE dataset.

While several of the factors we examined boosted the identifiability of individuals on the basis of their functional connectome fingerprints, the prediction of brain-behaviour relationships in this developmental population did not improve. This suggests that more unique connectome fingerprints do not necessarily translate to better prediction of brain-behaviour relationships. Future work will expand this examination to other models of brain-behaviour relationships.

3-B-6 - Youth ADHD and dysregulation as predictors of default- and frontoparietal network-amygdala connectivity: An ABCD study

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Details

Objective

Behaviorally, it is well-established that youth with ADHD experience poorer emotion regulation (ER) compared to peers (Graziano & Garcia, 2016; Shaw et al., 2014). Emerging work has examined associations between brain functional connectivity and ER among youth with ADHD (Posner et al., 2013, 2014). Functional connectivity between the amygdala and frontoparietal network (FPN; involving dorsolateral prefrontal cortex [dlPFC]) has been associated with attention and cognitive control (i.e., explicit ER), while amygdala-default mode network (DMN; involving ventromedial PFC [vmPFC]) connectivity has been associated with emotional reactivity (i.e., implicit ER; Etkin et al., 2015; Sylvester et al., 2020). Healthy youth develop strong, negative amygdala-PFC connectivity during the transition to adolescence (Gee et al., 2013), whereas youth with ADHD show weaker functional connectivity involving

the FPN and DMN (Tao et al., 2017). In one study, youth with low dysregulation exhibited greater amygdala-PFC connectivity during an ER task compared to those with high dysregulation (Bertocci et al., 2012). Given the still limited understanding of the neural circuits involved in ER among youth with ADHD, the current study aimed to examine youth ADHD diagnosis and dysregulation as predictors of resting-state functional connectivity (rs-fc) between the DMN and FPN and bilateral amygdalae.

Method

4,673 youth ages 9-10 years old with and without ADHD (915 with ADHD) completed the ABCD Study baseline visit with their caregiver. To account for potential family effects, only children and oldest sibling in the family were included in this study. Youth underwent a magnetic resonance imaging (MRI) scan during which rs-fc data were acquired. For the current study, correlations between the 13 Gordon parcellation cortical networks (e.g., DMN and FPN) and bilateral amygdalae were used in analyses (Gordon et al., 2016). A caregiver completed the child behavior checklist (CBCL; Achenbach & Rescorla, 2001). Anxious/Depressed, Aggressive Behavior, and Attention Problems subscale T scores were summed as the CBCL dysregulation profile (CBCL-DP; Kim et al., 2012).

Results

Youth with ADHD had significantly weaker, negative DMN-right amygdala (RA; M=-.017, SD=.089) and stronger, positive FPN-RA (M=.0534, SD=.11) rs-fc compared to youth without ADHD (M=-.021, SD=.083; M=.0530, SD=.10) when accounting for child age, sex, race and ethnicity, pubertal status, anxiety, conduct disorder, oppositional defiant disorder, and site (F(1,4556)=4.65, p=.03; F(1,4563)=4.97, p=.03). Youth with ADHD did not differ from their non-ADHD peers with respect to DMN- or FPN-left amygdala (LA) rs-fc (all F<.92, all p>.34). Across all youth, dysregulation was not significantly associated with DMN- or FPN-amygdalae rs-fc (all p>.05). However, youth dysregulation predicted FPN-RA rs-fc only in the context of moderation by ADHD diagnosis (B=-.41, p=.02), whereby this association was positive among typically developing youth and negative among youth with ADHD.

Conclusion

Youth with ADHD demonstrated significantly weaker, negative DMN-RA rs-fc and stronger, positive FPN-RA rs-fc compared to peers, consistent with prior work implicating altered DMN and FPN connectivity in this population. Although youth dysregulation was not directly associated with FPN-amygdalae rs-fc, ADHD diagnosis moderated this association, such that FPN-RA connectivity increased with higher dysregulation among youth without ADHD, whereas FPN-RA rs-fc decreased with higher dysregulation among youth with ADHD. Therefore, weaker FPN-RA rs-fc may be a marker of high dysregulation (i.e., low explicit ER) and reveal potential neural mechanisms underlying ER among youth with ADHD. Future work should examine these associations longitudinally and assess connectivity in specific brain regions (e.g., vmPFC vs. DMN).

3-B-7 - Functional Connectivity Changes of Default Network Subcomponents following the COVID-19 Pandemic Stressor Associated with Depressive Symptoms in Youth

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Details

Neurodevelopmental processes including brain network connectivity mature during adolescence, at least partially according to environmental demands, and may alter risk trajectories for internalizing pathologies. The onset of the COVID-19 pandemic and widespread shutdowns represented a substantial stressor that could impact such brain network maturation and influence emerging internalizing psychopathology. In particular, neural systems supporting affective self-generated and self-referential cognition like the default network (DN), thought to be highly-related to repetitive negative thought and additional risk mechanisms for internalizing psychopathology, may demonstrate significant changes in response to such a stressor. Of three subcomponents of the DN, the core component consisting of anterior medial prefrontal and posterior cingulate cortex has demonstrated significant involvement in the ruminative process over and above the medial temporal DN subcomponent, consisting of ventral medial prefrontal cortex, posterior inferior parietal lobule, retrosplenial cortex, parahippocampal cortex and hippocampal formation, which is more involved in episodic judgments and simulations (Zhou et al., 2020). The current study examines functional connectivity (FC) changes with these two DN subcomponents before and during a major stressor, hypothesizing specifically increased widespread core DN connectivity concurrently associated with depressive symptom change using the Mood and Feelings Questionnaire - Short (MFQ-S: Î”M=1.22, SD=5.60, range [-15, 23]; Angold et al., 1995).

We use the Development of Anxiety in Youth Study (DAYS; GalvÃ¡n & Peris, 2020) with 65 youth (38M/27F; age: pre- M=11.75, SD=1.53; peri- M=13.85, SD=1.40) with an 8-minute resting-state fMRI prior to COVID-19 shutdowns (pre: Feb 2019-March 2020) and once in-person procedures resumed (peri: Jan 2021- April 2022). Youth scans were approximately 2 years apart (SD=140 days), thus age was included in models to account for age-related changes over time. Using DN seeds from prior work (Andrews-Hanna et al., 2010), analyses used seed-to-whole-brain FC from core (2 bilateral) and medial temporal (5 bilateral) subcomponents of the DN reflecting self-referential processing and episodic judgments, respectively, as primary dependent variables in two mixed effects analyses implemented with 3dLMEr in AFNI examining changes in FC from pre- to peri-pandemic associated with both between- and within-subjects depressive symptoms while controlling for side, seed, age, and gender.

Thresholding at FWE p=.005 (k>32, p<.001) based on 3dClustSim results, core DN demonstrated significant FC changes from pre- to peri-pandemic with primarily increasing connectivity with midline structures associated with between-subjects greater depressive symptoms. Within-subjects depressive symptom fluctuations over time were not significant in core DN. However, medial temporal DN showed significant FC changes over time associated with both between and within-subjects differences in depressive symptoms, primarily in the left hemisphere. Between-subjects medial temporal DN FC changes associated with depressive symptoms included bilateral superior temporal, left inferior frontal triangularis, left cuneus, left inferior parietal lobule, and left middle frontal gyri. Within-subject increases in depressive symptoms were associated with medial temporal DN FC changes with primarily left inferior parietal lobule.

These findings suggest increased core DN, often associated with repetitive negative thought, is primarily a between-subjects effect; changes in FC during a stressor with the medial temporal DN may hold better promise for within-person prediction of depressive symptom changes in youth. Longitudinal studies with additional timepoints following such stressors are needed for more causal interpretations of the impact of significant stressors on mood regulation and brain network connectivity.

3-B-8 - The development of rich-club organization in neurodevelopmental disorders: an MEG study

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Details

Background: Rich-club organization is a topographical property of functional brain networks that is characterized by the tendency for a set of hub regions to be more densely connected to one another than to other regions. This type of organization is essential for the global integration of information across the brain to support cognition, and disruptions in its development have been related to neurodevelopmental disorders (NDDs) such as attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and obsessive-compulsive disorder (OCD); however, existing studies have only used functional magnetic resonance imaging. With superior temporal resolution, magnetoencephalography (MEG) can provide important information about the neural dynamics underlying rich-club organization in NDDs.

Objective: This study is the first to use MEG to investigate the development of rich-club organization in a large sample of children and adolescents with ADHD, ASD, OCD, or who are typically developing (TD).

Methods: Resting-state MEG data were obtained in 636 children and adolescents (4-19 years of age) with ADHD (*N*=125), ASD (*N*=251), OCD (*N*=38), or who were typically developing (*N*=260). Functional connectivity networks were constructed for each of the canonical frequency bands (theta: 4â€“7Hz, alpha: 8â€“14Hz, beta: 15â€“29Hz, low gamma: 30â€“55Hz, and high gamma: 65â€“80Hz), and the degree of rich-club organization in each network was quantified. Multiple linear regression models were used to investigate the effects of diagnosis, age, and their interactions on rich-club organization in each frequency band, separately for males and females. Significance was held at $p<0.05$, with Tukey post-hoc comparisons between the diagnostic groups for simple effects and simple slopes.

Results: In the males, rich-club organization increased with age in the lower frequency bands (theta: $p=.002$, $\hat{I}^{2}=.02$; alpha: $p<.001$, $\hat{I}^{2}=.15$; beta: $p<.001$, $\hat{I}^{2}=.07$) across all participants; no diagnostic differences were observed. In the females, this positive association was also observed across all participants in beta ($p=.002$, $\hat{I}^{2}=.05$); however, in theta, an age-by-diagnosis interaction was significant ($p=.006$, $\hat{I}^{2}=.04$), with only the TD females showing increasing organization with age.

In the higher frequency bands (low and high gamma), males showed no diagnostic or age-related effects in rich-club organization. In the females, a main effect of diagnosis was observed in low gamma ($p=.027$, $\hat{I}^{2}=.05$), with children and adolescents with ASD having increased rich-club organization compared to the TD females. Finally, an age-by-diagnosis interaction was significant in high gamma ($p=.049$, $\hat{I}^{2}=.04$), with only the TD females showing decreasing organization with age.

Conclusions: Over childhood and adolescence, diagnostic differences in rich-club organization amongst those with and without NDDs are exclusive to females. Future work will investigate the association between rich-club organization and behavioural characteristics.

3-B-9 - Structural connectome gradients and cognition relationships in early childhood

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Details

Objective

One of the fundamental goals in neuroscience study is to establish the association between the individual differences in brain and cognition/behavior. Although it is widely known that the structural connectome (SC) computed from diffusion MRI is related to cognition/behavior in adults and adolescents, little is known about their relationships in early childhood.

A continuous spatial representation across the cortical surface, known as connectome gradients, allows the investigation of topographical organization of the cortex and their association with cognition. A substantial body of research has shown that the functional connectome gradient runs from primary sensory to higher-order transmodal regions. Unlike the extensive work characterizing the functional connectome gradients and their association with cognition, the associations between structural gradients and cognition remain largely unexplored.

We hypothesize that SC gradients are one of the salient features to predict individual cognition in early childhood. We aim to predict the individual's cognitive scores from their structural gradients at age 1 via deep learning models.

Methods

We computed SC gradients using the BrainSpace toolbox (https://brainspace.readthedocs.io/en/latest/) after harmonizing SC using ComBat with gestational age at birth, sex, and the number of remaining diffusion-weighted volumes after quality control as covariates that need to be preserved. The SC matrix was converted to an affinity matrix using a normalized angle kernel, and then the diffusion map embedding, a non-linear dimensionality reduction technique, was applied. Since each subject's gradients represent relative distances between nodes, we applied Procrustes rotation approaches to align the individual gradient axis to the group-averaged gradient template.

For the individual-level prediction model, we applied multi-layer perceptron (MLP) on the input structural connectome gradient to predict each individual's cognitive scores. A new loss function was proposed to make sure that the subjects having similar cognitive scores have higher agreement in their prediction. This regularization helps to preserve inter-subject variability, avoiding the case that the prediction converges to the group-averaged value.

We used the dataset from UNC Early Brain Development Study, collecting longitudinal neuroimages as well as cognitive/behavioral assessments. Cognitive measures were assessed using 5th Edition of the Stanford-Binet Intelligence Scales.

Results

The SC gradients showed spatial patterns dissimilar from the FC gradients in literature. Our analysis shows that the principal SC gradient was anchored at one end by visual cortex and at the other end by somatosensory/motor regions, exhibiting sensorimotor-to-visual pattern. The first gradient component that was computed as the largest normalized eigenvalue explained 16% variance at age 1. The second gradient accounting for 14% variance, runs from anterior to posterior.

We performed 10-fold cross-validation (CV) for all available data. In order to assess the sensitivity with respect to the different training/test split, we repeated the 10-fold CV for 10 times with different random seeds. The average mean absolute error (MAE) and Pearson's correlation coefficients between the ground-truth and the predicted scores are summarized in Table 1.

Table 1. Quantitative results in terms of mean Pearson's correlation coefficients and mean absolute error predicting IQ from SC at 1 year of age.

Cognitive score	Mean Pearson's correlation (SD)	MAE (SD)
IQ at age 4 (N=72)	0.16 (0.06)	10.64 (0.43)
IQ at age 6 (N=80)	0.53 (0.04)	8.76 (0.33)
IQ at age 8 (N=73)	0.16 (0.06)	10.88 (0.58)
IQ at age 10 (N=51)	0.44 (0.06)	9.49 (0.61)

Conclusion

In this study, we identified structural gradients at ages 1, 2, 4, and 6 years, where principal gradient primarily distinguishes visual and sensorimotor regions. We developed a deep-learning prediction model and demonstrated that principal structural gradients at age 1 year can predict the individual cognitive scores at later ages.

3-B-10 - Functional connectivity of the speech network in relation to word reading skill development among school-age children

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Details

Learning to read accurately and efficiently relies on proficiency in earlier-developing communication skills, which include foundational abilities in processing and producing speech. Indeed, literacy outcomes have been strongly linked with speech subskills, such as the identification and manipulation of individual speech sounds; yet, it remains unclear how functional brain networks for speech may give rise to subsequent reading skills. Given that speech skills can be addressed prior to, or along with, formal reading instruction of particular importance for children with family histories of reading difficulty it is crucial to work towards a more comprehensive model of speech and its neural architecture, in relation to reading outcomes. This analysis leverages the large sample size and longitudinal data from the Adolescent Brain and Cognitive Development (ABCD) Study to investigate the relationship between functionally-defined cortical networks for speech (Tourville et al., 2019) and reading skill development. We will use the regions of interest (ROIs) from the parcellated speech network to conduct an ROI-to-ROI analysis examining the intrinsic functional connectivity (iFC) of the speech network at rest, and continuously model iFC in relation to behavioral performance on a word-reading task. We will report the relationship between speech network connectivity and word-reading performance during the baseline time point (age 9-10 years) and during the first two-year follow-up (age 11-12 years). We hypothesize that greater iFC within the speech network will be positively associated with reading performance at the first time point as well as with subsequent reading gains over the two-year longitudinal time frame. Findings from this study will contribute to our understanding of the role of speech and its supportive neural mechanisms in reading development.

3-B-11 - A longitudinal study of structural connectome uniqueness and its association with mental health in adolescence

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Details

Objective: This temporally rich, longitudinal study of early adolescents will examine structural connectome maturation by measuring its uniqueness in adolescents enrolled in the Longitudinal Adolescent Brain Study (LABS), who underwent brain scans longitudinally from 12 years of age every four months. LABS in an ongoing prospective study that has been collecting data from the same participants since 2018 and includes 146 unique individuals. Recently, in a LABS dataset of *N*=63, our team (Shan et al., 2022) demonstrated that functional connectome uniqueness (â€˜brain fingerprinting') is associated with subsequent psychological distress, suggesting that a brain signature may predict emerging mental health outcomes. The study presented here will build on these findings, as it has been noted that there are benefits to examining both structural and functional connectomes in understanding the relationships between neurobiology and behaviour in adolescence (Park et al., 2022).
Methods: LABS participants undertake T1-weighted magnetization prepared rapid acquisition gradient echo sequence (MPRAGE) and diffusion tensor imaging (DTI) scans, and complete self-reported wellbeing (COMPAS-W) and psychological distress (K10) scales every 4 months. Structural brain connectome techniques developed by Yeh et al. (2016), will be applied to existing MRI data from *N*=118 LABS participants (with a minimum of 2 and maximum of 13 scans, longitudinally). This technique has been shown to characterise white matter connectivity at the voxel level, with high accuracy in identifying individuals over time, as well as the ability to examine neuroplasticity (Yeh et al., 2016). The results from this analysis will be combined with self-reported psychological distress and wellbeing to investigate potential links in terms of predicative capacity - between this measure of neurobiology and mental health outcomes in early adolescence. **Results:** These findings will provide an indication of whether a unique whole structural connectome exists at 12 years and remains unique across subsequent (i.e., 4 to 52) months. We will examine whether an individual's structural connectome uniqueness indices are associated with self-reported K10 and COMPAS-W scores longitudinally.
Conclusion: This project will utilise a novel neuroimaging longitudinal design to examine possible links between neurobiological markers of structural connectivity and subclinical measures of mental health and wellbeing in early adolescence to determine the predictive capacity of â€˜structural brain fingerprinting'.

C – Brain function

3-C-12 - Neurological perturbations and language impairments in very preterm infants

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Details

Background: Globally, around 15 million newborns are born preterm (< 37 weeks of gestation) every year. Due to recent medical advances in neonatology, the survival rates for preterm newborns have risen threefold. The significant increase in survival rates has also made preterm birth the number one cause of short-term and long-term neurodevelopmental impairment in children, including language deficits and disorders. Prior approaches aiming to understand the mechanisms that underlie the variability in the language development of preterm infants have been met with limited success, suggesting the need for a novel set of predictors. Neuropathological biomarkers collected in the NICU have the potential to predict later delays. However, neuromonitoring data is not available for all infants, and its relations to longer-term outcomes remain unknown. Thus, the proposed study aims to provide a multi-disciplinary approach by examining noninvasive monitoring and imaging techniques that could

potentially become a vital part of neonatal neurocritical care to examine risk factors for adverse language outcomes.

Aims: As part of this proposed study, we aim to 1) determine the extent to which near-infrared spectroscopy (NIRS), amplitude-integrated electroencephalogram (aEEG), and functional NIRS (fNIRS) are concordant in detecting neurological perturbations and 2) examine the association between the functional neuroarchitecture of the language system and language skills in very preterm infants (â‰¤32 weeks of gestation).

Methods: The cohort for this study will include very preterm infants that were delivered at or before 32 weeks gestational age and received neonatal care. NIRS, aEEG, and fNIRS will be measured at 36 weeks post-menstrual age during the infant's NICU hospitalization. Concurrent NIRS recording will be leveraged to examine average cerebral regional oxygen saturation (rSO2) and cerebral fractional tissue oxygenation extraction (FTOE). Cerebral maturation will be assessed using the Burdjalov scoring system on aEEG recordings. Resting-state functional connectivity of the language network will be assessed using functional near-infrared spectroscopy (fNIRS). Language abilities will be measured via a standardized, clinician-administered assessment when the infant is 9 months corrected age.

Anticipated Results: Our working hypotheses are that 1) delayed cerebral maturation with normal cerebral oxygenation will be associated with abnormal functional architecture of the language system at 36 weeks post-menstrual age and 2) higher levels of atypicality in the functional architecture of the language system at 36 weeks post-menstrual age will be associated with poorer language abilities.

What is Complete: N/A

What is in Progress: Currently, we are in the process of finishing submission to the local Institutional Review Board.

What will be completed by Flux: By September, we will have orientated NICU staff to the noninvasive imaging methods used as part of this study and have completed pilot data on 5 to 10 families.

What is planned: After September, we plan to collect data on 30 very preterm infants that were delivered at or before 32 weeks gestational age and received neonatal care at the University of Iowa Stead Family Children's Hospital.

Conclusion: Improved prediction of risk for later language delays based on early neuromonitoring biomarkers at critical timepoints may lead to precision-focused preventative neurological care of very preterm infants. Unveiling the etiological mechanisms that influence language development in preterm-born children may pave the way for novel opportunities for prevention and intervention efforts to benefit later development.

3-C-14 - Data-driven identification of neurobiological phenotypes during threat learning in youth exposed to childhood trauma and associations with psychopathology

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Details

Objective: Childhood trauma (CT) alters patterns of neural activation and connectivity during threat conditioning in ways that contribute to psychopathology. Multimodal measures of brain function (e.g., activation, connectivity) offer complementary information about the neural basis of threat learning, and are typically analyzed separately. However, aspects of environmental experience and psychopathology may be more related to complex combinations of neural activation and connectivity profiles than single indicators. Additionally, group-level analytical approaches considering neural metrics separately fail to capture considerable individual variability within groups. Unsupervised machine learning techniques enable the simultaneous analysis of measures of interest, e.g., neural activation and connectivity, while addressing meaningful variability by identifying latent structures of similarity across all participants. This study leverages a data-driven approach to characterize differing profiles of neural functioning and describe the associations of these profiles with CT and psychopathology.

Methods: 147 youth (aged 8-16 years) with and without exposure to CT underwent a differential threat conditioning procedure during an fMRI scan. Dynamic patterns of learning were described by the habituation rate of activation of regions-of-interest to CS+>CS- over the blocks of the task, as previously. Functional connectivity was assessed with generalized psychophysiological interaction analyses. Right amygdala habituation rate (AHR) and right amygdala-hippocampus connectivity (AHC) were the selected neural measures for the present analysis, as both previously exhibited differences as a function of CT and were associated with psychopathology in separate analyses. A k-means clustering analysis was performed over AHR and AHC. A chi-squared test examined the distribution of CT-exposed youth over the clusters, and multiple regression was used to examine associations with psychopathology.

Results: Various fit statistics converged upon 3 as the optimal number of clusters. All 3 clusters displayed statistically unique mean values of AHR and AHC. Cluster 1 ('Reactive Profile') comprised those with increasing reactivity and medium connectivity levels; cluster 2 ('Extremes Profile') comprised those with the most habituation and least connectivity; and cluster 3 ('Adaptive Profile') comprised those with medium habituation and the greatest connectivity. CT-exposed youth were overrepresented in the Extremes Profile, and very overrepresented in the Reactive Profile. Cluster membership predicted psychopathology, such that the Extremes and Reactive Profiles were associated with greater levels of depression, panic, generalized anxiety, externalizing, and PTSD symptoms than the Adaptive Profile, and did not differ between themselves.

Conclusions: Neurobiological phenotypes during threat learning may be identified by allowing data-driven analyses to cluster participants with similar profiles of neural activation and connectivity. Importantly, CT was significantly associated with two differing phenotypes, highlighting individual variability following environmental exposure to threat. Both CT-related phenotypes were associated with transdiagnostic psychopathology, suggesting multiple neurobiological pathways to psychopathology. Some CT-exposed youth were clustered in the Adaptive Profile, suggesting a potential pathway to resilience. Differences in psychopathology were not identified between the CT-associated profiles in the present analysis. However, data visualizations (e.g., of PTSD symptoms) suggest that with even more highly powered studies, further clinically-relevant differentiation may be detected. Future work should move towards simultaneously analyzing multiple modalities of neural data in large samples to further elucidate the complex interplay of neural systems and how such patterns relate to environmental experience and psychopathology.

3-C-15 - Mother-child Relationship Quality and Conflict throughout Adolescence Predicts Neural Response to Peer Influence in Young Adulthood

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Details

Adolescence is a period of heightened sensitivity to social influence, particularly from peers. This second decade of life has been characterized by a shift in which the adolescent brain becomes increasingly sensitive to input from peers relative to parents (Nelson, Jarcho, & Guyer, 2016; Blakemore, 2008). However, parents (particularly mothers) still remain a primary agent of socialization, exerting impacts on behavior and neurobiological development. Prior work has shown that adolescents vary in neural susceptibility to peer influences (Schriber & Guyer, 2016), with aspects of the maternal-adolescent relationship implicated as a potential source of individual differences (Chan & Chan, 2011; Telzer et al., 2015). Two salient aspects of the maternal-adolescent relationship are self-reported levels of conflict, and perception of the quality of the relationship (Branje, 2018). Yet, little is known about the underlying neural correlates that may relate to these sources of social influence. The present study tested the effects of maternal-adolescent relationship conflict and quality throughout adolescence on young adults' neural response to peer influence, derived from others' preferences. Participants were 43 young adults (22 females, M_{age} = 19.2 *SD* = 0.54) recruited from a 15-year longitudinal study of Mexican-origin youth. Using a task adapted from Mason et al. (2009), participants first viewed a series of 20 abstract symbols that they were told 200 similarly-aged peers rated as being 'popularâ€ or 'unpopular.â€ Then, while undergoing fMRI, young adults completed two runs of 90 trials in which they viewed multiple presentations of the 20 previously socially-tagged symbols (instantiated to be either popular or unpopular) as well as 10 novel symbols (no prior social information), one symbol at a time. Self-reported adolescent-maternal conflict and relationship quality were assessed from ages 10-16 using the Parent-Adolescent Conflict scale (Jensen-Campbell & Graziano, 1996) and Relationship Quality with Mother Scale (Melby & Conger, 2001). Mean scores across these ages were used in analyses. Results indicated that higher self-reported adolescent-maternal conflict measured throughout adolescence (ages 10-16) was associated with greater neural activity in the left insula (t = 3.81, p < .05) and right ACC (t = 2.98, p < .05) when young adults viewed socially tagged vs. novel symbols. Higher self-reported adolescent-maternal conflict was also associated with greater activation of the right caudate (t = 2.44, p < .05) when young adults viewed popular vs. unpopular symbols. Regarding adolescent-maternal relationship quality, results indicated higher relationship quality was associated with less activation of salience (bilateral ACC, t =-4.05, p < .05) and reward (caudate, t =-4.47, p < .05) region response to socially tagged vs. novel symbols. These results suggest that aspects of the adolescent-maternal relationship (i.e., conflict and self-reported quality) are related to neural sensitivity to peer influence in brain regions that code for salience detection and reward processing. Specifically, greater reported adolescent-maternal conflict may sensitize the young adult brain to peer influence, whereas greater relationship quality may buffer this sensitivity. This has potential implications for family-based interventions designed to mitigate risks associated with heightened sensitivity to peer influences (e.g., risk-taking behaviors).

3-C-17 - Characterizing the effect of hearing loss on auditory entrainment in children

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Details

Objective: Even with early intervention, congenital hearing loss leads to variability in the integrity of auditory input that is transmitted to the primary auditory cortex. This is true in both children who are hard-of-hearing (CHH, i.e., children with mild-to-severe hearing loss) as well as those with profound hearing loss. CHH have also been shown to have academic and language difficulties through childhood, though an understanding of the exact mechanism underlying these difficulties is incomplete. More generally, it is unclear how the decreased fidelity of auditory input impacts central auditory processing in the brain. Previous research has shown that 40 Hz auditory stimulation leads to strong neural entrainment at the same frequency in the primary auditory cortices. Moreover, alterations in auditory entrainment have been identified in a number of clinical populations, supporting the notion that the integrity of this response has implications for upstream cognitive and affective processes. The objective of this study was to characterize the neural dynamics underlying auditory entrainment in children who are hard of hearing loss (CHH) relative to children with normal hearing (CNH) and explore any interactions with cognitive ability or behavior.
Methods: A total of 39 participants aged 7-15, (14 females), including 16 CHH and 23 CNH, received passive stimulation of a 1kHz click train presented at 40 Hz bilaterally during magnetoencephalography (MEG). Outside the scanner, participants also completed a number of neuropsychological tests, including the Wechsler Abbreviated Scale of Intelligence (WASI-II). Stimulus-induced entrainment responses were imaged using sLORETA, and response power was extracted from peak vertices in the left and right primary auditory cortices. The impact of hearing status, hemisphere, and time (i.e., slope of response throughout the stimulation) were then computed using a linear mixed-effects model. Finally, the relationship between auditory entrainment slopes and behavior were assessed.
Results: Linear mixed effects modelling revealed significant main effects of hemisphere (estimate(standard error) = .1306(.0393), $p < .001$) and time (-.0099(0.0026), $p < .001$), significant group*time (.0069(.0033), $p < .05$), group*hemisphere (.1280(.0512), $p < .05$), and time*hemisphere (-.0072(.0036), $p < .05$) interactions, as well as a significant hemisphere*time*group interaction (.0229(.0047), $p < .001$). Follow-up testing of the interactions showed that CHH had more negative entrainment slopes than CNH in the right hemisphere, while the effect was reversed in the left hemisphere. We also found a negative correlation between right hemisphere (RH) entrainment slopes and the full-scale IQ on the WASI-II (FSIQ-4) in CHH, suggesting that reduced entrainment was related to poorer performance $r(15) = -.640$, $p = .008$; this relationship was not found in CNH. The difference in these correlations between groups was significant, Fisher's $z = 3.00$, $p = .003$).
Conclusions: In this study, we found significant alterations in 40 Hz auditory entrainment dynamics in CHH relative to CNH, and that entrainment was uniquely correlated with cognitive outcomes in CHH. While preliminary, these data suggest that the integrity of the auditory cortical entrainment response is an important buffer against the reduced integrity of auditory input experienced by CHH. Future work should seek to identify the mechanisms that underlie the relationship between primary auditory dynamics and higher-order cognition, especially in the context of individuals with hearing loss.

3-C-18 - The role of parent-child interactions around number play in children's numerical processing skills

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Details

Background and Aims: Current literature suggest that math achievement, a skill deemed crucial to formal schooling, predicts children's academic achievement, over and above cognitive skills such as literacy. Many studies have highlighted variability in early math achievement to be influenced by parent-child numerical activities in a chil's home math environment (HME). Other studies have focused on the critical role of symbolic (i.e., comparing Arabic numerals) and nonsymbolic (i.e., comparing arrays of dots) numerical processing skills during early schooling. However, there is significant variability in children's numerical processing skills prior to formal schooling, and little is known regarding how parent-child interactions around numbers play a role in the neurocognitive basis of children's numerical processing skills prior to formal schooling. We aim to bridge these two bodies of work together, by investigating multiple aspects of children's numerical processing as a function of parent-child interactions around number play and parental talk about numbers. Stated differently, our objective in the current study is to investigate the neurocognitive patterns underlying children's numerical processing as a function of parent-child numeracy interactions.

Methods: As part of the study, parents are administered questionnaires assessing a range of parent-child numeracy interactions, and parents and children engage in a semi-structured play task aimed to elicit number talk. Lastly, children complete two numerical measures: symbolic and nonsymbolic numerical processing, during which we measure the hemodynamic response linked to neural activity via functional near-infrared spectroscopy (fNIRS). We plan to run a sequence of multiple linear regression models using the *lm* function in the *stats* package in R, to examine how parent-child numeracy interactions relate to oxygenated hemoglobin (HbO) concentration changes in our brain regions of interest (right frontal, left frontal, right parietal, left parietal). We will include the following covariates: child age at testing, parent education, gestational age, and schooling (kindergarten vs. not).

Anticipated Results: Our working hypothesis is that higher exposure to parent-child numeracy interactions will predict increased left parietal activation and lower frontal activation.

What is Complete: N/A

What is in Progress: Currently, we are in the process of data collection and pre-processing the fNIRS data.

What will be completed by Flux: By September, we will have completed data collection on 40 participants.

What is planned: After September, we plan to finalize data analyses and begin writing the manuscript for publication.

Conclusion: Overall, we hope our findings provide the groundwork for further studies that could break down the sources of variability in the developmental course of children's mathematical abilities. Future directions could also include further investigation into potential interventional programs to improve the numerical processing skills of children preparing to enter formal schooling.

D – Brain structure

3-D-19 - Sleep onset latency is associated with smaller hippocampal volume in the Adolescent Brain Cognitive Development (ABCD)SM Study

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Details

Objective: Sleep behavior and physiology are vital to emotional and physical health. Studies indicate sleep not only supports daily neuronal maintenance but may also support brain maturation, suggesting sleep may be particularly important during periods of significant neurodevelopment. Adolescence is one such developmental period with prior research indicating sleep characteristics, including sleep duration (i.e., total time asleep) and sleep onset latency (SOL [i.e., the time taken for an individual to fall asleep]) are associated with emotional and cognitive function (Galvan, 2020). Mounting evidence suggests alterations in neurodevelopment may underlie this relationship. Specifically, previous research has shown reduced hippocampal volume in adolescent rodents following sleep deprivation as well as in children with sleep apnea (Novati et al., 2011; Lee et al., 2023). Given the importance of the hippocampus in cognitive and emotional processes, the current study sought to examine associations between sleep duration and SOL and hippocampal volume in early adolescence.

Methods: Using the Adolescent Brain Cognitive Development[SM] Study (ABCD; data release 4.0 [Auchter et al., 2018; Feldstein-Ewing et al., 2018; Garavan et al., 2018]) database, we examined associations between average sleep duration and SOL and total hippocampal volume at year 2 (ages 11-12). Sleep duration and SOL were recorded over the course of one week using Fitbit Charge 4 devices. Only participants with complete Fitbit data (i.e., data recorded across all 7 days) as well as structural data passing quality control measures were used in the final analyses (n=4,736). Statistical analyses were conducted using linear mixed effects (LME) modeling in R. Covariates included age, sex assigned at birth, race, ethnicity, and hippocampal volume at baseline. Random effect of MRI scanner was included as well.

Results: Results of the analyses showed SOL was negatively associated with total hippocampal volume ($\hat{I}^2$=-0.01, t=-2.19, p<.05). Sleep duration, however, was not associated with total hippocampal volume (t=0.974, p=0.33).

Conclusion: During adolescence, sleep characteristics change as a result of both biological and environmental factors. While adolescents need an additional 60-90 minutes of sleep each day compared to at age 10, research suggests adolescents typically lose an average of 90 minutes of sleep per night throughout adolescence (Crowley et al., 2014), resulting in an overall deficit in sleep. Some of this loss in sleep can be attributed to increased SOL. Notably, the current study found SOL, but not sleep duration, was associated with hippocampal volume, suggesting SOL and factors related to SOL may influence neurodevelopment in other ways outside of limiting sleep duration. Given the paucity of research on SOL and adolescent brain development, additional research is warranted to better understand how changes in sleep during adolescence may influence neurodevelopment over this important developmental period.

3-D-20 - The Genetic and Environmental Factors Influencing Cortical and Subcortical Structure in Youth Exposed to Neighborhood Disadvantage

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Details

Though researchers have examined the relative contributions of genetic versus environmental influences on brain volumes in youth, fewer studies have examined multiple smaller regions of interest or structural measures other than volume, including surface area and thickness, with some exceptions (Schmitt et al., 2014, 2019, Strike et al., 2018). Also, existing studies have focused on relatively advantaged youth, leading to concerns about generalizability. Given research showing that disadvantage may modulate the heritability of 'highly heritableâ€ outcomes (e.g., IQ; Fischbein, 1980; Tucker-Drob & Bates, 2016), studies are needed that examine the heritability of brain structure in youth exposed to disadvantage. The current study aimed to augment recent literature by simultaneously examining both the environmental and genetic contributions to variability in brain structure in a representative sample of youth with enrichment for exposure to neighborhood disadvantage.

Methods: 708 twins (354 families; 7-19 years) were recruited from birth records to be representative of families living in neighborhoods with above average levels of neighborhood disadvantage. We applied the classic ACE model to our structural MRI data, examining cortical thickness, surface area, and volume for 34 regions of interest (ROIs), and subcortical volume for 7 ROIs. This model decomposes the observed phenotypic variance into components attributable to additive genetics (A), common or shared environmental (C), and unique or non-shared environmental factors (E), including measurement error (Neale and Cardon, 1992).

Results: Controlling for global brain structure (i.e., total gray matter volume, mean surface area, or mean thickness), ACE modeling indicated a *wide range* of heritability estimates across cortical ROIs. Heritability estimates ranged from *very low* (**<10%**: Volume cuneus, lateral occipital; Surface Area lingual, postcentral; Thickness pericalcarine) to *very high* (**>80%**: Volume lateral orbitofrontal; Surface Area rostral middle frontal; Thickness rostral anterior cingulate, caudal middle frontal). We also found wide variability in heritability estimates for subcortical volume ranging from *very low* (**<10%** right hippocampus) to *very high* (**78%** right thalamus). Relative to additive genetics, common environmental effects were much smaller ranging from *very low* (**<10%**: Cortical Volume: 64% of ROIs; Surface Area: 44% of ROIs; Thickness: 67% of ROIs; Subcortical Volume: 64% of ROIs) to *low-to-moderate* (Cortical Volume: **60%**â€"parahippocampal; Surface Area: **64%**â€"entorhinal; Thickness: **52%** pericalcarine; Subcortical Volume: **30%**â€"left caudate). Nongenetic variance was largely due to unique environmental factors and measurement error, which also varied widely across cortical and subcortical ROIs. Estimates for unique environmental effects across the cortex ranged from *very low* (**<10%**: Volume paracentral; Surface Area cuneus, rostral middle frontal; Thickness rostral anterior cingulate, caudal middle frontal) to *very high* (**>80%**: Volume medial orbitofrontal, caudal middle frontal; Surface Area isthmus cingulate, medial orbitofrontal; Thickness insula, pars triangularis). Unique environmental effects also ranged from *low* (**12%**right thalamus) to *high* (**75%** left putamen) for subcortical volumes.

Conclusions: In this study, we parcellated the brain into smaller regions than most previous studies. Within a sample of twins exposed to neighborhood disadvantage, we show that heritability and environmental influences vary widely across cortical regions for volume, area, and thickness (volume up to 96%; surface area up to 94%; thickness up to 93%) and the volume of subcortical structures (up to 78%). Overall, region-specific genetic factors accounted for much of the structural variation within several anatomically distinct cortical and subcortical regions, but environmental sources are clearly involved.

3-D-21 - Effects of an Early Parenting Intervention on Stop Signal Reaction Time through White Matter Integrity in Middle Childhood: A Randomized Clinical Trial among CPS-Involved Children

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Details

Background: Inhibitory control is an executive function that refers to one's ability to resist making a habitual or prepotent response to achieve a goal. Children who experience early adversities in the form of neglect or abuse are particularly vulnerable to difficulties or delays in the development of inhibitory control. Previous studies have found microstructural abnormalities in white matter tracts as measured by a reduction in fractional anisotropy (FA), comparing children with versus without a history of early adversities. Attachment and Biobehavioral Catch-up (ABC) was developed to mitigate such negative consequences of early suboptimal care. ABC is an early parenting intervention designed to promote sensitive caregiving in three main behavioral targets: increasing sensitivity to child signals, increasing nurturance to child distress, and decreasing frightening and harsh behaviors. Using the Stop Signal Reaction Time (SSRT) paradigm, we have shown that ABC can causally enhance inhibitory control development compared to a control intervention (DEF) among CPS-involved children at age 8. However, we have not tested white matter integrity as a candidate of processes underlying the enhanced inhibitory control development among children whose parents received ABC.

Objective: The present study sought to understand whether white matter integrity in tracts detected by diffusion MRI connectometry analysis can explain the effects of ABC on SSRT behavior during middle childhood.

Methods: A total of 178 children were included in this study. A subset of 70 children (23 ABC, 22 DEF, and 25 no CPS-involvement, comparison children) underwent diffusion-weighted imaging and 136 children (40 ABC, 46 DEF, and 50 comparisons) completed the SSRT task at age 10. A whole-brain connectometry approach in DSI Studio was utilized to track the white matter segments that have FA correlated with intervention group membership while controlling for scanning age and sex (*t*-threshold=2.0 using a deterministic fiber tracking algorithm, topology-informed pruning with 16 iterations, a length threshold of 30 mm, and an FDR threshold of .05 with 10000 randomized permutations). Post-hoc mediation analysis in lavaan SEM package with full information maximum likelihood was conducted with ABC as the main predictor and the stop-signal reaction time as the

outcome, mediated by the mean FA values of significant tracts detected from the connectometry analysis, while controlling for age, sex, and IQ scores.

Results: The connectometry analysis showed that children whose parents received ABC had white matter tracts with greater FA than children in the DEF condition in several local white matter bundles, including various sections of the corpus callosum; frontal, parietal, parolfactory, parahippocampal cingulum; inferior, middle, superior longitudinal fasciculus; arcuate fasciculus; thalamic radiation; and corticostriatal tract. No tracts were found greater for DEF than ABC. While ABC did not predict stop-signal reaction time (p=.199) at age 10, the mean FA values across the tracts showing ABC-greater-than-DEF effects mediated the association between the ABC intervention and stop-signal reaction time (indirect effect B=-.319, p=.043, total effect B=.275, p=.145, CFI=.948, RMSEA=.017, SRMR=.054). In other words, through increases in FA among the identified tracts, indicating better white matter integrity, children whose parents received ABC showed faster stop time in the SSRT task than those whose parents received DEF, indicating better inhibitory control.

Conclusions: We observed ABC's effects on white matter integrity 8 years after receiving the intervention. We also demonstrated that increased white matter integrity may be one of the mechanisms underlying improved inhibitory control for children whose parents received ABC. The present study adds to the evidence base supporting the long-lasting beneficial effects of ABC on children's brain and executive function development.

3-D-22 - Neuroendocrine Functioning and Adolescent White Matter Organization

Jose Guzman [1], **Felicia Hardi** [1], **Colter Mitchell** [1], **Christopher Monk** [1], **Nestor Lopez-Duran** [1], **Luke Hyde** [1]

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Details

Neuroendocrine Functioning and Adolescent White Matter Organization

Authors: Jose M. Guzman, Felicia A. Hardi, Colter Mitchell, Christopher S. Monk, Nestor L. Lopez-Duran, & Luke W. Hyde

The hypothalamic-pituitary-adrenal axis responds to acute stress and programs long-term patterns of responsivity through a set of physiological and neurobiological processes. Cortisol, the stress hormone, regulates neurobiological mechanisms involved in the development of gray matter structures, yet its impact on white matter connections is relatively unknown. Furthermore, few studies have examined how different dimensions of neuroendocrine functioning might contribute to white matter structural organization. Therefore, we used growth curve modeling with landmark registration as applied to neuroendocrine data to examine the relationship between different phases of the cortisol response to stress (reactivity, peak, recovery) and graph analysis metrics of white matter connectivity (measures of efficiency, clustering, and segregation) in a sample of 222 adolescents recruited from a sample with a

high representation of socioeconomically disadvantaged individuals. Across the whole sample, greater cortisol reactivity was associated with more efficient ($\hat{I}^2$ = .209, p = .006) and less segregated networks ($\hat{I}^2$ = -.111, p = .007), but was not associated with network clustering ($\hat{I}^2$ = 2.033, p = .143). There were no associations between cortisol peak activation and recovery slope and network efficiency, clustering, or segregation (all p's > .119). Additionally, the findings varied by whether the participant had an endocrine response to the stress task. Among the responders, greater cortisol reactivity was associated with less network clustering ($\hat{I}^2$ = -3.515, p = .035), but was not associated with network efficiency ($\hat{I}^2$ = -.138, p = .137) or segregation ($\hat{I}^2$ = -.051, p = .348). There were no associations between cortisol peak activation or recovery slope and network metrics in responders (all p's > .958). Among non-responders, there were no associations between cortisol measures and network metrics (all p's > .984). All these associations remained after adjusting for covariates (family income, mother's marital status, city, medication, puberty, time from wakening, age, gender, and race/ethnicity). Findings suggest a link between cortisol reactivity and structural network organization. Greater reactivity was related to more integrated and less segregated structural networks. Moreover, for those individuals with an endocrine response to the stress task, greater cortisol reactivity was associated with lower network robustness. These findings suggest that neuroendocrine functioning may play a role in structural white matter development. Future analysis will examine the relationship between cortisol and specific white matter tracts that may underlie the development of structural connectivity.

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Primary Submission Theme: Mechanisms (hormones, neurotransmitters, physiology)

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List of Themes: https://fluxsociety.org/abstract-submission/

3-D-23 - Cortical thickness in bilingual children from the ABCD study: Differences between home-learners and school-learners

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Details

As the world's population becomes increasingly bilingual, there is a growing body of research on the "bilingual brain". While there are numerous models about how bilingual experience shapes brain structure, most data comes from adults, and therefore these models do not explain or account for development.

The limited research that exists on bilingual brain structure during childhood has compared groups of bilingual and monolingual children to identify between-group differences. Research with adults increasingly emphasizes that bilinguals are not a homogenous group; there are many life experiences that may lead to proficiency in two languages by adulthood. In the U.S., English is the majority language and, unlike other parts of the world, monolingualism is the norm. There are two main ways that children in the U.S. learn a non-English language: at home or at school. Although both groups of children might ultimately become bilingual, it is important to note the differences between these two groups. Home-learners acquire the non-English language at a very young age and it likely has sociocultural significance in their lives. School-learners experience a monolingual environment at home and are exposed to the non-English language later in childhood in an academic setting. These differences highlight the importance of including both groups of children in theories of bilingual development without collapsing them into a single group. The current study makes use of the large and diverse sample of children ages 9-10 from the Adolescent Brain Cognitive Development (ABCD) Study to compare cortical thickness in bilingual home-learners (n = 686), bilingual school-learners (n = 457), and separate samples of monolingual children who are matched to the home-learners (n = 686) and school-learners (n = 457) on age, sex, pubertal status, non-verbal IQ, parent education, and household income. This is an extension of previous work comparing samples of matched bilingual and monolingual children from the ABCD study (Vaughn et al., 2021).

We hypothesized that both groups of bilingual children would differ in cortical thickness compared to their monolingual counterparts and each other. We expected that the home-leaners would be the most different from the monolinguals, and school-learners would have cortical thickness values that fall between the home-learners and the monolingual groups because their pre-school/home experience would be more similar to monolinguals.

To test these hypotheses, we conducted ANCOVAs for each region of the Desikan-Killiany Cortical Atlas with the four groups of children (i.e., home-learners & matched monolinguals; school-learners & matched monolinguals) as a factor and age, sex, pubertal status, non-verbal IQ, parent education, and household income as covariates, applying a false-detection rate (FDR) of 0.05. Results indicated that home-learners had thinner cortex than matched monolinguals in posterior temporal, parietal, and occipital regions, along with the left anterior cingulate cortex (ACC). School-learners had thinner cortex than matched monolinguals only in the right cuneus. Home-learners had thicker cortex than school-learners in the bilateral superior temporal gyri, right inferior frontal gyrus, left ACC, and bilateral occipital regions. There were no significant differences in cortical thickness between the two monolingual groups.

These results aligned with our hypotheses in the sense that the cortical thickness of home-learners differed more from monolinguals than the cortical thickness of school-learners. Interestingly, the school-learners differed from the home-learners in an unexpected direction (i.e., home-learners had *thinner* cortex than monolinguals, but *thicker* cortex than school-learners). This may reflect an interaction between brain development and bilingual experience that has been unexplored in previous research and should be considered in future models of bilingual brain development.

3-D-24 - Varied patterns of cortical expansion between very preterm infants and full term infants from birth to 9/10 years of age

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Details

Objective: The brain develops rapidly from the final trimester of pregnancy through school-age, with cortical surface area expanding greatly in the first few years of life. This increase in surface area has implications for cognitive and psychiatric outcomes in childhood. Given these implications, it is critical to understand how environmental, genetic, and birth-related factors, such as being born prematurely, impact cortical development. Importantly, infants born prematurely have been shown to have key differences in brain development, such as altered surface area at birth, decreased cognitive functioning in childhood, and increased rates of psychiatric and neurodevelopmental disorders. However, it is unclear exactly where and how cortical surface area changes occur from birth to school-age, and how prematurity affects these developmental trajectories. The WUNDER cohort, which is comprised of both very preterm (VPT) (gestational age at birth (GA) of 23-29 weeks) and full term infants, represents a unique opportunity to answer these questions.

Methods: 52 VPT (mean GA = 26 weeks, SD = 1.602 weeks) and 41 full term (mean GA = 39 weeks, SD = 1.202 weeks) infants from the WUNDER cohort were scanned as infants and at 9/10 years of age. VPT infants were scanned at term equivalent age (TEA) (36-40 weeks post menstrual age (PMA)) (mean PMA = 38 weeks, SD = 1.410 weeks), and full term infants (GA of 37-41 weeks) were scanned within the first four days of life (mean PMA = 39 weeks, SD = 1.167 weeks). For all infant scans, images were obtained using a Siemens Trio 3T scanner, and structural T2-weighted data were acquired with TR = 8600 ms, TE = 161 ms, and a voxel size of 1 x 1 x 1 mm^3. The M-CRIB-S pipeline was used to generate cortical midthickness surfaces. For the 9/10 year old time point, a Siemens Prisma 3T scanner was used, and structural T1-weighted data were acquired with TR = 2500 ms, TE = 2.9 ms, and a voxel size of 1 x 1 x 1 mm^3. Freesurfer was used to generate cortical midthickness surface outputs. In order to examine cortical surface area expansion, infant and 9/10 cortical surfaces were aligned using anatomically-constrained Multimodal Surface Matching (aMSM), a novel technique which allows for optimized point-correspondence between the infant and school-age surfaces. Finally, permutation analysis of linear models (PALM) was used to facilitate statistical comparisons of local growth patterns and to control for covariates of interest. For all analyses, we controlled for PMA at birth scan and used a threshold of $p < 0.05$.

Results: Using these techniques, we were able to compute average expansion across the brain's cortical surface for both the VPT and full term infant groups. Across both groups, cortical expansion was most pronounced in the frontal, temporal, and supramarginal/inferior parietal junction areas ($p < 0.05$). VPT infants showed greater cortical surface area expansion between birth and age 9/10 compared to their full term peers in medial and lateral frontal, precuneus, and the middle temporal/banks of the superior sulcus junction ($p < 0.05$).

Conclusions: Importantly, this is the first study to use aMSM to map developmental trajectories of cortical expansion between birth and school-age, and the first to show key differences in cortical surface area development between infants born VPT and those born full term. Given the crucial importance of cortical surface development for cognitive functioning and mental health, these results may help explain some of the key differences in neurodevelopmental and psychiatric outcomes for infants born VPT.

3-D-25 - Trajectories of gray matter volume development in toddlers and young children with prenatal alcohol exposure

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Details

Introduction: Prenatal alcohol exposure (PAE) occurs in ~11% of North American pregnancies (Popova et al. 2017) and is the most common preventable cause of neurodevelopmental disorders such as fetal alcohol spectrum disorder (~4% prevalence; May et al., 2018). While it is well understood that PAE has a significant effect on gray matter (Donald et al., 2015; Treit et al. 2020), longitudinal studies characterizing development trajectories are sparse (Moore and Xia, 2022), leaving a gap in knowledge for gray matter development in the toddler and preschool years. Rapid changes in gray matter volume occur in typically developing children between 2 and 8 years of age (Long et al. in prep), but it is unclear whether development follows a similar or different pattern in children with PAE during this same developmental period. The present study used an accelerated longitudinal design to characterize gray matter volume development in children with PAE and compare their development to unexposed control children.

Methods: We acquired T1-weighted MRI of the brain on the 3T GE MR750w scanner at the Alberta Children's Hospital in 54 children with confirmed PAE and 130 unexposed aged 2-8 years. We scanned most children longitudinally (498 total scans). MaCRUISE software (Huo et al. 2016) was used to define 116 regions and compute absolute (mm^3) and proportional volume (% intracranial volume). Using mixed effects models with previously defined normative trajectories (Long et al., in prep), we tested main effects of exposure group as well as age- and age^2-by-group interactions. When interactions were non-significant, we ran a reduced model (main effects only).

Results: We observed significant (FDR $q<.05$) group interaction effects in the right calcarine cortex (CC), medial temporal gyrus (MTG), putamen (PUT), and left lingual gyrus (LIG); Children with PAE showed proportional volume decreases in all four regions while volume was either stable or increasing in unexposed controls. Absolute CC volume decreased in the PAE group but increased in the control group. In the MTG and PUT, children with PAE had smaller volume increases with time than unexposed controls. Where interactions were not significant, most regions had significant main effects of group; the PAE group had smaller volumes than controls.

Conclusions: We characterized gray matter volume development in a novel sample of young children with PAE. Our findings concur with previous research in older children showing altered development trajectories and reduced gray matter volume in individuals with PAE. The altered developmental changes in gray matter observed in children with PAE may indicate reduced brain plasticity or accelerated maturation and underlie the cognitive/behavioural deficits often associated with PAE.

3-D-26 - Amongst initially healthy weight youth, smaller increases in subcortical volumes predict greater gains in BMI from 9-12-years-old: findings from the Adolescent Brain Cognitive Development Study

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Details

Background: Variation in brain structure (e.g., smaller subcortical volume) and function (e.g., impulsivity) are associated with maladaptive behaviors like overeating and weight gain. Yet, the cause vs. consequence mechanism is poorly understood. To our knowledge, no studies have evaluated these associations 1) during periods of time when the brain is undergoing extensive maturation and weight gain risk is highest: adolescence; nor 2) amongst youth who do not yet have excess weight. Previously, we showed that amongst initially healthy weight (HW) youth, those who were more impulsive 1) consumed more fat and sugar, and, 2) had, on average, a greater increase in the rate of change in body mass index (BMI) from 9/10 (baseline) to 11/12-years-old (Year 2; Y2). These findings partially support the idea that underlying differences in brain structure and function may lead to obesogenic behaviors.

Objective: The current study evaluated whether differences in subcortical brain regions associated with impulsivity and appetite control related to the rate of change in BMI from 9-12-years-old in initially healthy weight youth (100% $HW_{Baseline}$, 10.8% overweight by Y2; n=3615, 50.7% male, 15.9% Latino/a/x, 29.4% caregivers < 4-year college degree).

Methods: Magnetic resonance imaging (MRI), height (in), and weight (kg) were collected at baseline and Y2; height and weight were converted to BMI (kg/m^2). T_1w images were parcellated with FreeSurfer to obtain estimates of subcortical volume for each region of interest (ROI; n=16). Mixed-effects models were conducted to examine if the average rate of change in BMI was explained by changes in subcortical volume over time; models accounted for sex, puberty, caregiver education, and intracranial volume and allowed for nested random effects for MRI scanner and subject ID. The Benjamini-Hochberg method was used to correct for multiple comparisons.

Results: As expected, average BMI increased from baseline to Y2. However, results showed robust significant Time*ROI interactions on BMI in 6 bilateral subcortical regions (e.g., accumbens, amygdala, hippocampus, pallidum, thalamus, ventral diencephalon all *p*'s<0.01), while a unilateral Time*ROI interaction was observed for the right caudate (p=0.04). That is, across all ROIs, youth who had smaller increases in subcortical volumes had greater increases in the average rate of change in BMI from baseline to Y2.

Conclusions: These data suggest that amongst youth who were initially of a healthy weight, smaller increases in subcortical volumes in brain regions associated with appetite control (e.g., thalamus) and impulsivity (e.g., amygdala) related to a greater rate in change in BMI. Across several studies, a decreased rate in subcortical enlargement has been associated with various maladaptive health and behavior outcomes, like obesity and mental health disorders. Although variation in subcortical volumes have been associated with overeating and weight gain, for the first time, we showed that this variation exists *prior to* major unhealthy weight gain. Combined with the previously reported behavioral results in these youth, this finding suggests that underlying differences in the brain and impulsivity may be driving more impulsive food choices. This finding also provides baseline evidence of variation in brain structure prior to obesity during a time in which these subcortical regions are undergoing normative development and weight gain risk is high. Future studies are warranted to understand the implications of weight gain during adolescence on later brain development and behavior as well as the relationship to objective food intake.

3-D-27 - Neurobiological changes across pregnancy

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Details

Reproduction-related neuroplasticity has been observed in non-human animal species. However, the extent to which pregnancy affects the human brain remains largely unexplored despite more than 80% of the women experiencing pregnancy and childbirth in their lifetime. An accumulating body of research indicates that hormones known to rise during pregnancy can modulate neuroplasticity in both humans and non-human animals. The present study aims to chart the neurobiological changes throughout pregnancy, including morphometric features, white matter microstructure, resting state functional activity, and associations with hormones.

Hormone levels and multimodal images were collected from 10 women (mean age=28.97 yrs) repeatedly throughout pregnancy (mean gestational age=23.90 weeks and range=12.43-35.43 weeks; mean number of repeated measures=2.6 times, range=1-6 times). Waking salivary samples (cortisol, progesterone, and estradiol) across 2 mornings, 3D-QALAS (enable quantification of both T1- and T2-weighted MRI), diffusion-weighted MRI (DWI; 12 b=0 volumes, 12 b=500 volumes, 47 b=1500 volumes, and 70 b=2500 70 volumes), and two 10-minute-run resting-state fMRI were acquired. Brain volumes were quantified using FreeSurfer (v7.1.0) longitudinal pipeline. After preprocessing by FSL (v6.0) and MRtrix3, DWI data was segmented into 50 well-described tracts by TractSeg. Neurite Orientation Dispersion and Density Imaging metrics were estimated using Accelerated Microstructure Imaging via Convex Optimization. Specifically, intra-cellular volume fraction (ICVF), isotropic volume fraction (ISOVF), and orientation dispersion (OD) were extracted for each tract. Resting-state fMRI data were preprocessed using fMRIPrep 21.0.1. Processed functional time series were post-processed by eXtensible Connectivity Pipeline to estimate the amplitude of low-frequency fluctuation, and functional connectivity between each pair of brain network based on the Gordon atlas. Linear mixed-effects

models were fitted for each metric, with a fixed effect of gestational week, necessary covariates, and a random subject intercept.

Our main results revealed significant effects of gestational week on total brain volume (*B*=-0.11, *SE*=0.03, *p*=.004), total gray matter volume (*B*=-0.19, *SE*=0.05, *p*=.002) respectively. On average, total brain volume decreased by 0.45% per week (if constant over the full course of pregnancy it would translate to 18.11% estimated total decrease), and total gray matter volume decreased by 0.41% per week (a total estimated decrease of 16.58% across gestation; see Fig 1). The decrease was primarily driven by reductions in cortical volume as opposed to subcortical volumes. Progesterone levels were significantly related to total brain volume (*B*=-0.10, *SE*=0.03, *p*=.006) and total gray matter volume (*B*=-0.19, *SE*=0.05, *p*=.003). Additionally, we observed consistently increasing trends of ICVF and ISOVF in all tracts during pregnancy, with OD remaining relatively stable (Fig 2). ICVF and ISOVF of most tracts were significantly and positively associated with estradiol levels (Fig 3).

Our preliminary findings indicate that pregnancy may exert significant impacts on brain structure and white matter microstructure. Additionally, our study revealed a potential involvement of progesterone and estradiol in these changes. These results could have implications for understanding the neural basis of maternal behavior and mental health issues that may arise during peripartum.

3-D-28 - Comparing structural and functional maturity in middle childhood

Cassidy McDermott [1], **Morgan Botdorf** [1], **Maayan Ziv** [1], **Austin Boroshok** [1], **Anne Park** [1], **Dilara Berkay** [1], **Adrianna Jenkins** [1], **Allyson Mackey** [1]

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Details

Background and hypotheses: In this study, we will examine regionally specific associations between structural and functional maturity in middle childhood. Brain structure and function both become more ‘adult-likeâ€ through childhood and adolescence, yet little is known about how structural and functional maturation occur in relation to one another across development. We hypothesize that in early-developing sensorimotor areas, increased functional maturity will be associated with more mature structure. In contrast, we hypothesize that in later-developing association cortex, greater functional maturity will be associated with less mature structure.

Participants: Data collection for this study is ongoing; the projected sample size is approximately 80 4-10 year-old children with usable structural and functional neuroimaging data. The adult sample used in intersubject correlation (ISC) analyses includes 43 participants.

Methods: Structural maturity will be characterized by cortical thickness, as the cortex is known to undergo a protracted period of thinning from early childhood through young adulthood; thus, thinner cortex can be considered more ‘adult-like.â€ Structural analyses will be conducted in FreeSurfer version 6.0. Functional maturity will be characterized by comparing the similarity of functional activation during movie-watching between each child and an average adult sample. All participants will watch an animated movie, ‘Piperâ€ by Pixar, in the scanner. fMRI preprocessing will be conducted with Nipype. Functional maturity will be defined using ISC (Brainiak toolbox). For each child, each voxel’s timeseries

will be correlated with the average adult time series in that voxel; a stronger positive correlation will indicate that a chil's functional activity within that voxel is more 'adult-like.â€⍰ The average adult timeseries will be created using 3dMean in AFNI.

Exclusions: Participants will be excluded from structural analyses for low image quality resulting in inaccurate surfaces. Participants will be excluded from functional analysis for the following reasons: not completing the movie fMRI scan, technical issues during the scan, or average motion exceeding 0.5 mm.

Planned analyses: In order to compare structure-function associations along the sensory-association axis, we will focus on average cortical thickness and ISC extracted from the seven Yeo networks (Yeo et al., 2011). Within each cortical network, we will correlate children's cortical thickness and their functional maturity, controlling for age. A negative correlation will indicate that children with more mature structure (i.e., thinner cortex), also have more mature function (i.e., more highly correlated with the adult time-series) in a given network. A positive correlation will indicate that children with more mature structure have less mature function, consistent with the theory that structural maturation constrains functional development.

3-D-29 - Social wariness trajectories across early childhood and their relation to brain morphometry

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Details

Background

Cortical thickness and surface area reach their peak during childhood and then continue to decrease over adolescence (Wierenga et. al., 2014, Ducharme et. al., 2016). During this period, socially anxious behaviors, particularly towards peers, also begin to develop (Lijster et. al., 2017). However, it remains unclear whether individual differences in brain structure are related to these emerging anxious behaviors.

Social wariness (SW) is characterized by socially withdrawn behaviors and shyness when interacting with peers and prevalent in children that displayed high behavioral inhibition (BI) in infancy (Fox et. al., 2005). Prior research has shown that individual differences in BI (Sylvester et. al., 2016), negative reactivity (a precursor to BI; Filippi et. al., 2020), and anxiety (Newman et. al., 2015) are related to individual differences in brain structure. Individuals who exhibited temperaments in infancy characterized by distress to novelty (e.g., BI and negative reactivity) had thinner dorsolateral anterior cingulate cortices in adulthood (Sylvester et. al., 2016) and stunted amygdala growth in adolescence (Filippi et. al., 2020). Although previous research has established a relation between temperament in infancy and brain structure in later childhood, it remains unclear whether SW across childhood is related to brain development in adolescence. The aim of this study is to identify associations between SW trajectories over early childhood and cortical thickness and subcortical volume in later childhood. We hypothesize that high-stable SW will be associated with amygdala volume and thickness in regions of the salience network.

Methods

Participants were part of a larger longitudinal study that followed infants from 4 months of age to 12 years of age. T1-weighted magnetic resonance imaging (MRI) images were acquired at age 9 (n = 62) and age 12 (n = 66). Two subjects from the age 12 group were excluded due to incomplete data (n=64). Images were pre-processed using FreeSurfer 6.0 and cortical thickness and subcortical volume will be extracted using FreeSurfer's group analysis pipeline. At ages 2, 3, 4, 5, and 7, the children were observed during a free-play session with peers. The proportion of time spent displaying SW was computed (Degnan et. al., 2008) for each age.

To model changes in SW over time, latent class growth analysis will be conducted. This method will allow us to identify groups of individuals who exhibit similar developmental trajectories. To identify brain-behavior associations, linear mixed effects modeling will be conducted using Permutation Analysis of Linear Models. All models will control for sex and age at MRI and models examining subcortical volume will also control for intracranial volume. Linear mixed effects modeling allows us to examine associations between SW and brain structure at age 9, age 12, and the structural change from age 9 to 12. Correction for multiple comparisons will be applied to control the family-wise error rate. The analysis described above will be completed prior to the conference.

Implications

Identifying neural correlates of SW could shape our understanding of risk for social anxiety and inform early interventions aimed at preventing the development of psychopathology. Future analyses could investigate the associations between SW, brain morphology, and social anxiety to understand whether altered brain development mediates the relationship between SW and later anxiety.

3-D-30 - Identifying developmental mismatches in the child and adolescent brain: a multimodal study

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Details

Introduction. Neurodevelopment varies regionally, with subcortical areas developing rapidly in early childhood, while the prefrontal cortex (PFC) develops more gradually in adolescence. The Developmental Mismatch Hypothesis posits that this contrast results in a maturity gap that underlies the timing of adolescent behaviour development (Mills et al., 2014). Existing literature shows that amygdala and PFC trajectories are non-linear and mismatched to a variable extent. However, these findings are limited by small sample sizes (~30), older participant ages (>6 yrs), the use of singular imaging modalities, and a lack of sex comparisons (Galvan et al., 2006; Mills et al., 2014; Mills et al., 2021). Sex differences in trajectories are critical to examine, as pubertal hormone changes may influence neurodevelopment. Investigating mismatches using a large longitudinal dataset and multiple modalities will improve our understanding of neurodevelopment and behaviour.

Objective. Quantify and compare the developmental trajectories of amygdala and PFC macrostructure and amygdala-PFC tract microstructure in typically developing children and adolescents.

Hypotheses. **1.** The differences between the development rates of metrics (i.e., slopes) will be biggest in early adolescence (10-14 yrs). **2.** Compared to females, males will experience higher trajectory peaks at older ages.

Methods. Magnetic resonance (MR) imaging scans were obtained from prior longitudinal studies (Geeraert et al., 2020; Lebel et al., 2021; Reynolds et al., 2020). Pending final quality inspection, we will include approximately 707 scans from 148 typically developing children and adolescents aged 2.34 17.71 (74 females). T1-weighted (FSPGR BRAVO, 0.8-0.9mm isotropic voxels, TR~8.2ms, TE~3ms, total imaging time~5min) and diffusion-weighted scans (spin-echo echo planar, ~2.2mm voxels, TR=6.3-12s, TE=55-88ms, 5 images with b=0 and 30 images with b=750, 900 and/or 2000 s/mm^2, total imaging time=4-7min) were acquired on a 3T GE Discovery MR750w system with a 32-channel head coil. T1-weighted images have been preprocessed using Advanced Normalization Tools (ANTs) and Analysis of Functional Neuroimages (AFNI) software and will be segmented by Multi-atlas Cortical Reconstruction Using Implicit Surface Evolution (MaCRUISE) software. Amygdala and PFC volumes will be extracted from MaCRUISE volumetric labels in MATLAB. Diffusion-weighted images will be preprocessed using FMRIB Software Library (FSL) and MRtrix3. Fractional anisotropy and mean diffusivity of the amygdala-PFC white matter tract will be computed. ComBat correction will harmonize data collected with different MR sequences.

Analysis. Generalized additive mixed-effects models (GAMMs) will be performed in R to fit non-linear trendlines that describe metric development. Developmental rates will be calculated from the first derivative of the trendlines at 1-year intervals. Periods with significant age-related changes will be identified when the trendline 95% confidence intervals do not include zero. **1.** GAMMs will assess the overall relationships between regions and metrics. Developmental trajectories during each time interval will be compared between regions and metrics using the differences between trendline 95% confidence intervals. **2.** GAMMs will test sex-by-age interactions for each metric. Trendline peaks will be identified and compared between sexes. All comparisons will be completed by the 2023 Flux Congress.

Implications. To our knowledge, this is the first project to compare the developmental trajectories of the amygdala, PFC, and connecting tracts using a large longitudinal dataset and two imaging modalities. The project will establish fundamental methods that can be used to identify novel mismatches across the whole brain. This information is essential for understanding behaviour development and the etiologies of neurodevelopmental and mental health disorders.

3-D-32 - Does Adolescent Brain Structure Mediate the Association between Maternal and Paternal Parenting Behaviors and Adolescent Internalizing Symptoms

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Details

Parenting behaviors are established as important in shaping adolescent brain development and mental health. While maternal parenting is at the forefront of this literature, changes in parental roles and social norms have demonstrated that fathers now play a more hands-on role in caregiving. Yet, investigation into fathers still represents a substantially smaller portion of the overall parenting

literature. This study aimed to investigate the unique and interacting role of maternal and paternal parenting behaviour in the prediction of adolescent brain structure and internalizing problems. We will use a subset of data from two-parent families within the longitudinal Adolescent Brain and Cognitive Development study (*N*=2908).
Structural equation models will be employed to test our aims. We hypothesize that maternal and paternal acceptance (and their interaction) at age 9-11 (measured by the Acceptance/Rejection subscale of the Children's Report of Parent Behavior Inventory) will predict volumetric changes in the amygdala, hippocampus, and prefrontal cortex 2 years later, with these structural changes mediating the relationship between maternal and paternal parenting behaviors and adolescent internalizing symptoms 3 years later (measured by the Child Behavior Checklist). Additionally, supplementary analyses will be performed on prefrontal cortical regions, to identify whether cortical thickness mediates the relationship between maternal and paternal parenting behaviors and subsequent adolescent internalizing symptoms. While we anticipate unique and interactive effects of maternal and paternal parenting, given the lack of prior literature, we do not make specific hypotheses.
Preliminary analyses have suggested that maternal and paternal parenting behaviors may hold differential influences on adolescent internalizing symptoms dependent on adolescent gender, however further investigation is underway to test this finding across all brain regions, with consideration for the mediating role of brain structure. Our research will provide new insight into the independent roles of maternal and paternal parenting in influencing adolescent mental health and development. We anticipate that these findings may have implications for refining parenting interventions, which are largely based on research in mother-child dyads. Further, the findings may also be relevant for policy changes (such as deeper consideration for the role of fathers in custody arrangements and the introduction of paid paternity leave).

E – Clinical populations

3-E-33 - Differential developmental contributions of limbic and motor connectivity underlying fine motor function in preschool-age children with and without ADHD: a longitudinal study.

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Details

Objective: While diagnosis of attention-deficit/hyperactivity disorder (ADHD) is primarily characterized by symptoms of hyperactivity and inattention; it is highly associated with fine motor delays and difficulties. Fine motor development in the preschool age is well characterized on a clinical level, but its neural underpinnings are not well understood. In this study, we employ a longitudinal approach to examine development of structural connectivity and fine motor skills and examine their association and how it differs in children with ADHD.

Methods: This study employed linear mixed-effects models to characterize developmental (i.e., age-related) changes in fine motor function (e.g. overflow, as measured by the PANESS instrument), and structural connectivity using diffusion tensor imaging (DTI). Data were drawn from a longitudinal study of preschool-age children with and without ADHD, with an overall sample of 127 children and adolescents (ages 4-7 at start of study) either with an initial diagnosis of ADHD (n=72, 29 girls) or

typically developing (TD) controls (n=55, 23 girls) with MRI scans collected at a single site. There were a total of 376 time points, from which there were 208 usable DTI scans across 94 subjects. DTI data were run through FSL TBSS pipeline, and ROIs were defined from JHH DTI atlas. Outliers removed on a within-model basis (residual >2.5sd from mean), fit using natural splines, with Holm test for multiple comparisons (consistent with methods from Simmonds et al., 2014).

Results: Consistent with prior studies, developmental increases in fractional anisotropy (FA, higher values reflect greater integrity of white matter tracts) were seen broadly across the brain. Neuroimaging analyses revealed differences in development of connectivity by diagnosis, with some regions (corpus callosum, internal capsule, corona radiata) showing greater early developmental FA increases (age 4-7y) in ADHD than controls. Further, associations were seen in the interaction of age, diagnosis, and fine motor function. In limbic circuitry (cingulum), early developmental increases in FA were associated with better fine motor function in ADHD group, and poorer function in TD group. In contrast, in motor circuitry (internal capsule), the TD group showed that FA development during this time was associated with better fine motor function, while the opposite association was seen in ADHD.

Conclusions: These findings suggest differences in the development of motor circuitry in preschool-age children with ADHD. However, differences in fine motor development in ADHD seem to be underpinned by a dissociation in the development of motor and limbic circuitry, such that connectivity with the limbic system supports fine motor development in controls but not in ADHD.

3-E-34 - A shifting role of thalamocortical connectivity in the emergence of large-scale functional brain organization across early lifespan development

Shinwon Park [1], **Koen Haak** [2], **Han Byul Cho** [3], **Kyoungseob Byeon** [3], **Bo-Yong Park** [4], **Phoebe Thomson** [1], **Adriana Di Martino** [1], **Haitao Chen** [5], **Wei Gao** [6], **Ting Xu** [1], **Sofie Valk** [7], **Michael Milham** [1], **Boris Bernhardt** [8], **Seok Jun Hong** [3]

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Details

Introduction. How does the brain acquire specific functions across different areas (i.e., functional specialization), and how do functionally specialized areas organize major processing architectures such as cortical hierarchy across development? While the interplay between intrinsic (i.e., genetic patterning) and extrinsic (i.e., sensory experiences relayed through thalamic connections) mechanisms have been, for long, considered critical for such developmental processes during the embryonic stages, our understanding of the postnatal brain development is still limited. Given thalamocortical circuitry (established during early development) plays a fundamental role in sensory processing and continues to evolve throughout the lifespan, it may play a critical role in shaping functional organization throughout postnatal development. Accordingly, in this study, we examined the developmental effects of thalamocortical connectivity on large-scale functional brain organization across infancy, childhood, adolescence, and young adulthood.

Methods. First, we employed connectopic mapping to comprehensively chart the gradually changing functional relationship between the thalamus and the neocortex in two large-sample developmental cohorts: developing Human Connectome Project (HCP) cohort consisting of 195 infants (39.7 Â± 3.0 weeks), and the HCP development cohort comprising 603 participants (14.8 Â± 3.9 years). We then employed mechanistic approaches, such as genetic transcriptomic association analysis and developmental brain simulation based on generative network modeling, to interpret the developmental changes. Through thalamus-centered (e.g., core and matrix genes) and whole-brain (i.e., Allen Human Brain Atlas) analyses, we comprehensively delineated subcortical-cortical gene influences, and then leveraged generative network modeling to simulate brain development. Finally, perturbing the network simulations allowed us to identify the age window significantly contributing to the emergence of large-scale cortical hierarchies.

Results. We found that the development of thalamocortical connectivity showed diverging patterns across age, indicating a developmental change in the relationship between the thalamus and macroscale cortical functional organization. During infancy, thalamocortical connectome topology showed strong anchors in low-level sensory regions while the other end was spread out across undifferentiated higher-order cortical regions, indicating that the thalamocortical connections lay the basis for the development of cortical hierarchy. We also found a significant interaction with cortical genes involved in developmental processes during infancy, but not childhoodâ€“young adulthood. However, during childhood to adolescence, these thalamic projections undertake a unique role of differentiating between internally- and externally-oriented functional processes, suggesting the emergence of mature functional systems. Specifically, the salience network forms a stable anchor that differentiates between external-oriented networks such as dorsal attention, visual and sensorimotor networks on one gradient, and the default mode network on the other gradient. Moreover, this differentiation reflected the distinct patterns of underlying thalamic projections based on the relative density of â€˜core' and â€˜matrix' cells. Finally, we demonstrated that the thalamocortical connectivity is a major player in scaffolding the emergence of a continuous internal-external functional brain stream (i.e., 'functional gradientâ€ by Margulies, et al. PNAS 2016) and modular structures using generative network modeling. Specifically, our perturbation analysis revealed its highest influence in later age groups (i.e., above 12 years), particularly in the development of cortical hierarchy, including the internal processing areas such as the default mode network.

Conclusion. Our findings provide compelling evidence of the active role of thalamocortical connectivity in shaping large-scale functional brain organization, emphasizing its significant impact across the early developmental stages. These results may provide new insights into developmental neuroscience, as well as clinical conditions that are related to atypical interaction between intrinsic and extrinsic mechanisms, such as autism and schizophrenia. Additionally, our study challenges the prevailing cortico-centric models of large-scale functional brain organization by highlighting the importance of examining subcortical brain structures, particularly the thalamus.

3-E-35 - A dimensional investigation of response time variability in children with and without ADHD

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Details

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder of childhood. Its core symptoms of inattention, hyperactivity, and impulsivity are often accompanied by deficits in cognitive control, which is critical for regulating thoughts and behaviors. Prior investigations have conceptualized ADHD categorically, comparing clinically diagnosed children to age-matched, typically developing controls. This categorical framework does not consider that ADHD symptoms and associated cognitive control deficits transcend diagnostic categories, nor that children without ADHD diagnoses also experience ADHD symptoms and cognitive control impairments. Thus, the goal of this project was to use a dimensional approach to examine performance on a cognitive control task and ADHD diagnostic status across symptom-based clusters of children with and without ADHD. We hypothesized that clusters would differ in cognitive control performance, but not in the proportion of individuals with an ADHD diagnosis. To probe these hypotheses, 555 children (7-18y) from two independent datasets were included. All participants completed a go/no-go task, and their parents completed the Child-Behavior Checklist (CBCL). Cognitive control performance was operationalized as response time variability on the go/no-go task. Participants were categorized as having ADHD in one of two ways: 1) if a formal diagnosis of ADHD existed; or 2) if there were elevated scores on the hyperactive/inattentive subscale of the Strengths and Difficulties Questionnaire (i.e., score >11). Data from the eight subscales of the CBCL, which is used to assess a range of emotional and behavioral symptoms, was used to create a matrix of child-by-child correlations. Walktrap, a random walk community detection approach, was applied to this matrix. While there were significant differences in the proportion of children with ADHD across all clusters (Rao-Scott's Chi square, F=6.2, *p*-value=.0004), the clusters transcended diagnostic categories, such that there were children with ADHD in all clusters. Unsurprisingly, the cluster whose profile was characterized by elevated thought problems, attention problems, rule-breaking behavior, and aggressive behavior captured the highest proportion of children with ADHD. When assessing cognitive control performance, however, there were no differences across clusters. These findings suggest that examining transdiagnostic subgroups of individuals with similar symptom profiles, instead of diagnosis-based subgroups, may allow for a more nuanced understanding of the symptom heterogeneity observed in individuals with and without ADHD.

3-E-36 - Prediction & Sensory Processing in Autism Spectrum Disorder: an fMRI Study

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Details

Objective

Sensory over-responsivity (SOR) is a heightened negative response to sensory stimuli such as loud noises. SOR is present across neurodevelopmental disorders and is particularly prevalent in autism spectrum disorder (ASD), affecting more than half of youth with ASD (Ben-Sasson et al., 2009). Previous functional magnetic resonance imaging (fMRI) studies have found greater activation in response to sensory stimuli in ASD youth with SOR in several brain areas including primary sensory cortices and the amygdala (Green et al., 2015). SOR is associated with reduced habituation to sensory stimuli in relevant sensory cortices and the amygdala (Green et al., 2015; Green et al., 2019). Similarly, a key feature of typical predictive processing is reduced reactivity to predicted stimuli (Koster-Hale & Saxe, 2013). The

reduced habituation in SOR could be due to a deficit in predictive coding, which has previously been proposed in ASD (Pellicano & Burr, 2012). Here, we examined the role of prediction in sensory processing of mildly aversive stimuli in ASD by examining brain responses to predictable versus unpredictable sensory stimuli. We hypothesized that there would be less reactivity in the predictable compared to the unpredictable events and that this effect would be stronger in the TD group due to predictive processing deficits in ASD.

Methods

Brain responses to predictable and unpredictable stimuli were examined using fMRI in 20 young adults with ASD and a control sample of 21 neurotypical (NT) young adults (aged 13 to 25 years) matched on age, IQ, and sex. Concurrent auditory and tactile stimulation varied between four types of aversive auditory stimuli (helicopter, firetruck, construction, or school bell sounds) and four types of tactile stimuli (a toothbrush or sponge rubbed on the palm or forearm). In 'predictableâ€ trials, stimulation was preceded by an image indicating which type of auditory and tactile stimuli will be applied. This visual cue was not present prior to 'unpredictableâ€ trials. We compared activation to the predictable and unpredictable stimuli thresholded at Z>2.3 and cluster corrected for multiple comparisons at p<.05.

Results

As expected, the ASD group had significantly higher SOR measured by parent report (t=4.42, P<0.001), confirming a high prevalence of sensory processing difficulties in this group. In both the ASD and TD groups, there was significantly lower activation in the fusiform gyrus, a high-level vision area, in response to predictable compared to unpredictable stimuli. In the ASD group only, there was significantly higher activation to predictable compared to unpredictable stimuli, specifically in the cerebellum, a key region implicated in predictive processing (Gatti et al., 2021), as well as in frontal and somatosensory cortices. In the TD group, there were no areas with significantly higher activation to predictable compared to unpredictable stimuli. Finally, compared to ASD, the TD group displayed higher activation in visual areas in response to the prediction cue images prior to the predictable trials.

Conclusion

Overall, these findings suggest that modulating the expectancy of aversive sensory stimulation results in significantly different brain responses to the stimuli in both ASD and TD individuals. As expected, the TD group displayed less reactivity to predicted stimuli, which is a key feature of predictive processing. Notably, only the ASD group displayed *higher* activation to predictable stimuli, particularly in regions involved in prediction, top-down mechanisms, and tactile processing. Thus, in the ASD group, expectancy of oncoming stimulation may not facilitate less reactivity. This may be due a deficit in the ASD group in using the image to precisely predict oncoming stimuli. These findings suggest that predictive processing deficits may play a role in sensory features of ASD such as SOR or reduced sensory habituation.

3-E-37 - Neural correlates of smartphone-based communication in adolescents with and without depression

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Details

Standard Submission:

Background: Existing research suggests that particular linguistic markers, such as greater use of first-person pronouns and negative emotion words, detected in naturalistic language are associated with depression symptoms. Smartphones, which are ubiquitously used among adolescents, offer a penetrating window into naturalistic language used in social communication in this population and thus provide an opportunity to passively detect ecologically valid markers of depression-related language patterns in adolescents. Given the impact of depression on social interactions, it is likely that linguistic features of social communication in particular differ between adolescents experiencing depression and those who are not. We do not yet know, however, the underlying neural correlates that might explain naturalistic communication patterns that covary with depressive disorders.

Objective: In this preregistered study (https://osf.io/u2k6h), we assessed the extent to which neural correlates of adolescent-onset depression are associated with *in vivo* smartphone-based social communication expressed through naturalistic language among a sample of 34 adolescents (ages 13-18 years, 65% female) with and without Major Depressive Disorder (MDD; 23 participants with MDD). The objective of this study is to identify the neural correlates of linguistic features of social communication that are associated with a diagnosis of MDD.

Methods: Linguistic markers were derived from keyboard data (n=263,399 messages across 2,093 daily observations) entered into social media, text message, and e-mail smartphone applications acquired through a passive mobile sensing smartphone app, the Effortless Assessment Research System (EARS). Clinical assessments were used to determine MDD diagnosis. All participants completed resting-state fMRI scans prior to downloading the EARS app. Based on prior literature examining neural correlates of depression, we examined within- and between-network connectivity of the default mode network (DMN), central executive network (CEN), cingulo-opercular network (CO), and the salience network (SN). The Linguistic Inquiry Word Count (LIWC) software was used to identify first-person pronouns and negative emotion words, calculated as proportions of daily total words entered into social communication apps. Linear multilevel models (accounting for repeated measures of daily linguistic features) were constructed to examine associations between linguistic features and resting-state fMRI network connectivity, covarying for age, sex, diagnostic group, and time period (i.e., pre- or peri-pandemic).

Results: Participants with MDD had higher average daily use of first-person pronouns and negative emotion words in smartphone social communication (all *ps*<.05). Lower left CEN within-network connectivity was associated with higher average daily use of first-person pronouns (*p*=0.0005).Greater within-network connectivity of the DMN, greater within-network connectivity of the right CEN, and greater SNâ€“CO between-network connectivity were associated with higher average daily use of negative emotion words (all *ps*<0.05).

Conclusions: Our findings indicate that adolescent depression is associated with certain linguistic features derived from naturalistic smartphone communication, particularly those related to self-focused attention and negative emotion words. Further, these linguistic patterns are associated with many of the same neural patterns that have been documented in adolescent-onset depression, suggesting that individual differences in language use in smartphone social communication is reflected in specific neural patterns that are commonly linked with depression. While this cross-sectional study cannot draw conclusions about causal relationships between these variables, this proof-of-concept study represents an important step in identifying potentially scalable digital and brain-based biomarkers of depression in adolescence.

3-E-38 - Stability of the intrinsic brain architecture across sleep and wakefulness in children with autism

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Details

Evidence suggests that spatial resting state fMRI (R-fMRI) maps obtained during sleep in infants and young children are similar to those observed in older children and adults during wakefulness. This has supported the use of natural sleep R-fMRI to probe multiple functional systems in young and/or clinically challenging populations. Nevertheless, studies employing within-subject designs in adults have shown R-fMRI differences between sleep and wakefulness, and knowledge of the stability of brain functional architecture between states within children remains limited. Accordingly, we examined the stability of connection- and voxel-wise R-fMRI metrics in children with autism completing MRI scans while awake and asleep.

Two MRI sessions â€" one in wakefulness and one in natural sleep â€" were completed by 28 children with autism (22 male) aged 5-8 years (inter-session mean time=12Â±12 days). Scans were conducted on an Allegra 3T scanner (TR=2s, TE=15ms, voxel size=3x3x3mm) and included one 6-min awake and at least 12-min sleep R-fMRI. Data with median framewise displacement (medFD)<0.2mm were preprocessed using the Configurable Pipeline for the Analysis of Connectomes (CPAC) version 1.8.4. Functional connectivity was extracted between pairs of regions from Schaefer-400 cortical and Tian-54 subcortical parcellations. Additionally, voxel-wise measures were investigated given their relevance to typical development and autism, including amplitude of low-frequency fluctuation (ALFF), degree centrality (DC), regional homogeneity (ReHo) and voxel-mirrored homotopic connectivity (VMHC). Intra-class correlation coefficients (ICC) between-states were calculated using a one-way random model in Reliability Explorer (covariates: awake MRI age, inter-session time interval, sex, medFD). Given prior findings of the impact of scan duration on ICC, we first computed between-state ICC using 6, 9 and 12-min sleep segments. As a qualitative stability benchmark, within-state ICC was also computed using two 6-min segments within each state separately (n=16 wakefulness, n=28 sleep).

Across all R-fMRI metrics, keeping awake R-fMRI duration constant, between-state ICC was higher with 12 minutes of sleep data compared to 6 or 9 minutes. Thus, results from between-state ICC analyses are reported based on 12 minutes sleep data. Across measures, ICC within state (either wakefulness or

sleep) was higher than that computed between states. Across parcels, whole-brain summary measures of ALFF and DC had between-state ICC in the moderate range (i.e., .4 â‰¤ ICC â‰¤ .7). In contrast, ReHo, VMHC and connection-wise measures at the whole-brain level showed low between-state ICC (i.e., <.4). However, ICC substantially varied by region/circuit examined. For most voxel-wise measures, moderateâ€“high ICC was most observed in the visual and default mode networks, as well as in the salience and dorsal attention networks for ALFF and DC. Connection-wise, moderateâ€“high ICC occurred predominantly within and between higher-order functional networks.

Consistent with prior reports, within-state R-fMRI findings are generally reliable. While our results of moderateâ€“low ICC between states suggest caution in studies combining sleep and wakefulness data, results of improved ICC with at least 12 minutes of sleep data, and variable ICC by measure and spatial location can provide a guide for interpretation. For example, moderateâ€“high consistency across sleep and wakefulness were observed in the default mode network (particularly for ALFF and DC measures) and functional connectivity within and between high-order functional networks was more consistent across the two states.

3-E-39 - Identifying latent neuroanatomical factors associated with severe temper outbursts in children with ADHD: A Bayesian modeling approach

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Details

Introduction. Frequent and intense temper tantrums that exceed what is expected for a child's developmental stage are referred to as severe temper outbursts (STO). STO can pose significant challenges for a child's ability to navigate social situations, including interactions with peers, family members, and within academic settings such as school. This phenomenon is particularly prevalent in children diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD), and as such, serve as a notable source of both current and future impairments, despite not being included as part of the diagnostic criteria (Roy et al., 2013). In this study, we quantified the heterogeneity in structural (i.e., cortical thickness) and functional (i.e., resting-state connectivity) patterns related to STO and ADHD to reveal latent factors and examine their neurobiological correlates, with an aim of discerning the key contributing mechanisms underlying these highly comorbid and heterogeneous symptoms. .

Methods. In a sample of 123 children (47 STO with ADHD (STO+ADHD), 39 ADHD-controls (ADHD), 37 neurotypical-controls (NT)), we collected behavioral symptom assessments and neuroimaging data *(i.e.,* structural MRI & resting-state fMRI). For heterogeneity quantification, we first 1) performed a factor analysis on the behavioral assessments and then 2) utilized the Latent Dirichlet Allocation (LDA), a fully unsupervised Bayesian analysis framework, to parsimoniously summarize the neuroanatomical profiles into multiple latent pathological brain factors. To test for behavioral associations of the derived latent brain factors, we implemented a canonical correlation analysis between the behavioral factors and neuroanatomical brain factors. Finally, we investigated possible group differences within the latent brain

factors and conducted a resting-state seed-based connectivity analysis using the regions that showed significant group differences to gain insight into underlying functional mechanisms.

Results. The dominant factor with the highest variance explained from the behavioral assessments revealed a construct that reflects representative aspects of STO and ADHD (e.g., anger, aggression, externalizing problems, bullying, etc.). Consistent with this, significant group differences were observed, with the STO+ADHD showing the highest scores followed by the ADHD and NT groups. The 3-factor solution from the LDA analysis of cortical thickness revealed latent brain factors that showed an overall thinning, thickening and a mixture of both. Results from the canonical correlation analysis indicate a significant association between the dominant behavioral factor and the latent brain factor showing a mixture of cortical thinning and thickening. Moreover, a significant group difference (STO+ADHD>NT) was found in the dorsolateral prefrontal region of this mixed latent brain factor. Using this region as a seed for functional correlation analyses, we found reduced functional connectivity mostly concentrated in the default mode network, showing significant differences among the STO+ADHD, ADHD, and NT groups.

Conclusion. Our study sheds light on the underlying neurobiological mechanisms of STO and its frequently co-occurring condition, ADHD, highlighting the potential for novel clinical implications. Through the quantification of heterogeneity by enabling an individual to express multiple latent pathological brain factors (i.e., categorical subtype) in varying degrees (i.e., continuous), our study demonstrated the potential to reconcile the dimensional and categorical models of STO-related heterogeneity in ADHD. Revealing these latent factors and probing its neurobiological correlates provides an opportunity to tease apart the key contributing mechanisms for these highly comorbid and heterogeneous symptoms.

3-E-40 - The effects of prematurity on patterns of cortical maturation in toddlers indicated by resting EEG

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Consistent evidence has shown that early childhood adversities have detrimental influence on child behavioral and socioemotional outcomes (Sheridan & McLaughlin, 2014). One of the neural mechanisms underlying the adverse effects is cortical maturation (Sheridan et al., 2012). In the early years of a child, their brain will go through major structural and functional changes. The maturation of cortical structures in the brain is important for the neurodevelopmental processes (Deoni etal., 2015). Most studies focus

on the effect of environmental risks on child cortical maturation, yet little is known about how organic adverse conditions, e.g., being born preterm, would affect child cortical maturation. Children who are born prematurely are known to be at higher risk of dealing with abnormalities compared to children who are born at the end of their term (Jarjour, 2015). However, the neural mechanism associated with risk is unclear. To fill in the gap, we used electroencephalogram (EEG) to measure cortical maturation as a risk mechanism in toddlers who were born prematurely. To participate in the study, toddlers had to have been born before 36 weeks of pregnancy. Children were excluded if they had a history of neurological complications or serious illness. The sample was composed of 35 toddlers who were born prematurely (18 male children, *M* = 1.89 years, *SD* = 0.45 years). Within the sample, 20 participants were considered 'extremelyâ€ preterm, meaning that they had a gestational age of 22-27 weeks. The remaining 15 participants were considered 'veryâ€ preterm as they had a gestational age of 28-33 weeks. As part of the research visit, a 64-channel EEG cap was placed on the chil's head. The electrodes' impedance was verified before initiating the resting task, which consisted of the child sitting on their caregiver's lap, watching a research assistant spin a bingo cage that is filled with stuffed animals. The caregiver was given a visor to place on their head and instructed to refrain from speaking to their child or directing their attention to the cage. The resting EEG task lasted for a duration of three minutes, during which data was recorded using Brainvision ActiCHamp system with a sampling frequency of 1000 Hz. Child behavioral outcomes were assessed using parent report. Parents were asked to report their chil's vocabulary using MacArthur-Bates Communicative Development Inventories (MB-CDIs; Fenson et al., 2006). The resting EEG will be analyzed according to standard practices, using the Harvard Automated Processing Pipeline for Electroencephalography (HAPPE) pipeline (Gabard-Durnam et al., 2018). In line with prior studies, we hypothesize that toddlers in the extremely premature group will demonstrate more delayed patterns of cortical maturation, evidenced by more low-frequency (theta) activity and less high-frequency (alpha) activity, during the resting task than toddlers in the very premature group. We also expect that immature cortical maturation would be associated with delayed language development indicated by McArthurBates, suggesting higher risks of academic and behavioral maladjustment in later childhood.

3-E-41 - Differences in Brain Age in Adults with ASD as a Step Towards Understanding Atypical Brain Maturation Across the Lifespan

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Autism spectrum disorder (ASD) is a highly prevalent lifelong neurodevelopmental disorder with preliminary evidence of accelerated cognitive and neurological decline in later adulthood. Neuroimaging research, however, has almost exclusively been conducted in children and young adults with ASD. In children with ASD, previous studies have often interpreted neuroimaging findings as indicative of maturational mistiming. It is important to understand if the maturational process is disrupted only in childhood or across the lifespan in ASD and how such disruptions are related to changes in cognitive and

neurological function. Estimated ‘Brain Ageâ€ (derived from normative models trained using machine learning), has been increasingly explored as a predictor for symptoms of various neuropsychological and neurodegenerative disorders, cognitive deterioration with age, and mortality. As such, it is also a promising measure to study differences in brain maturation in ASD. We, therefore, propose a pre-registered cross-sectional study in which we hypothesize 1) that middle-aged and older adults with ASD will display a ‘positiveâ€ brain age gap (BAG; the difference between estimated brain age and chronological age) as compared to age and sex matched typically developing (TD) adults, 2) that BAG will show an increase with age in the ASD but not TD group, and 3) that a positive BAG will be associated with poorer cognitive function in the ASD group. Structural T1-weighted MRI data will be used (TR=8.78ms, TE=3.66ms, resolution=0.8mm^3, 3T GE MR750), available from an ongoing longitudinal study on middle-age and aging in ASD. Scans will be visually inspected and only data passing rigorous quality control will be used. The sample will include at least 70 participants between 40 and 70 years old (n=30 with ASD, n=40 TD, mean age=52.88). Brain age will be estimated using BrainageR (Cole et al. 2017) which first processes raw structural MRI data through SPM12 to derive individual tissue probability maps and then compares these to a normative model trained on data from 18-90 year-olds (n=3377) from multiple open-source datasets. A linear model, including factors for diagnostic group, age and age-by-group interaction, will test for differences in BAG between the ASD and TD groups (Hypothesis 1) and for group differences in the effect of age on BAG (age-by-group interaction; Hypothesis 2), while controlling for data quality (gray-white contrast). Additional analyses will test for effects of sex, co-occurring medical conditions (e.g. cardiovascular disease) or SES to rule out potential confounds. Partial correlations (controlling for data quality and non-verbal IQ) will be performed to (Hypothesis 3) test for associations between BAG and executive function (assessed using the Delis-Kaplan Executive Function System [DKEFS]) and verbal learning (using the California Verbal Learning Test [CVLT-II]). Preliminary data will be presented for a subset of participants who have completed a second longitudinal timepoint (â‰¥ 5 years after initial enrollment) to test if BAG increases longitudinally with age in the ASD group. Establishing whether there is an increased brain age gap in adults with ASD compared to typically developing adults may establish reference points for improved understanding of lifespan changes in brain structure and function in autism. If our hypotheses are confirmed, further research will be required to explore the causes of brain age gaps in the ASD population longitudinally in larger cohorts and across a wider age range.

3-E-42 - Testing the generalisability of transdiagnostic latent patterns in functional brain networks to a Norwegian sample of youth

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Details

Introduction

Replicability and generalisability of neuroimaging findings across samples remains a challenge in the field (Botvinik-Nezer & Wager, 2022). While it is becoming increasingly common to validate results using unseen data from the same sample, fewer studies attempt to validate their results across samples. Recently, wederived brain informed dimensions of psychopathology based on covariance in functional brain networks in a developmental clinical sample from the US (Voldsbekk et al., 2023). These

dimensions recapitulated the psychopathology hierarchy, with a general psychopathology factor and increasingly narrow dimensions. Similar dimensions of psychopathology have been identified in a population-based sample of children, using measures of both brain structure and functional connectivity (Kebets et al., 2023), alluding to a generalisable link between brain measures and the psychopathology hierarchy. However, it remains to be clarified whether these patterns have predictive utility across samples.

Objectives

The current study aims to address this question of generalisability and predictive utility by investigating whether the previously identified link between functional connectivity (FC) and psychopathology can be detected in a Norwegian convenience-based sample of youth. Specifically, we aim to not only validate the association in a new sample, but also to investigate whether the identified latent pattern has predictive utility. Specifically, we will investigate whether a) the FC side of the latent pattern can be replicated in a new sample, and b) if this pattern can predict levels of psychopathology in the new sample.

Methods/Analysis plan

In the previous work, we used partial least squares (PLS) (Krishnan et al., 2011) to identify latent variables (LV) between FC and symptom scores obtained from the Child Behaviour Checklist (Achenbach & Rescorla, 2001). Each LV represent a distinct pattern that relates a weighted set of symptoms to a weighted set of FC connections (i.e., edges). The sample consisted of children and adolescents aged 5-21 (n = 1880, 62% male) from the Healthy Brain Network study (HBN) (Alexander et al., 2017). Brain networks were derived using the Schaefer parcellation (Schaefer et al., 2018), resulting in 4950 unique partial correlations (i.e., edges). This work identified five LVs linking distinct patterns of functional connectivity to the following dimensions of psychopathology: a general psychopathology factor, externalising-internalising, neurodevelopment, somatoform and thought problems, respectively.

In the current work, we will perform out-of-sample validation of these detected patterns in the BRAINMINT sample, an independent convenience-based sample of Norwegian youth aged 9-25. To do this, we will first estimate corresponding brain network edges in BRAINMINT resting-state fMRI data. Then, we will decompose the BRAINMINT FC edges by multiplying them with the imaging weights estimated in the HBN PLS analysis. Then, to establish whether the resulting FC maps in BRAINMINT overlap with those in HBN, we will correlate them and test their significance using permutations. Next, we will correlate the derived BRAINMINT FC pattern with symptom scores in BRAINMINT, to test the generalisability and predictive utility of the FC pattern in a new sample. To do this, we will correlate the connectivity loadings in BRAINMINT with symptom scores obtained from the Strength and Difficulties Questionnaire (Goodman, 1997). To assess the reliability of the associations between BRAINMINT connectivity loadings and symptom scores, we will run 1000 bootstraps using resampling with replacement.

General implications

This work aims to determine the degree to which the link between FC and psychopathology in a US developmental clinical sample can be extended to a Norwegian convenience-based sample of youth. The implication of this work is to establish the degree of generalisability and reproducibility of brain-behaviour associations across samples. This represents an important contribution to the neuroimaging field, in which reproducibility long has remained an untouched issue.

3-E-43 - Connectivity Between Striatum and Task Positive Networks is Modulated by Long-term Stimulant Exposure in Childhood ADHD, an ABCD study

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Details

Background

Stimulants (methylphenidate and amphetamines) are the first-line pharmacological treatment for Attention-Deficit/Hyperactivity Disorder (ADHD) and their acute administration attenuates symptoms via upregulation of striatal dopamine activity. An emerging area of research uses resting-state functional connectivity (rs-FC) to test the neural correlates of stimulant exposure and points to potential modulatory effects on rs-FC. However, progress is stymied by relatively small sample sizes and methodological heterogeneity, with little known about the effects of long-term exposure. We explored striatal-cortical rs-FC correlates of long-term stimulant exposure in youth with ADHD and their relation to symptom improvement across two years. Advantages of our approach include a large sample size as well as a focus on long-term outcomes, both made possible by use of data from the Adolescent Brain Cognitive Development (ABCD) study.

Methods

We selected children (n=202; 77 F; mean age at baseline=9.9 years [sd=0.65]) from the ABCD study with moderate to severe ADHD symptoms at baseline (based on the Kiddie Schedule for Affective Disorders and Schizophrenia and T score>=60 on the Child Behavior Checklist ADHD Problems Scale) who had complete data and were recommended by the ABCD study for rs-FC data analysis. Using pretabulated rs-FC data, in which striatal seeds were 6 ROIs from the ASEG atlas and cortical networks were 10 networks from the Gordon atlas, we constructed Bayesian hierarchical models in which change in striatal-cortical rs-FC across two years (2-year follow-up baseline) predicted stimulant exposure (n=89), controlling for head motion, gender, and socioeconomic status. Given the comorbidity and polypharmacy in the sample, sensitivity analyses tested the specificity of initial results and tested for associations with amount of stimulant exposure. Lastly, for striatal-cortical connections associated with stimulant exposure, we explored correlations with ADHD, externalizing, and internalizing symptom improvement.

Results

Bayesian hierarchical models revealed strong evidence, as defined by 0 falling outside the 95% credible interval for an estimated effect, for associations between stimulant exposure and change in 2 striatal-cortical functional connections at rest, which demonstrated specificity in two sets of control analyses. These were left caudate-frontoparietal network (Est.=-5.13, sd=1.86, 95% QI=[-8.86,-1.58]) and left putamen-ventral attention network (Est.=-2.94, sd=1.19, 95% QI=[-5.35,-0.63]). Additional associations emerged which were strong but weakened when analyses were limited to children exclusively exposed to stimulants, including with left putamen-cinguloparietal network (Est.=2.00, sd=0.73, 95% QI=[0.61,3.48]) and left nucleus accumbens-dorsal attention network (Est.=-4.13, sd=1.96, 95% QI=[-8.05,-0.34]). We did not identify any associations with the amount of stimulant exposure, however, there was an interaction between exposure and rs-FC change for left putamen-ventral attention network when predicting ADHD symptom improvement at the 2 year follow-up, controlling for baseline symptoms (Est.=5.22, sd=2.47, 95% QI=[0.47,10.22]). Post-hoc tests indicate this was driven by the non-exposed group, for whom left putamen-ventral attention network rs-FC attenuated over 2 years for children whose symptoms no longer met clinical criteria (t(110)=2.2, p=.030).

Discussion

Results contribute to the burgeoning literature on the modulatory effects of stimulants on rs-FC, and our study is among the first to investigate the effect of chronic stimulant exposure. Specifically, results reveal the stimulant effect on the longitudinal rs-FC changes between left caudate and putamen and canonical task-positive networks, such as frontoparietal and ventral attention networks. More broadly, the study highlights the diversity and particularity of questions that can be addressed using large multi-site datasets such as ABCD.

F- Education

3-F-44 - Positive parenting buffers the negative impact of weaker inhibitory control network connectivity on adolescents' school performance

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Details

In past decades, the positive role of self-control in students' academic success has attracted plenty of scholarly attention (for a review, see Duckworth et al., 2019). However, fewer studies have linked adolescents' neural development of inhibitory control system in the brain and their academic achievement, especially using a longitudinal approach. Moreover, less is known about the role of parents in this association. Therefore, using the large-scale longitudinal data from the Adolescent Brain Cognitive Development (ABCD) study, the current study took an integrative biopsychosocial approach to explore the longitudinal link between inhibitory control network and adolescents' school performance, with attention to the moderating role of parental monitoring and parental acceptance.

Data were obtained from baseline (T1) and two-year follow-up (T2) of the ABCD study (data release 4.0). Among the full sample of 11876 adolescents at T1, a total of 9627 adolescents (mean age = 9.94 years; 50% girls) who passed imaging quality control criteria of resting-state fMRI were included in the analyses. At T1, adolescents underwent a 20-minute resting-state fMRI scan. The ABCD team has

calculated cortical networks' within- and between- network connectivity and the connectivity between cortical network and subcortical regions (Casey et al., 2018). Following prior research (Chen et al., 2023; Nee, 2021), the current study focused on the within-network functional connectivity of the frontoparietal network (FPN) and the connectivity between FPN and striatum. At both T1 and T2, parents reported on how well their adolescents do in school. At T1, adolescents reported on *parental monitoring* (5 items on parents' monitoring and knowledge of adolescents' daily behavior) and *parental acceptance* (5 items on parents' warmth, acceptance, and responsiveness).

Analyses were conducted using mixed-effect models with participants' site and family included as random intercepts and demographic variables (i.e., adolescents' age and gender, parents' educational attainment, marital status, and household financial adversity) included as fixed-effect covariates. Results showed that lower FPN within-network connectivity was associated with worse school performance at T2 ($\hat{I}^2$ = .02, p = .03), controlling for school performance at T1. However, the longitudinal association between adolescents' FPN-striatum connectivity and school performance was, albeit in the same direction, not significant ($\hat{I}^2$ = .01, p = .19). Notably, parental monitoring moderated the link between FPN within-network connectivity and school performance (interaction term: $\hat{I}^2$ = -.02, p = .02), as well as between FPN-striatum connectivity and school performance ($\hat{I}^2$ = -.02, p = .03). Follow-up simple slopes analyses found that the associations between inhibitory control network connectivity and school performance were only significant when parental monitoring was low (i.e., 1 SD below the mean), but not when parental monitoring was high (i.e., 1 SD above the mean), suggesting the buffering role of parental monitoring. Moreover, a similar pattern was found with regard to the moderating role of parental acceptance, although the interaction effects were only marginally significant (parental acceptance Ã— FPN-FPN: $\hat{I}^2$ = -.02, p = .07; parental acceptance Ã— FPN-striatum: $\hat{I}^2$ = -.02, p = .06).

Taken together, our findings demonstrate underdeveloped inhibitory control network as a risk factor for adolescents' academic development and highlight positive parenting practices as protective factors for academic development among adolescents with delayed development of inhibitory control network.

3-F-45 - Exploring Differences Between Movement and Math Performance in Timed and Untimed Math Tasks and its Relationship with Anxiety

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Details

Background: Mathematics can be a difficult concept for students to grasp and the development of math skills is impacted by many factors. This necessitates an interdisciplinary approach to understand what impacts math performance. Math anxiety is a factor known to have a negative effect on performance (Zhang et al., 2019). Based on recent research approximately 41% of students experience some level of math anxiety (SzczygieÅ, & Pieronkiewicz, 2022). Timed math tasks also had a negative effect on performance when compared to untimed tasks, though this relationship to anxiety is not well-known (Tsui & Mazzocco, 2006). Anxiety can manifest physically in many ways. Trembling, general body movements, and restless body movements are all associated with anxiety (Paulick et al., 2018).

Combining behavioral and biopsychological data could be a novel approach to understanding math performance and math anxiety.

Objectives: The purpose of the current study was to integrate behavioral and biophysiological data to evaluate how timed versus untimed tasks, movement, and anxiety relate to overall math performance.

Methods: Data were collected as part of a larger study assessing brain synchrony of parent and child dyads. For the current analyses, participants were 39 children aged 6-12 years (M = 8.85, SD = 1.91) with average IQ. The Woodcock Johnson Achievement test was used to gather information on math performance in both timed and untimed tasks. These assessments were video recorded to gather motion energy analysis (MEA) data. To assess math anxiety, children answered questions about the degree of anxiety they experience when practicing or talking about math.

Results: Participants performed significantly better on untimed math tests (M = 102.51 standard score, SD = 17.59) than on timed subtests (M = 92.87 standard score, SD =12.93); $t(38) = 4.38$, $p < .001$, with standard scores falling in the average range for both timed and untimed subtests. Additionally, participants overall moved significantly less in untimed math subtests mean MEA (M = 206.62, SD = 45.90) than on timed subtests (M = 238.73, SD =193.42); $t(38) = -1.875$, $p < .05$, though there were no differences between maximum MEA variability in timed and untimed tasks. Math performance during untimed subtests was significantly negatively related to anxiety, $r(37) = -33$, $p < .05$, though this relationship was not found for timed tasks. In examining the correlations between movement, performance, and anxiety during untimed and timed tasks, there was a moderate negative correlation between maximum movement variability and math anxiety, $r_S(37) = -39$, $p < .05$.

Conclusions: There were significant overall movement differences between timed and untimed math tasks, with participants moving more overall during timed tasks than untimed tasks. There was also a significant difference in performance, with performance on untimed math tasks being significantly higher than performance on timed tasks. The higher the overall movement variability, the lower self-reported math anxiety was, suggesting that movement may serve as a coping strategy for anxiety. Despite this, overall movement and anxiety did not appear to impact performance during timed or untimed math tasks. These results add to the general knowledge of the factors that impact math anxiety and potentially math performance. The implications of this research could lead to new interventions and promote math performance. However, more research is needed to elucidate the relationship between movement, math anxiety, and math performance.

3-F-46 - Exploring the relationship between Latinx American youth's familism values and school disengagement: Identifying potential neural moderators

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Details

Cultural values play a significant role in shaping Latinx American youth's development over time (e.g., Rivas-Drake et al., 2014). More specifically, familism, which is a cultural construct that involves one's beliefs about familial obligation and familial closeness, has been theorized to serve as an important protective factor for Latinx youth (Sabogal et al., 1987). For example, previous research has shown that among Latinx American families, youth's endorsement of familism values consistently predicts their academic outcomes, including school engagement and academic achievement (Constante et al., 2019; Esparza & SÃ¡nchez, 2008; Valenzuela & Dornbusch, 1994). However, given that adolescent brain development is sensitive to sociocultural input (Foulkes & Blakemore, 2018), it is unclear how cultural values such as familism interact with youth's neural systems to shape their academic outcomes. Therefore, the present study examined the association between Latinx American youth's familism values and their school disengagement, with attention to the moderating role of youth's neural sensitivity to personal reward.

Data were obtained at the two-year follow-up of the Adolescent Brain Cognitive Development (ABCD) study, which was the first wave that the ABCD study measured youth's familism values. A total of 1258 Latinx American youth (mean age = 11.90 years; *SD* = .65 years; 47% girls) were included. The Monetary Incentive Delay (MID) task was used to assess youth's ventral striatum and amygdala activity during reward processing (i.e., reward anticipation and reward receipt) (Casey et al., 2018; Knutson et al., 2000). Youth reported on their familism values using the Mexican American Cultural Values Scale (Knight et al., 2010), which includes items from three subcategories (i.e., family support, family obligation, and family as referent). In addition, youth reported their school disengagement using the School Risk and Protective Factors questionnaire (Zucker et al., 2018).

Analyses were conducted in the context of structural equation modeling (SEM) with youth's familism values specified as a latent variable with three indicators (i.e., family support, family obligation, and family as referent). Results indicated that youth's familism values were associated with lower school disengagement when controlling for demographic covariates (Î² = â€“.16, $p < .001$). We further examined whether youth's neural sensitivity to reward modulated the link between their familism values and school disengagement. Results suggested that youth's ventral striatum activation during both reward anticipation and receipt moderate this link (interaction term: Î²s > .06, *p*s < .05). In addition, youth's amygdala activation during reward receipt also had a similar moderating effect (interaction term: Î² = .09, $p = .001$). Follow-up simple slopes analyses suggested that the associations between youth's familism values and school disengagement were stronger when youth's neural sensitivity to reward was low (i.e., 1 SD below the mean) (Î²s < -.24, *p*s < .001), but were weaker or insignificant when youth's reward sensitivity to reward was high (i.e., 1 SD above the mean) (Î²s > -.11, *p*s > .01).

Taken together, these findings further bolster the notion that familism values may significantly influence Latinx American youth's school adjustment. More importantly, these results indicate that youth's heightened affective neural sensitivity to reward may dampen the protective role of familism on their academic adjustment, suggesting that neural reactivity in the ventral striatum and amygdala may serve as notable markers of youth's neurobiological susceptibility to sociocultural context. Ultimately, such work may have important implications for developing neurobiologically informed policies or interventions which aim to promote positive development among minority youth.

3-F-47 - Functional Connectivity Profiles in 1st Graders Identified for Math Support in the Classroom

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Details

Mathematics achievement predicts future life outcomes, but many children persistently struggle to develop this essential skill. Previous studies have shown that children with math learning disabilities identified in lab settings have increased resting state functional connectivity (rsFC) between frontal and parietal regions when compared to typically developing peers matched on other cognitive abilities. However, it still needs to be determined how rsFC relates to children whose mathematics learning difficulties may have a broader etiological basis. We will explore rsFC differences between students with typical mathematics achievement and students identified for intensive mathematics support in their school settings using a searchlight and a region-of-interest (ROI) approach. We hypothesize that each method will indicate connectivity differences in a set of frontal and parietal regions typically associated with domain-general cognitive abilities, such as executive functions, and domain-specific abilities, such as number processing. **Methods:** Data has already been collected and preprocessed. 60 1st graders with typical mathematics achievement, and 47 1st graders identified for intensive mathematics support took part in the study. Participants completed a standardized mathematics achievement (ASPENS) task to confirm their mathematics achievement. After a mock scan, participants completed a high-resolution anatomical T1-volume scan (GRAPPA accelerated MPRAGE, TR = 2500ms, TE = 3.43ms, TI = 1100ms, flip angle = 7Â°, 1 mm isotropic resolution) and a resting-state fMRI (TR = 780ms, TE = 32ms, flip angle = 55Â°, 2.5mm in-plane resolution, 2.5mm slice thickness, and multiband acceleration factor = 3) in a Siemens 3T Skyra scanner. In the resting-state data acquisition, participants were instructed to keep their eyes open and 'do nothing and let your mind wander.â€ The FIRMM software was used to assess motion in real time and ensure sufficient high-quality data. Data preprocessing was conducted with FSL. Framewise displacement (FD) was identified with FSL Motion Outliers. Motion was treated with a combination of volume censoring and independent component analysis denoising, using FLS Melodic and FMRIB's ICA-based Xnoiseifier (FIX). FSL brain extraction tool (BET) was used, and skull-stripped anatomic scans were then registered to a 2mm MNI space. **Analyses Plan:** We will conduct a searchlight-based MVPA analysis using CoSMoMVPA toolbox. We will define the searchlight with a 4mm radius and run the vector classification analysis for each searchlight position within a 10-fold cross-validation design. A leave-pair-out-cross-validation approach will be adopted, such that 2 participants will be kept for testing the classifier, and the remaining participants will be used to train it. All possible combinations of participants will be tested. The observed results will be randomly resampled 10,000 times using Monte Carlo permutation, and a 95% confidence interval will be adopted as a cut-off. We will also conduct an ROI analysis using the CONN toolbox. ROI analyses will use subregions of the intraparietal sulcus, angular gyrus, and hippocampus as seeds. First, the time course across all voxels within these regions will be averaged. Then, a resting-state connectivity map will be created for each participant by correlating the average time course of the seed regions with the time course of every other voxel in the brain. Using Fisher-to-z transformation, we will convert the correlation scores to z-scores and then perform group comparisons. **Implications:** Results will inform us about how rsFC differs across students with typical mathematics achievement and students identified for intensive mathematics support in the first year of elementary school. Understanding the underlying mechanisms related to mathematics learning may have implications for mathematics difficulties diagnosis and interventions.

G – Environment (Stress, SES)

3-G-48 - The role of early social adversity on neural function during emotional (or threat-related) interference: implications for depression and suicidality.

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Details

Introduction: Adolescence is a period of heightened risk for the development of depression. Recent work indicates that the presentation of depression during adolescence is highly heterogeneous, including fluctuations in the severity of symptoms and suicidality. There is a critical need to understand the mechanisms by which experiences in childhood and adolescence confer risk for the development of mood symptoms and psychopathology. Social adversity and increased neural reactivity to social threat and altered emotion regulation are known risk factors for adolescent depression and suicidality. Therefore, we propose a model in which greater neural activity in subcortical regions and reduced activity in prefrontal cortical regions while resisting interference from threat-related distracters mediates the relationship between history of childhood social adversity and increased adolescent depressive and suicidal symptom severity. **Methods:** Participants include 154 adolescents (ages 12-18; *M* = 15.17-years-old, 65% female) with and without clinical depression from a completed 5-wave (baseline and 4 follow-up assessments at 6, 12, 18 and 24 months) longitudinal study examining the associations between neural, emotional, cognitive and behavioral factors and trajectories of mood symptoms among depressed youth. Data will include: (1) baseline past social adversity assessed via the emotional abuse and neglect items from the child Childhood Trauma Questionnaire (CTQ), (2) baseline current emotional interference as indicated by slower reaction times and reduced amygdala ventrolateral prefrontal cortex connectivity during the 2-back threat-related (vs. neutral) emotional face distracters of an emotional working memory fMRI task (Manelis et al, 2022), and (3) baseline and 12-month follow-up depressive and suicidal symptom data from the child Mood and Feelings Questionnaire (Costello and Angold, 1988). **Results:** Using linear regression, we will analyze whether past social adversity as measured at baseline is associated with increased depressive and suicidal symptoms at the 12-month follow-up visit. We will analyze whether this relationship is partially mediated by behavioral and neural markers of emotional interference at baseline, after taking into consideration covariates such as age, sex, baseline depression symptoms, and medication status. This design and analysis plan will be presented for feedback, but no data analysis of main study aims will take place before the conference. **Conclusion:** Results will inform our understanding of mechanisms by which early stressful social experiences contribute to increasing depression severity and suicidality in adolescents varying in levels of depressive symptoms. Findings could thus provide insight into novel and earlier neural and behavioral targets for intervention for adolescents with a history of early adversity.

3-G-49 - Dimensions of early-life adversity co-occurrence and associations with cortico-limbic functional connectivity in the ABCD Study

Alexis Brieant [1, 2], **Anna Vannucci** [3], **Hajer Nakua** [4], **Jenny Harris** [5], **Drew Ward** [2], **Nim Tottenham** [3], **Dylan Gee** [2]

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Details

Background. Early-life adversity (ELA) has profound consequences for youth neurodevelopment and adjustment. Experiences of adversity are heterogeneous and interrelated in complex ways that can be difficult to operationalize and organize in developmental research. Data-driven approaches are one way to characterize the co-occurring nature of ELA and to elucidate associations with brain function. The cingulo-opercular (CO) network is a cortical executive network involved in self-regulation, and prior research has shown that resting-state functional connectivity (RSFC) between the CO network and the amygdala is sensitive to global indices of adversity exposure (Brieant, Sisk, & Gee, 2021). However, increasing theoretical and empirical work suggests that different types and features of adversity may have distinct neurodevelopmental effects (e.g., McLaughlin et al 2021; Ellis et al., 2022). Thus, we expected that distinct dimensions of ELA co-occurrence would differentially relate to CO-amygdala RSFC.

Method & Results. In a subsample of participants (*N* = 7,115) from the Adolescent Brain Cognitive Development (ABCD) Study at baseline (9-10 years of age), we identified 60 environmental and experiential variables that reflect adverse experiences. An exploratory structural equation model identified 10 robust dimensions of ELA co-occurrence pertaining to 1) caregiver psychopathology, 2) socioeconomic disadvantage and lack of neighborhood safety, 3) secondary caregiver lack of support, 4) primary caregiver lack of support, 5) child report of family conflict, 6) caregiver substance use and biological separation, 7) family anger and arguments, 8) family aggression, 9) trauma exposure, and 10) caregiver lack of supervision. This 10-factor solution provided excellent fit to the data ($Ï‡^2$ = 4260.83, *df* = 1215, $p < .001$, RMSEA = 0.02, CFI = .97).

Next, we tested associations between these factors and RSFC between the CO network and the amygdala (i.e., correlations between within-network connectivity and amygdala ROI). Specifically, we tested a Bayesian multivariate multilevel model with the 10 ELA factors as independent variables and CO-amygdala RSFC (left and right hemispheres) as dependent variables (controlling for age and sex). We split the sample into discovery (*n* = 4,687) and replication (*n* = 1,996) sets to assess the reproducibility of results. In the discovery set, the model accounted for approximately 5-8% of the variance in CO-amygdala connectivity ($R^2_{left\text{-}amyg}$ = .08, 95% *CI* = .06, .09; $R^2_{right\text{-}amyg}$ = .05, 95% *CI* = .04, .06). There were small, significant correlations between predicted RSFC (from the discovery set model) and actual RSFC in the independent replication set (*r*s = .14 - .22, *p*s< .001). Associations between ELA dimensions and RSFC were largely consistent across the discovery and replication sets. The factor representing socioeconomic disadvantage/lack of neighborhood safety was the only significant factor and demonstrated a small but robust association with RSFC (b = -.02, 95% *CI* = -.02, -.01) such that greater disadvantage/lack of safety was associated with stronger negative connectivity between the CO network and left amygdala.

Conclusions. Our findings suggest that family and neighborhood economic disadvantage and lack of neighborhood safety are associated with stronger negative CO-left amygdala connectivity. Prior research has shown this pattern of connectivity to be associated with broad stress exposure, and we expand upon this work to show how specific types of adverse experiences may be most salient for this circuitry. This may be consistent with observations that smaller cortical volumes and greater cortical thinning are linked to both socioeconomic disadvantage and neighborhood violence (e.g., Machlin et al., 2019; Miller et al., 2022; Whittle et al., 2017). Limitations and future directions (e.g., extensions with longitudinal imaging data) will be discussed.

3-G-50 - Differentiating the influence of socioeconomic status and negative live events on the functional brain development in children and adolescents.

Brianna Hughes [1], **Bobby Stojanoski** [1]

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Details

Objective: Childhood and adolescence is marked by significant changes to the functional properties of the brain that support various aspects of higher-level cognition. This developmental period is also sensitive to environmental factors, which can have an outsized influence on brain development and the cognitive processes they support. **For instance, l**ow socioeconomic status (SES) and adverse experiences have been shown to have detrimental effects on neurocognitive development. However, measures of SES often encompass aspects of adversity, but it is likely that SES (finances) and adversity (negative life events) have unique contributions to the developing brain. In the current study, we examined the differential influences of financial resources from negative adverse experiences on the inherent functional architecture of the developing brain. **Methods:** Independent components analysis on resting state fMRI data from children and adolescents aged 6 to 19 (n=79; acquired from the Healthy Brain Network) was computed to identify seven networks (Auditory, Default Mode Network, Left Executive Control Network, Right Executive Control Network, Hippocampal, Language, and Salience) of interest. Spatial and temporal properties of the seven networks were compared to a large cohort of adult (total of 1200; separately for male and female) resting state data to compute a measure of neural maturity (degree of similarity between the child and adolescent brains with the adult brains). Regression analysis was used to determine the association between age, parental education (SES), number of negative life events, and executive functioning (WISC) on neural maturity value. **Results:** We found a strong positive relationship between Age and Parental Education (SES) and neural maturity in the Right Executive Control Network (ECN) (R^2 = .065). We also found a strong relationship between parental education and executive functioning (r = .264, p= .027). Interestingly, we failed to find an association between neural maturity (across the seven networks) and executive functioning and the number of experienced negative life events. **Conclusion:** We found children and young adolescents had an underdeveloped central executive network (more distributed), but becomes adult-like by 18 years of age. We also found that parental education, but not adversity, was associated with the maturity of the central executive network, and executive functioning, suggesting that SES and adversity have differential influences on functional brain development.

3-G-51 - Is breastfeeding associated with individual differences in resting brain activity of one-month old infants?

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Details

Breastfeeding is considered the "gold standard" food source in the first months of postnatal life. The World Health Organization and American Academy of Pediatrics recommend breastmilk as the only source of sustenance for infants from birth to six months old. In addition to being a critical source of nutrition, a large body of evidence suggests that breastfeeding has important consequences for an infant's cognitive and socio-emotional development, as well as their long-term physical and mental health. However, it is not yet clear whether breastfeeding is associated with individual differences in infants' brain function. Moreover, breastfeeding is correlated with family characteristics and postnatal experiences that may shape infant brain function, such as family socioeconomic status and postpartum bonding, but it is not well understood whether breastfeeding may affect the developing brain independent of these factors. The goal of this study was to examine whether breastfeeding is associated with individual differences in infant brain activity approximately one-month after birth (N = 159; $M_{ageinweeks}$ = 5.61; 40% White; 55% female). Maternal age, parental education, family income, and postnatal bonding were collected from mothers, and resting EEG (theta, alpha, beta, and gamma power) was collected from infants. 67 mothers reported exclusive breastfeeding (42.1%), 24 mothers reported exclusive formula feeding (15.1%), and 68 mothers reported mixed breastfeeding and formula feeding (42.8%). Infants who were exclusively breastfed had parents who reported more years of education compared to infants who were mixed-fed, $t(133)=4.68$, p <.00, or formula-fed, $t(89) = 6.11$, p <.001; higher income-to-need compared to infants who were mixed fed, $t(126) = 3.46$, p <.001, or formula fed, $t(83) = 5.35$, p <.001; have older mothers compared to infants who were formula-fed, $t(89) = 3.58$, p <.001; and have parents who reported better postpartum bonding compared to infants who were formula-fed, $t(89) = 2.91$, p <.001. Infants of mothers who were exclusively breastfed showed higher relative gamma power (M = 0.031, SD = 0.017) compared to infants of mothers who were exclusively formula-fed (M = 0.020, SD = 0.007, $t(89) = 2.94$, p = 0.004). However, when controlling for income-to-needs, child age, maternal age, parental education, and postpartum bonding, group differences were no longer statistically detectable $F(2,140) = 1.65$, p = 0.197. There were no significant differences in relative theta, alpha, and beta power between infants who were exclusively breastfed compared to infants who were mixed-fed or formula-fed, ps > .10. Taken together, these data suggest that family characteristics and experiences associated with breastfeeding may have a stronger influence on infant brain function than breastfeeding in and of itself. Future directions will be to further investigate these relationships longitudinally across the infants' first three years of life.

3-G-52 - Childhood socioeconomic status and the pace of structural neurodevelopment: Accelerated, delayed, or simply different?

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Details

Adverse childhood experiences and access to resources in childhood, as measured by socioeconomic status (SES), have been consistently linked to children's neurodevelopment. Recent theories have proposed that experiencing adversity or low SES early in life may alter the pace of neurodevelopment. While most of these models focus on adversity broadly, they have been expanded to include SES, given that SES likely impacts neurodevelopment via similar pathways (although note that adversity and low SES are related but not interchangeable constructs). Importantly, these theories make contrasting predictions about whether adverse environmental experiences are associated with an acceleration or

delay in the pace of neurodevelopment. While some models propose that adversity and/or low SES may lead to an acceleration in the pace of brain maturation, another recent model argues that delayed development is also a possibility. Empirically testing these predictions has been challenging as a clear articulation of specific evidence that would align with either acceleration or delay has not been provided. Further, most studies have relied on cross-sectional designs that cannot be leveraged to investigate these questions.

To adjudicate between these competing hypotheses, our review contextualizes theoretical predictions within the context of normative structural neurodevelopment during infancy, childhood, and adolescence. We then systematically review extant evidence from longitudinal studies to ascertain whether low SES is associated with an accelerated, delayed, or a simply different trajectory of neurodevelopment. We find that while none of these theories completely explain observed SES-related differences in structural neurodevelopment, current evidence indicates that low SES is linked to brain structure trajectories that are more in line with a delayed or simply distinct developmental pattern rather than an acceleration in neurodevelopment. Based on the empirical evidence, we argue that low SES is associated with simply different developmental trajectory characterized by lower cortical thickness and volume at all ages from infancy through adolescence as well as slower growth and slower thinning over time. This trajectory is most consistent with the evidence, which shows lower thickness, volume, and surface area and slower rates of change in individuals from low SES backgrounds at all ages. Accordingly, we present a novel framework that suggests that low SES may be associated with a distinct pattern of brain maturation that is not only about the pace of the attainment of milestones (i.e., slower or faster) but also the milestones themselves.

3-G-54 - Co-creating programmatic developmental neuroscience research with communities under study

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Details

Background: Although influential neurodevelopmental work has addressed effects of trauma and other forms of adversity on the neurobiology of threat learning and anxiety in youth, effects of stressful experiences specific to ethnically and racially marginalized groups have received scant consideration in extant research. Our lab is beginning to address this gap with a longitudinal study of effects of ethnic-racial discrimination in 150 10â€“13-year-old Mexican-origin Latina girls, a historically understudied population that encounters unique and compounding cultural stressors like sexism, racism, and economic marginalization. We plan to use computational fMRI techniques to examine the effects of cumulative stress exposure on neurodevelopment due to ethnic-racial discrimination. This presentation highlights two foundational components of our research program: (1) the creation of a Community Advisory Board (CAB) to formalize researcher-community partnerships by placing the concerns of the community on our agenda and (2) initial evidence documenting links between parental experiences of ethnic-racial discrimination and children's anxiety symptoms. Together, these components will set the stage for subsequent waves assessing longitudinal associations with threat neurocircuitry and anxiety.

Methods: Well-validated measures assess parental reports of experiencing ethnic-racial discrimination, including the Perceived Discrimination Scale, the Everyday Discrimination Scale, and the Experiences of Discrimination Scale, assessing the frequency and the appraisal of discriminatory events. Parents also report their children's anxiety symptoms, via the SCARED-Parent total and subscales. A latent discrimination score will be constructed from item-level responses and hierarchical regression analyses will test associations between parental discrimination experiences and children's anxiety symptoms, over and above age, socioeconomic status, and parental education. One hundred and fifty Mexican-identifying caregivers have completed the first wave of data collection. The presentation will describe efforts by our lab to form a CAB. I will discuss insights gleaned from three meetings and share how community members can act as key collaborators who can help inform research protocols, provide us with real life examples of issues under study, voice the concerns of the community, assist in developing community education resources and help disseminate scientific findings.

Discussion: Community-based participatory research includes community members in the scientific co-creation at multiple steps in the research process. However, they are rarely, if ever, used in neuroscience research. Fostering a full partnership between the research team and the community under study ensures that researchers gain an understanding of the context in which community members assess the risks and benefits of research.

3-G-55 - Infant White Matter Cingulum Microstructure Moderates the Association of Maternal Anxiety Symptoms with Infant Behavioral Outcomes

Lauren Costello [1, 2], **Jessica Buthmann** [2], **Ian Gotlib** [2], **Emily Dennis** [3], **Lauren Borchers** [2], **Julian Joachimsthaler** [2]

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Details

Background: Infant vocal reactivity is an index of the amount of vocalization exhibited by infants in their daily lives. Researchers have found infant vocal reactivity to be associated with maternal sensitivity and infant behavioral development, as well as with language development. Maternal symptoms of anxiety have been linked to aberrant infant white matter microstructure in regions important to cognitive-emotional responses, sensory processing, and socio-emotional functioning, and to maladaptive infant behaviors. Few studies, however, have examined the role of the cingulum bundle, a tract that supports cognitive and affective processing, in infant development. We hypothesized that fractional anisotropy (FA) of the cingulum bundle will moderate the relation between maternal anxiety symptoms and infant vocal reactivity at 6 months.

Methods: At six months postpartum, 38 mothers (*M*=32.58, *SD*=4.75) completed the Beck Anxiety Inventory (BAI). Infant vocal reactivity was assessed through maternal report at 6 months of age using a subscale of the Infant Behavior Questionnaire (IBQ). Diffusion-weighted MRI was acquired from 38 infants born full-term (18F, *M*=6.73, *SD*=0.42), and deterministic tractography was performed to

segment the cingulum bundles. We used hierarchical multiple regression to test whether infant cingulum bundle FA moderates the association of maternal anxiety symptoms with infant vocal reactivity, covarying for infant gestational age at birth, infant age at scan, and infant race.

Results: Infant cingulum FA moderated the association of maternal anxiety symptoms with infant vocal reactivity (ð›½=.-.589, 95% CI [-.984, -.193], *p*<. 005). Simple slopes analysis revealed that infants with lower cingulum FA values born to mothers who reported higher anxiety symptoms had higher vocal reactivity scores (ð›½=-.194, 95% CI [-.187, .575], p =.307). whereas infants with higher cingulum FA values born to mothers who reported higher anxiety symptoms had lower vocal reactivity scores (ð›½=-.984, 95% CI [-1.698, -.270], *p*<.009).

Discussion: The extent to which infants vocalize depends on their everyday social interactions with caregivers; these interactions, in turn, help them learn that their vocalizations have effects on the social behaviors of those in their environment (e.g., eliciting maternal responsiveness). Our finding that infant cingulum FA values moderated the relation between maternal anxiety symptoms and infant vocal reactivity at 6 months indicates that levels of FA in the cingulum bundle are a possible risk or protective factor; whereas low levels of FA may mitigate the negative effects of maternal anxiety on infant vocal reactivity, high levels of FA may increase the risk of lower vocalization in infants whose mothers have high anxiety symptoms. Our results highlight the importance of the early environment in the development of infant white matter microstructure and its relation to behavioral outcomes and have important implications for caregiving interventions aimed at improving maternal regulation behaviors to optimize infant temperament.

3-G-56 - Longitudinal effects of early life stress on pubertal development in the ABCD study

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Details

Background:

Pubertal development marks a youth's transition to physical, emotional, social, and neural maturity, and the timing of pubertal development has substantial social and biological implications. Early life exposure to adverse experiences has been shown to impart multi-system influences on developmental trajectories, including pubertal onset and timing. Specifically, life-history principles suggest that early exposure to adverse environments may alter the trajectory of pubertal development in order to optimize reproduction and survival. Most studies demonstrate this phenomenon following more severe forms of adversity (e.g., institutional rearing), though other common, everyday stressors that are lower in intensity but experienced frequently have also been shown to impact maturational processes. Therefore, this study will aim to test whether exposure to chronic forms of early adversity also induce a 'fasterâ€ pattern of pubertal developmental trajectories over adolescence within a large-cohort,

nationally-representative sample. Additionally, since puberty is inherently a sexually dimorphic process, this study also aims to explore the role of biological sex on early adversity-related changes in pubertal developmental timing and trajectory.

Methods/Analyses:

Mixed effects models will be employed to examine these longitudinal changes in pubertal development over the course of 3-4 years. Since the timing and trajectory of puberty varies greatly, mixed effects models will be used to conduct these analyses, which can appropriately capture the variability that occurs both between- and within-subjects. These models will test the hypotheses that exposure to chronic early life stressors will accelerate patterns of pubertal development.

Data will be drawn from the Adolescent Brain and Cognitive Development (ABCD) Study. Longitudinal data from the baseline visit through the 3-year follow-up will be used (n = 11,790; ages 9-14), which covers the period of development where most youth begin the pubertal transition and exhibit the most dynamic ranges of pubertal developmental stages. Puberty will be quantified with both self-report and physiological measures (Pubertal Development Scale (PDS), salivary pubertal hormones). In line with the adverse childhood experiences framework, dimensions of abuse, neglect, and household dysfunction will be extrapolated as measures of early life stress, in addition to other widely experienced chronic stressors (e.g., financial adversity, discrimination, etc.). Early-life exposure to adverse experiences will be examined in both cumulative and dimensional analysis approaches and compared between males and females for any sex-specific effects.

Discussion:

Findings from this study are expected to illuminate the roles of chronic early life stress on the trajectory and subsequent outcomes of pubertal developmental processes. Since extreme adverse conditions are shown to induce accelerated patterns of pubertal development, this study aims to uncover how less severe (yet more common) experiences of adversity could also elicit changes in the timing and tempo of puberty. Since this study will focus on chronic stressors widely experienced throughout the United States, these findings may provide additional insight into how broad public health concerns may influence biological pubertal development, which may ultimately promote or interfere with later health outcomes.

3-G-57 - Neural correlates of attachment learning: The role of caregiving instability.

Nicolas Murgueitio [1], **Margaret Sheridan** [1], **Kathryn Garrisi** [1], **Maresa Tate** [1], **Celina Meyer** [2], **Summer Motton** [1], **Helen Milojevich** [1], **Amanda Mitchell** [1], **Regina Sullivan** [3], **Katie McLaughlin** [4], **Tracy Dennis** [5], **Sarah Myruski** [6]

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Details

Altricial species rely on caregivers to survive and develop properly. Attachment learning is the tendency for young offspring to seek proximity and show preference to caregiver cues. Rodent studies show this preference to be true, even for cases when aversive conditioning occurs in the presence of the mother. In these cases, young pups develop approach behavior to the learned cue, in sharp contrast to adult that learn to avoid. Similarly, human children have been shown to display behavioral preference to aversive conditioned stimuli when the learning occurred with their parents. Additionally, neuroimaging studies show that children exhibit differential reactivity and activation when cued with maternal stimuli. This preference is likely to be related to the stability of attachment relationships. The present study explores the neural correlates of caregiver stimuli in comparison to non-caregiver stimuli. In addition, we report explorations of the association between these responses and caregiving instability. We recruited 4-8 years old (*M*=6.23, *SD*=0.84; N=53; 26 female) children to participate in a neuroimaging visit. Children underwent fMRI scanning on a 3T Siemens Prisma during an emotion regulation paradigm where they heard stories that helped them regulate their emotions evoked by negative pictures. Prior to hearing these stories and seeing pictures, children hear a 'scaffoldâ€ prompt which encourages them to use the stories to regulate their responses. This prompt was voiced by either their caregiver or a research assistant while also looking at a picture of their caregiver or a sex and race matched stranger. We examined differences in neural activation while children listened to scaffold prompts given by caregiver and strangers. Secondarily we examined caregiving instability as a predictor of differential activation for this contrast. We examined neural activation to these contrasts using a whole-brain analyses with cluster-level corrections using FSL (*voxel level correction z*=3.1). We coded a binary variable from a caregiver report on the number of changes in in primary and secondary caregiver children have had (0= no changes in caregivers, 1=at least one change in caregiver).When children listened and saw their caregiver deliver the scaffolded prompt they exhibited increased activation of the anterior insula, medial prefrontal cortex, nucleus accumbens, precuneus, and inferior and middle temporal gyri relative to listening to a stranger deliver similar prompts. In contrast when observing a stranger, children exhibited greater activation of the middle frontal and superior frontal gyri, superior parietal, and lateral occipital cortex relative to when observing their caregiver. Finally, children with caregiving instability show greater activation in the superior and middle frontal, and supramarginal gyri, and superior parietal cortex, when listening and viewing strangers' prompts relative to those with no caregiving instability. Taken together, these findings suggest that children may preferentially recruit regions commonly associated with complex emotional and higher-order cognitive processing when viewing and listening to caregiver stimuli, in comparison to non-caregiver stimuli. When viewing non-caregiver stimuli relative to their caregiver children recruited regions associated with cognitive control. Children with caregiving instability show greater recruitment of regions associated with higher-order cognition when processing non-caregiver stimuli. These findings support the notion that children process, and experience emotional information delivered by caregivers and non-caregivers differently. This differential neural recruitment of caregiver vs. non-caregiver information may form the neural substrate of attachment learning. Additionally, these results suggest that children with caregiving instability might exhibit enhanced processing of non-caregiver stimuli relative to peers without caregiving instability.

3-G-58 - Prenatal economic strain and neonate subcortical volumes: The mediating role of prenatal maternal psychological symptoms.

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Details

There is a growing body of literature regarding the effects of mothers' prenatal psychological experiences on the developing brain, though these relations and potential underlying mechanisms are presently underexplored. Previous studies have indicated associations between prenatal psychopathology (e.g., anxiety and depression) and volumetric differences in various fetal and infant brain structures, and others have shown that economic strain can contribute to prenatal anxiety and depression. Effects of socioeconomic status on social and emotional development are well-documented, as are the related environmental factors thought to mediate these relationships; however, it remains unclear how economic strain and accompanying anxiety and depressive symptoms during pregnancy may affect very early neuroanatomical development, specifically of the amygdala and hippocampus, two key structures associated with socioemotional behavior.

The objectives of the present study are to evaluate a) the relation between economic strain and prenatal maternal psychological symptoms (i.e., anxiety and depressive symptoms); b) the relation between prenatal maternal psychological symptoms and neonate amygdala and hippocampal structure; and c) whether prenatal maternal psychological symptoms mediate the association between economic strain and neonate amygdala and hippocampal structure.

A diverse sample of 102 women participated in study visits during their third trimester of pregnancy. They completed the Economic Strain Questionnaire (ESQ) to report levels of financial stress and the Brief Symptom Inventory (BSI) to report the quantity and severity of anxiety and depressive symptoms. Neonates underwent a 3T magnetic resonance imaging (MRI) scan at two weeks of age. Bilateral amygdala and hippocampal volumes were extracted jointly from T1- and T2-weighted images via the UNC MultiSeg pipeline with multi-templates and checked manually.

Path analyses were conducted to test for associations between economic strain, prenatal maternal anxiety and depressive symptoms, and infant amygdala and hippocampal volumes. Economic strain significantly predicted more anxiety symptoms (B = .17, p = .003). More anxiety symptoms were predictive of smaller amygdala volumes (B = -26.44, p = .02). Indirect and total effects were calculated using bootstrapped standard errors (1,000 draws). The total effect of economic strain on amygdala volume through maternal anxiety symptoms was significant (B = -18.01, p = .02). No significant associations were found with hippocampal volumes.

The finding that prenatal maternal anxiety mediates the impact of economic strain on neonate amygdala volume adds to increasing evidence that the effects of financial insecurity on offspring neurodevelopment begin prenatally. Greater understanding of how maternal experiences with socioeconomic disparities affect the developing brain has important implications for prenatal mental health care, public assistance, and interventional strategies for low-income families. Consistent with prior research demonstrating sex differences and lateralization in amygdala development, further analyses using this model will include testing for an effect of fetal sex and comparing left and right amygdala volumes.

3-G-59 - The combined role of maternal childhood maltreatment and maternal depression during pregnancy for newborn global white matter microstructure

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Details

Objective: Maternal depressive symptoms during pregnancy are highly prevalent and have consequences for offspring cognitive and social-emotional development. These effects are likely mediated by variation in gestational biology. However, gestational biological correlates of MDS may differ depending on the presence or absence of a history of childhood maltreatment (CM). We aim to investigate the independent and interactive associations of maternal depressive symptoms in pregnancy and maternal history of CM on newborn global brain microstructure.

Methods: In a sample of N=90 mother-infant dyads from two cohorts, maternal depressive symptoms were assessed serially across pregnancy with the Edinburgh Postnatal Depression Scale. CM was assessed with the Childhood Trauma Questionnaire or the Adverse Childhood Experiences scale, respectively, and harmonized into one binary indicator variable of abuse and/or neglect exposure. Diffusion tensor imaging (DTI) was performed in the infants within 90 days of birth. Fiber profiles of fractional anisotropy (FA), axial diffusivity (AD), radial diffusivity (RD) and mean diffusivity (MD) were computed and for each DTI metric a global mean across the brain was computed for use in the statistical analyses.

Results: After adjusting for age, sex, race and ethnicity, and study site, neither depressive symptoms nor CM were independently associated with global newborn white matter microstructure. There was a significant interaction effect of maternal depression and CM on newborn global FA (*B*=-.001, *p*=.026) and RD (*B*=5.94e-6, *p*=.012) but not MD (*B*=2.90e-6, *p*=.053) or AD (*B*=2.21e-6,*p*=.116). More specifically, in infants born to women with a history of CM, higher maternal depressive symptoms were associated with lower fractional anisotropy, and with higher radial diffusivity, a pattern suggesting lower microstructural integrity and myelination. In contrast, infants of women without CM exhibited the reverse pattern of associations between depressive symptoms and DTI metrics.

Conclusions: The present findings suggest that maternal depressive symptoms during pregnancy may affect offspring brain development via different mechanisms depending on whether mothers were exposed to CM. Future studies should explore whether these different patterns in newborn brain microstructure associated with maternal depression and CM also translate into differences in cognitive and social-emotional developmental trajectories. These findings may inform future prevention strategies and highlight the importance of monitoring the psychosocial well-being of pregnant women.

3-G-60 - Corticolimbic Neural Underpinnings of Neighborhood Environment Unpredictability in Relation to Adolescent Behavioral Motivation

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Details

Recent early adversity theories increasingly adopt a dimensional model and examine the distinctive dimensions of threat vs. deprivation (McLaughlin et al., 2014), and harshness vs. unpredictability (Belsky et al. 2012). Since the COVID-19 pandemic, unpredictability has been increasingly acknowledged as a core dimension of early adversity that drastically increases in social contexts (Liu & Fisher, 2022). The corticolimbic neural circuitry, which is responsible for integrating emotion and cognition, has been identified as a key mechanism linking unpredictable social experiences and behavioral maladaptation (Gee, 2021). In typical development, corticolimbic connectivity (e.g., between amygdala and PFC) shifts from positive (immature) to negative (mature) as an indicator of matured inhibitory control and emotional behaviors (Gee et al. 2013). Early unpredictability is found to induce accelerated corticolimbic maturation, as indicated by earlier negative amygdala-PFC connectivity, among young children (Gee et al., 2021). However, this association is less clear among adolescents due to the lack of evidence, and considering that the unpredictability effects may vary given possibilities of neurobiological recalibration in puberty.

The current study investigated the direct and interaction effects of harshness and unpredictability, particularly in the neighborhood environment, on youth's corticolimbic resting-state function connectivity (rsFC). We further examined the implications of this neural signature on youth behavioral motivation, including inhibition in response to punishment or removal of reward, and approach in response to reward or removal of punishment. Data were from the ABCD study release 4.0, including 11,875 youths (47.9% female, 15% Black, 20.4% Latino[a], 9-10 in baseline). Neighborhood safety was assessed annually via one item from the PhenX Toolkit. Using the 3-year data, we obtained neighborhood harshness with mean scores, and calculated the unpredictability indicator using the coefficient of variance. Youth corticolimbic connectivity was indicated by fMRI rsFC of the cingulo-opercular (CO) network and the amygdala, assessed at baseline and year-2. The behavioral motivation constructs were captured via the BIS/BAS scale (Carver & White, 1994) at baseline and year-2.

The structural equation model revealed no direct, but significant interaction effects, of neighborhood harshness & unpredictability on CO-right amygdala rsFC. Higher levels of negative CO-right amygdala rsFC were also significantly linked to increased quick goal-pursuit and fun-seeking behavioral approaches. Simple slope tests revealed that, for youth in low-harshness neighborhoods, no difference in CO-right amygdala rsFC was discovered. However, significant differences were exhibited in highly harsh neighborhoods. Youth in highly harsh but not unpredictable neighborhoods exhibited accelerated corticolimbic maturation as indicated by stronger negative CO-right amygdala rsFC, which was further linked to increased behavioral approaches. This finding may be explained by the Life History Theory (Ellis et al., 2009): When environments are harsh and resources are scarce, youth perceive the environment as adverse and may be more likely to quickly pursue their goals or seek fun experiences, once rewards are present, to enhance their fitness levels (in an evolutionary sense). In contrast, youth in highly harsh and highly unpredictable neighborhoods showed delayed corticolimbic maturation as indicated by weaker negative CO-right amygdala rsFC, which was further linked to decreased behavioral approaches. It is likely that under unpredictable social contexts, youth may be hesitant to act on goal-pursuit or fun-seeking motivations given the uncertainty of how long the rewards/resources would stay. We will also look into the potential impact of puberty development in these associations and report in the poster/presentation.

3-G-61 - Parent emotion socialization is associated with neural correlates of implicit emotion regulation in early adolescents

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Details

Background: Early adolescence is a developmental period marked by significant biological and social-emotional changes, and is also a time of heightened vulnerability to emotion regulation difficulties. During this period, neural networks supporting emotion regulation undergo dynamic alterations, rendering early adolescents particularly sensitive to environmental influences. Parent emotion socialization behaviors play a critical role in shaping the healthy development of emotion regulation in young people; however, the impact of such behaviors on the neural correlates of emotion regulation in early adolescents is not well understood. In this study, we aimed to examine the association between parent emotion socialization behaviors and neural activity during both implicit and explicit forms of emotion regulation in early adolescents. **Methods**: Participants were 47 female adolescents aged between 10 to 12 years, who were experiencing some emotion regulation difficulties (i.e., with elevated depressive and/or anxiety symptoms). Adolescents reported on their parents' emotion socialization behaviors using the Emotions as a Child questionnaires, and performed two fMRI tasks: an affect labeling task (implicit emotion regulation) and a cognitive reappraisal task (explicit emotion regulation). We performed both hypothesis-driven region of interest (prefrontal cortex [PFC], amygdala) analyses, in addition to exploratory whole-brain analyses, to investigate associations between supportive and unsupportive parent emotion socialization behaviors and adolescent brain function during emotion regulation. **Results**: Supportive parent emotion socialization behaviors were associated with greater activation in the dorsomedial and ventromedial PFC (dmPFC, vmPFC) and dorsal anterior cingulate cortex (dACC) during implicit emotion regulation (affect label vs shape label). Unsupportive emotion socialization behaviors were associated with less activation in the dmPFC, vmPFC, and right hippocampus during implicit emotion regulation. Parent emotion socialization was not associated with neural activation during explicit emotion regulation (cognitive reappraisal vs passive viewing of negative pictures). **Implications**: Findings from this study suggest that both higher levels of supportive emotion socialization (e.g., validating children's emotions, modeling adaptive emotion regulation) and lower levels of unsupportive emotion socialization (e.g., dismissing and punishing emotions, intolerance towards children's emotional expressions) may influence emotion regulation neurobiology in adolescents experiencing emotional difficulties. Associations with brain function during implicit but not explicit emotion regulation may indicate that neural infrastructure underlying explicit emotion regulation typically develops during adolescence. As such, early adolescents may vary in their ability to employ cognitive reappraisal, which may explain why we did not observe any significant association between parent emotion socialization and neural activity during explicit emotion regulation. However, given the relatively small sample size of the current study and its correlational nature, further research is needed to establish causal associations.

3-G-62 - Effects of sleep & stress on early childhood structural brain development & self-regulation

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Details

Self-regulationâ€“a multidimensional construct that encompasses aspects of executive function (EF), self-control, effortful control, delay of gratification, and emotion regulationâ€“is a developmental process associated with both cognitive development and psychosocial wellbeing in childhood (Ursache et al., 2011; McClelland et al., 2018). Previous work has highlighted the role of sleep and stress on the development of self-regulation in childhood, indicating that adequate duration and quality of sleep supports self regulation, while experiences of stress negatively impact self regulation development (Bernier et al., 2013; Blair & Raver, 2012; Williams et al., 2017). The prefrontal cortex (PFC) is a key brain region underlying self-regulation processes (Blair & Ursache, 2011; Heatherton & Wagner, 2011) and is shaped by the environmental factors of (1) stressâ€"via cortical thickness (CT) (Feola et al., 2020), volume (V) (Hanson et al., 2012), and surface area (SA) (Stomby et al., 2016)â€"and (2) sleepâ€"via CT (Goldstone et al., 2018) and V (Kocevska et al., 2016; Urilla et al., 2017). The amygdala and hippocampus are also key regions associated with sleep and stress, and may have implications for self regulation development (Gunnar & Quevedo, 2007; Hansen & Simon et al., 2022; McEwen, 2007; Oshri et al., 2019). However, it is unclear whether the structure of these brain regions mechanistically links experiential measures (stress, sleep) and self regulation development during childhood. The present, pre-registered study (https://osf.io/dn9pg) fills this gap by investigating whether and how sleep and stress influence self-regulation in early childhood, and whether the structure (CT, SA, and V) of neuroanatomical regions of interest (PFC, amygdala, hippocampus) mediate these relationships. Specifically, we examine three hypotheses:

- H1: Greater cumulative childhood stress will be associated with lower self-regulation.
- H2: Less sleep/lower quality sleep will be associated with lower self-regulation.
- H3: The relationships described in H1 and H2 will be mediated by (a) CT, SA, and V of the PFC bilaterally, and (b) volume of the amygdala and hippocampus bilaterally.

Participants were 76 children (59% male) aged 4-7 years old (M=5.7 years, SD=0.7) enrolled in either pre-K or Kindergarten, and were socioeconomically, racially, and ethnically diverse. Caregivers reported family income-to-needs ratio, and completed standardized questionnaires about child stress (LES-C; Coddington, 1972), child sleep quality and duration (TCSQ; McGreavey et al., 2005), and self-regulation (BASC-2; Kamphaus & Reynolds, 2011; BRIEF-2; Gioia et al., 2015). Children also completed whole-head, high resolution T1 MPRAGE MRI scans, and automated and manual quality checks were applied. Freesurfer will be used to extract CT, SA, and V of the bilateral PFC (superior, middle, and inferior frontal gyri), and the V of bilateral hippocampi and amygdalae. Hypotheses will be evaluated using multiple regression models and bootstrapped mediation analyses, controlling for child age, sex, and income-to-needs ratio. Additionally, supplementary, exploratory analyses will examine hypotheses in whole-brain analyses using general linear models in Freesurfer.

Results will help elucidate the neuroanatomical mechanisms by which sleep and stress influence the development of self-regulation in early childhood, which has implications for reducing disparities in this key developmental capacity that is crucial for school readiness and child wellbeing. Additionally, because both sleep and stress are affected by structural inequities (e.g., noise exposure, violence exposure, income inequality), this work also has important implications for focusing interventions on structural factors that may ultimately lead to broader social and educational equity.

3-G-63 - The association of maternal cortisol concentration during pregnancy and offspring white matter microstructure in one-month old neonates

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Details

Background

Maternal stress during pregnancy can alter the developmental trajectory and impact the physiological and psychological health of the fetus. Some of these changes are believed to be mediated by changes in the structure and functioning of the brain. Under conditions of high maternal stress during pregnancy, increased amounts of cortisol cross the placenta exposing the fetus to higher cortisol concentrations. Elevated maternal cortisol levels have been associated with offspring adverse health outcomes, cognitive delays, and behavioural problems. While maternal depression during pregnancy, a condition likely accompanied by an increase in cortisol concentrations, has been associated with alterations in white matter microstructure in infants and children in the limbic and prefrontal regions of the brain, the association of variation in maternal cortisol concentrations during pregnancy with the development of offspring white matter microstructure has not been extensively studied in humans. Evidence for white matter integrity being susceptible to variation in glucocorticoid concentrations comes from preclinical work that has shown that oligodendrocytes and myelination are adversely affected by high levels of glucocorticoids.

Objective

The aim of this project is to investigate the association of variation in endogenous maternal cortisol concentrations during pregnancy and the white matter microstructure in the corpus callosum (CC) and uncinate fasciculus (UF) in one-month old infants.

Hypothesis

Higher maternal cortisol concentrations during pregnancy are associated with lower fraction anisotropy (FA) and higher axial diffusivity (AD) and radial diffusivity (RD) in the CC and UF in one-month old neonates.

Methods

Complete:

The study consists of 85 mother-infant dyads from across three sites, University of Rochester and Magee-Women's Research Institute & Foundation in the United States of America and CharitÃ© UniversitÃ¤tsmedizin Berlin, Germany. The same MRI scanner and imaging protocol was used at all sites. Diffusion weighted imaging was performed in the one-month-old neonates and pre-processed using DMRIPrep to remove artifacts and to correct for the effects of eddy currents and subject motion. The diffusion images were visually quality controlled in DMRIPrep to remove any further bad gradients, and tensors were estimated using a weighted least square algorithm. Maternal saliva samples were collected three times a day, for at least one and up to four days, at one to three timepoints throughout pregnancy to measure cortisol diurnal profiles. The cortisol data from all three sites was harmonized to account for timing differences in the daily saliva collection protocol. Area under the curve with respect to ground, a measure of total cortisol output, was calculated at each trimester cortisol was measured during pregnancy for each participant.

In progress/Will be completed by flux:

A neonatal DTI atlas will be created using DTIAtlasBuilder and the white matter tracts of interest will be defined in the atlas. The individual subjects DTIs will then be registered into atlas space and the resulting deformation field will be used to map the white matter tracts into individual space. FA, mean diffusivity, AD and RD profiles will be computed for each white matter tract. Every tract from each subject will be quality controlled using FADTTSter and subjects will be excluded from statistical analyses on a tract-by-tract basis if the individual profile has a low correlation to the average tract profile. General linear models will be used to test if maternal cortisol concentration is associated with the microstructural profiles of the white matter tracts. All models will be adjusted for gestational age at birth, scan age, site and sex. In a second step the moderating role of sex will be explored. Further covariates, including race and ethnicity, obstetric risk and socioeconomic status will be included in post hoc analyses.

3-G-64 - Gut Microbiome: Associations with Caregiving Adversity and Alexithymia in a Peri-Adolescent Sample

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Details

Early life caregiving adversity (ECA) is a strong risk factor for alexithymia, a cognitive-emotional trait characterized by difficulty identifying and describing feelings that is linked to deficits in neural emotion processing and internalizing disorders. Prior research has found that gut microbiome composition is related to alexithymia in adults. A developmental perspective is imperative given that there may be a sensitive period of microbiome development in adolescence which programs gene expression in brain regions implicated in alexithymia. When studying the gut microbiome, measuring both composition and functional potential (i.e., what functions can the gut microbial community perform?) can help uncover mechanistic implications of taxonomic differences for brain-gut-microbiome communication. This study's objective is to examine how ECA is associated with microbiome composition and functional potential, and how these microbiome features are related to alexithymia, in a peri-adolescent sample of 163 children ages 6-16 years. Half of the children were exposed to ECA (e.g., foster care). Preliminary analyses in this sample found children exposed to ECA had higher alexithymia.

The following analyses will be complete by Flux conference. To maximize statistical power, we will first take a hypothesis-driven approach. We hypothesize (H1) that gut microbiome potential for GABA and glutamate metabolism will be associated with ECA and alexithymia. We also hypothesize (H2) that lower abundance of *Lachnospiraceae* species, higher abundance of *Prevotella, Fusobacterium*, and *Veillonella* species, and (H3) lower alpha (community-level) compositional diversity will be associated with more ECA and alexithymia. To test H1 and H2, we will use MaAsLin2, a generalized linear model framework that appropriately handles microbiome features and corrects for the false-discovery rate. To test H3, we will use linear regressions. If our hypotheses are not supported, we will examine all functions and species within the gut microbiome in exploratory analyses. Findings will inform models of brain-gut-microbiome interactions related to adversity and mental health-related cognition. Follow-up analyses in this cohort will examine relations with brain function.

3-G-65 - The role of socioeconomic status in shaping associations between sensory association cortex and prefrontal structure and implications for executive function

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Details

Background and Introduction:

Socioeconomic status (SES) has been linked to differences in brain structure, including cortical surface area, cortical thickness, and cortical volume throughout temporal, parietal and frontal cortex. We and others have proposed that sensory processing regions in particular visual association cortex (VAC) precedes and predicts development of the prefrontal cortex (PFC; Amso & Scerif, 2015; Rosen, Amso, & McLaughlin, 2019). Important experiences including cognitive stimulation correlated with SES may drive development of the visual system which in turn provides the first opportunities for the PFC to resolve conflict for example between stimuli with overlapping features. We have further proposed that SES-related differences in these regions may in part explain SES-related differences in executive function (EF) skills. While this conceptual model has focused on VAC, it is also possible that differences in development of other sensory association regions also are important for the development of the PFC. In particular, the auditory association cortex (AAC) may be critically involved given that language development is important for the development of EF (Romeo et al., 2022).

Current Study:

In this preregistered analysis (https://osf.io/quy2n/) we will leverage the ABCD Study to investigate how SES is related to differences in development of AAC and VAC and whether these differences explain SES related differences in structure of the PFC and change in PFC development over time. Furthermore, we will investigate whether these neural differences explain SES-related differences in EF.

SES: SES will be a latent factor of the following indicators:

Average parental education in years, income-to-needs ratio, and area deprivation index.

Brain Structure: Cortical thickness and surface area will be based on the Destrieux parcellation. We will use average cortical thickness and total surface area for VAC (middle occipito-temporal gyrus, lateral occipito-temporal gyrus, anterior occipital sulcus, middle occipital-temporal sulcus and lingual gyrus) AAC (supramarginal gyrus, lateral aspect of superior temporal gyrus, planum temporale, superior temporal sulcus, transverse temporal sulcus) and PFC(middle anterior cingulate gyrus and sulcus, triangular part of the inferior frontal gyrus, middle frontal gyrus, inferior frontal sulcus, middle frontal sulcus, superior frontal sulcus) at Time 1 and Time 2.

Executive Function: EF will be latent factor with performance on the NIH Toolbox Flanker and Processing Speed as indicators. Performance on the Flanker is measured by the difference in RT for Incongruent and Congruent trials. Processing speed is calculated by taking the total number of correct responses that are completed within 90 seconds.

Analysis: We will use a latent growth curve model using the lavaan package in R to test whether the association between SES and EF is mediated by structure of the sensory association cortex and related differences in structure of the PFC. SES and EF are latent factors made up of the indicators described above. Intercepts and slopes of VAC, AAC, and PFC are also latent factors of at T1 and T2. We will use SES at Time 1 to predict the intercept and slope of VAC and AAC structure. The model will also use VAC and AAC structure at Time 1 to predict PFC structure at Time 1 (intercept), and PFC structural change (slope) as well as change in VAC and AAC structure at Time 2 predicting change in PFC structure at Time 2. The model will also use PFC structure at Time 1 to predict EF at Time 2 and change in PFC structure at Time 2 predicting EF at Time 2. Intermediate direct paths will also be modeled. We will test models for cortical thickness and cortical surface area separately and all models will covary for main effects of age, sex, and scanner type. The significance of the indirect paths will be evaluated using 99% bias-corrected bootstrap confidence intervals based on 10,000 replications.

3-G-66 - Gut microbiome dysregulation as a mechanism of reward circuitry differences in youth exposed to early adversity

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Details

Exposure to early adversity increases risk for health outcomes, such as major depression or substance use disorders, that are linked to differences in corticostriatal reward circuitry. In order to develop treatments and interventions that promote adaptive development of reward circuitry in youth exposed to early adversity, researchers must identify manipulable mechanisms linking adversity to reward processing. The gut microbiome may be one such mechanism. This ecosystem of microorganisms that inhabit the gut performs crucial metabolic functions, including monoamine precursor synthesis and immune regulation, that may affect reward circuitry in youth. Moreover, gut microbiome differences following early adversity exposure have been extensively documented, both experimentally in animal models and observationally in humans. The ability of the microbiome to be manipulated via probiotics, prebiotics, and dietary changes makes its study as a potential treatment target particularly compelling. We collected resting-state functional magnetic resonance imaging (fMRI) (N=94) and stool samples

(N=52), which were sequenced using 16S amplicon target gene sequencing, from youth (ages 5-18) oversampled for early adversity exposure. We will examine the total effect of early adversity on resting state functional connectivity (rs-FC) between the nucleus accumbens and ventromedial prefrontal cortex using a multiple linear regression model controlling for age. Using distance-based methods and central log ratio-transformed relative abundance models controlling for age, we will test associations between microbiome composition and rs-FC. Additionally, as an exploratory analysis, we will use both a distance-based mediation model and an abundance-based linear decomposition mediation model to test the extent to which gut microbiome composition mediates the relationship between early adversity exposure and rs-FC. Data collection for this project is complete at the time of abstract submission and preprocessing and analysis are underway. The results of this project will provide a foundation for longitudinal work that examines the role of the microbiota in reward circuitry following adversity exposure and, ultimately, inform treatments and interventions to promote health in this group.

3-G-67 - Resting state neural activity in the first year of life and associations with household chaos

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Details

Household chaos is a construct in psychological science that includes factors such as noise, crowding, routines, clutter, and predictability within a family's household and neighborhood environment. Reliably, when measured in relation to behavioral child outcomes, higher levels of household chaos have been shown to be associated with poorer performance on cognitive tasks and greater socioemotional and behavioral challenges for infants, children, and adolescents (Marsh et al., 2020 for a review). Comparatively, research on how household chaos, or the factors that comprise it, impacts infant and child brain development is very new but demonstrates observable effects at the neural level (e.g., Brito et al., 2021; Simon et al., 2022; Werchan et al 2022). This emerging work at the level of brain development has focused on chaos factors of noise and predictability of input, finding that children exposed to excessive noise show reduced cortical thickness (Simon et al., 2022) and infants who experienced more predictable auditory input displayed increased sustained attention, behaviorally and neurally as early as 3 months of age (Werchan et al., 2022). In the proposed study, we seek to investigate how this environmental factor of household chaos may be related to entropy in the EEG signal, a marker of unpredictability in the neural signal that may be particularly sensitive to environmental chaos and unpredictability.

Proposed study participants are 3- and 6-month-old infants (*N* = 250) drawn from a larger longitudinal study on infant development. Families were recruited for the larger study from an established pregnancy registry site at the Gugulethu Midwife Obstetrics Unit, located in Gugulethu, an informal urban settlement in the Cape Town metropole in South Africa. High-density (128 channels) resting state EEG data was recorded in a dimly lit room while participants were seated on their caregivers' laps. The resting state EEG video was presented via E-Prime software and consisted of a 3-minute long silent video of different colorful and engaging clips. Parents completed a modified version of the short form Chaos, Hubbub, and Order scale (Matheny et al., 1995).

Presently, data from the 3-month data is entirely collected and pre-processed. Data from the 6-month time point is expected to be completely collected by May 2023. All EEG files will be processed using the Harvard Automated Processing Pipeline for EEG (HAPPE), an automated preprocessing pipeline designed for infant EEG data (Gabard-Durnam et al., 2018). Household chaos scores are computed as an average of items collected on the questionnaire. Regression analyses will be run to examine longitudinal development of entropy in the EEG signal and associations with household chaos. Relevant controls will include gestational age and family SES. We expect to find an increase in entropy with age, signaling neural maturation. We expect that this association may be dependent on levels of chaos reported in the home.

3-G-68 - Identifying Prenatal Psychological Influences on Infant Neural Signatures

Tara Rutter [1], **Kelly Molloy** [1], **Madelyn Heise** [2], **Joel Nigg** [1], **Sarah Karalunas** [2], **Elinor Sullivan** [1], **Hanna Gustafsson** [1]

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Details

Background: Frontal EEG asymmetry, a neural index of behavioral approach and withdrawal, is related to risk for depression (Allen & Reznik, 2015). Infants of birthing parents who are depressed in the postnatal period demonstrate greater right frontal asymmetry (Field et al., 2011), a pattern that has been associated with impaired emotional processing and risk for psychopathology. While several studies have linked greater infant frontal right asymmetry with birthing parent depression postnatally, the effects of prenatal depression on infant brain development are not well understood, despite evidence that prenatal depressive symptoms exert unique effects on other metrics of infant brain development (Dufford et al., 2021). Research guided by the Developmental Origins of Health and Disease framework (Wadwha et al., 2009) has shown that birthing parent psychological states during pregnancy can alter gestational-fetal-placental biology in ways that influence fetal brain development. While preliminary studies suggest that prenatal depression is associated with greater right infant frontal asymmetry (Goodman et al., 2021), several questions remain and constitute **our study objectives**: 1) Depression and anxiety commonly co-occur in the perinatal period, yet no study has examined whether prenatal anxiety also relates to infant frontal asymmetry. Given that depression and anxiety have similar biological correlates in the perinatal period (and these biological sequelae are the purported mechanism of effect), we hypothesize that both symptom types will contribute to infant right frontal asymmetry, independent of the effect of postnatal symptoms; 2) Previous research has almost exclusively examined diagnostic group differences (i.e., clinically depressed vs. controls), but evidence suggests that variation in subclinical levels of anxiety and depression also exert meaningful effects on infant brain development (Graham et al., 2020). If dimensional measures of depression and anxiety are related to infant frontal asymmetry, this would suggest that a broader approach to screening and intervening on perinatal symptomatology may be effective for reducing offspring psychopathological risk; and 4) The postnatal environment has potential to perpetuate, exacerbate, or ameliorate the effects of prenatal symptomatology (Pluess & Belsky, 2011), yet interactions between prenatal and postnatal symptomatology remain underexplored. We hypothesize that infants whose mothers endorsed high levels of anxiety and depression in both prenatal and postnatal periods will have greater right frontal asymmetry than those whose mothers only endorsed high symptoms during pregnancy.

Methods: Birthing parents (N=100) completed the Spielberger State-Trait Anxiety Inventory (Spielberger et al., 1999) and Center for Epidemiologic Studies-Depression Scale (Radloff, 1977) during the 2nd and 3rd trimesters and at 1 month postpartum. Infant resting state EEG was recorded using a 32-channel system ($M_{ChildAge}$=1.44 months), as described previously (Karalunas et al., 2022). Frontal asymmetry was calculated within the 3-12 Hz band by comparing power at right (F3) and left (F4) frontal sites. Hypotheses will be tested using multiple regression. Independent and interactive effects of a) anxiety and depressive symptoms and b) pre- and post-natal symptoms will be tested. Trimester-specific and child-sex effects will be explored in secondary analyses. Covariates (e.g., child age, sex, demographics) will be included in models as appropriate. FIML will be used for missing data.

H – Executive functioning

3-H-69 - The relationship between irritability and neural circuitry related to emotion regulation in adolescents

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Details

Irritability, or a lowered threshold for frustration when a goal is blocked (i.e., frustrative non-reward), increases in adolescence and is a robust transdiagnostic risk factor for the development of psychopathology. Emotion regulation strategies, such as cognitive reappraisal, have been thought to mitigate irritability. Given that emotion regulation capacity is neurobiologically instantiated, and adolescence is a period of tremendous neurocognitive and emotional development, clarification of the neural mechanisms underlying the relationship between emotion regulation and irritability in adolescence is critical. However, the neural mechanisms underlying this relationship are not well understood. Therefore, the current study examined the relationship between irritability, measured by the Child Behavior Checklist (CBCL), and fMRI brain activation during an explicit emotion regulation task in a sample of 91 adolescents. Participants were instructed to either (i) naturally react to or (ii) regulate their emotions while viewing images of negative or neutral social scenes in the MRI scanner. Results revealed that irritability moderated neural responses in the right inferior frontal gyrus, a region tied strongly to inhibitory control. Specifically, irritability was negatively related to activation when encountering negative (but not neutral) stimuli during the react (but not regulate) condition. These findings suggest that adolescents with heightened irritability may have difficulty activating top-down control related brain regions when experiencing negative emotions and not explicitly told to regulate beforehand, whereas their neural regulatory capacity may remain intact if activated before the negative emotional experience. Overall, this study provides novel insights into the association between irritability and emotion regulation during adolescence in a brain region related to top-down control.

3-H-70 - The unity and diversity of brain connectivity underlying executive function tasks

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Details

Executive function (EF) is a broad set of cognitive processes that drive attention and control abilities, and aid in facilitating goal directed behaviors. EF ability is predictive of numerous important life outcomes in childhood and beyond. EF is exerted across many different domains, such as inhibition, working memory, and switching. These domains share common and unique variance and can be described within the Miyake unity (common) and diversity (unique) framework of EF. The neurobiological systems that support EF are in place as early as late childhood and show unity and diversity aspects. EF domains have been found to mature at different rates and relate to different mental health disorders. Therefore, understanding diversity in the neurobiological mechanisms of EF is crucial for promoting healthy development.

Here, we examine the neurobiological diversity of EF in childhood and adolescence by analyzing patterns of functional connectivity in the developing brain (*n*=62, M_{age}= 12.2, *age range*= 8.8-17.2, 30 F). All participants completed at least one run of a resting-state task, a working memory task, a cognitive flexibility task, and an inhibition task while in a MRI scanner. We estimated functional connectivity within each of the 4 states by computing the pairwise correlations of time courses derived from 333 cortical parcels. We then computed two graph metrics for each state, global efficiency; quantifying the integration between brain regions, and modularity; quantifying how the brain segregates into distinct systems. Mixed effects models were used to test for differences in graph metrics between rest and the three EF tasks.

We found brain connectivity differed across the four states. Global efficiency at rest was significantly lower than during the working memory and inhibition tasks. We found that modularity at rest was significantly different from modularity during a working memory task, an inhibition task, and a cognitive flexibility task, with rest having the highest modularity, and the working memory task having the lowest modularity. We found age was related to brain connectivity, with older youth having higher modularity during cognitive flexibility and inhibition, and lower global efficiency during inhibition. Performance on the inhibition task was also related to global efficiency, such that better performance on the task was related to higher global efficiency. Additionally, the difference in brain connectivity between rest and inhibition states was predicted by performance on the inhibition task.

Taken together, this work shows the brain significantly changes in its functional organization across EF tasks. However, the nature of this change differs by EF domain, with working memory and inhibition requiring more integration, and cognitive flexibility requiring more segregation. Additionally, age was related to functional connectivity during some EF domains, suggesting distinct maturational trajectories of brain function. Task performance predicted brain connectivity during the inhibition task and the change in connectivity between inhibition and rest, suggesting brain configuration and reconfiguration matters for performance. In sum, though there is unity in the neural architecture of EF in adolescence, we see diversity in functional brain organization across EF tasks.

3-H-71 - Integrating multimodal neuroimaging measures of error monitoring to predict future anxiety among behaviorally inhibited adolescents

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Details

Background: Behavioral inhibition (BI) is a temperament style identified in the first years of life and characterized by fear or distress to novel people or stimuli. BI is one of the strongest and earliest known risk factors for future anxiety; yet, only around half of all children with this temperament will go on to develop an anxiety disorder, underscoring the importance of identifying moderating factors that further influence anxiety risk among children with a history of BI. Among these children, previous work has found concurrent associations between error-monitoring-related brain activity and anxiety. However, to maximize clinical utility, neural measures should not only relate to current anxiety but also predict future changes in anxiety. The present study tested whether integrating multimodal measures of error monitoring (EEG and fMRI) could improve prediction of anxious outcomes among children with a history of BI.

Methods: Adolescents with and without a history of BI temperament completed an arrow flanker task at age 13 years with EEG (n=123), non-simultaneous fMRI (n=42), or both (n=41) to assess error-related brain activity. Anxiety was assessed via self-report, parent-report, and diagnostic interview, which were combined via a latent factor score. Participants returned to the lab two years later, at which time all assessments were repeated. EEG analyses focused on the error-related negativity (ERN), a negative voltage deflection that is larger following errors than following correct trials and is maximal over frontocentral electrode sites. For integration with fMRI data, the neural generators of the ERN were estimated via source localization in brain space. For each participant, fMRI-weighted ERN scores were obtained by multiplying ERN source estimates by the participant's error-related fMRI beta weights. Prediction of future anxiety change was tested via a series of latent change score models.

Results: Among youth with a history of high BI, fMRI-weighted ERN scores in two major generators of the ERN the dorsal anterior cingulate cortex (dACC) and posterior cingulate cortex (PCC) significantly predicted future anxiety changes two years later. However, activity from each brain region predicted future anxiety in opposite directions. That is, greater fMRI-weighted ERN activity in the dACC predicted greater anxiety increases among those with high BI, whereas greater activity in the PCC instead predicted decreased anxiety for these youth. The reverse was observed among youth with a history of low BI. When examining EEG or fMRI separately, effects did not survive correction for multiple testing.

Conclusions: Overall, results suggest disentangling error monitoring signals from distinct brain regions via integration of multimodal neuroimaging can improve prediction of future anxiety outcomes.

Furthermore, given the opposite findings observed among youth with vs. without a history of BI, results support the existence of distinct developmental pathways toward anxiety as a function of temperamental history. These distinct developmental pathways may help explain previous findings of inconsistent associations between error monitoring and anxiety among adolescents.

3-H-72 - Edge-centric control theory applied to neonatal structural connectivity in term and preterm neonates predicts cognitive and social outcomes at 18-months

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Details

The brain undergoes extensive development during infancy to gain future cognitive and social skills. However, it remains unclear if brain structure at birth can predict these future skills. Network control theory is a promising framework for studying brain development. The controllability of structural networks is associated with cognitive outcomes in infants and adolescents. We have recently extended network control theory to assess the controllability of specific structural connections (or edges). Edge controllability better predicts cognition in adults compared to traditional controllability measures. We investigated whether edge average controllability (eAC) and edge modal controllability (eMC) can predict developmental outcomes in neonates. eAC measures each edge's ability to drive nearby brain state transitions. eMC measures each edge's ability to drive distant brain state transitions. We then generalized these models to preterm neonates at high risk of poor neurodevelopmental outcomes.

We applied edge-centric network control theory to structural connectomes of 530 neonates (448 terms, 82 preterms) from the developing Human Connectome Project. Term neonates were scanned at birth. Preterm neonates were scanned twice at birth and term-equivalent age. 349 term and 63 preterm neonates underwent cognitive testing (BSID-III) and autism risk screening (Q-CHAT) at 18 months old. Standard DWI preprocessing was performed. Structural connectivity for each subject was constructed with the 90-node infant atlas based on the quantitative anisotropy between any two nodes. We calculated eAC and eMC and used Connectome-based Predictive Modeling (CPM) to predict BSID-III and Q-CHAT scores from eAC and eMC. Prediction models controlled for sex, brain volume, and head motion.

We first trained 10-fold CPM models to predict the BSID-III and Q-CHAT scores from the term neonates. Edge controllability predicted BSID-cognition (eAC: $r=0.19$, $p<e-3$; eMC: $r=0.18$, $p<e-3$) and language (eAC: $r=0.22$, $p<e-4$; eMC: $r=0.20$, $p<e-3$) scores, but not BSID-motor scores. Edge controllability also predicted Q-CHAT scores (eAC: $r=0.24$, $p<e-5$; eMC: $r=0.22$, $p<e-4$). Using the pre-trained model on term infants, we predicted Q-CHAT scores (eAC: $r=0.31$, $p=0.013$; eMC: $r=0.27$, $p=0.030$) in preterm infants.

We used edge-centric network control theory and CPM to predict 18-month outcomes from neonatal structural connectivity. Edge controllability predicted later individual cognitive and social abilities. Overall, edge-centric network control theory holds promise as a brain-based marker of future developmental risk.

3-H-73 - Trajectories of Early Postnatal Cortical Thickness Development and Associations with Executive Function in Late-Childhood

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Details

Objective. The early postnatal period is a critical stage of human brain development. Neurodevelopmental theories argue that the first several years of life represent a sensitive period during which experience and learning shape synaptic proliferation and pruning in ways that set the stage for cognitive development across the lifespan. Current evidence from early intervention studies and animal models suggests that the impact of experience in early postnatal life on long-term changes in brain structure and function applies even to regions with protracted developmental trajectories such as the prefrontal cortex. However, little research has directly examined associations between trajectories of early cortical development and later cognitive function, although this association is a primary prediction of sensitive period models. In part this is because there is limited data with dense enough sampling during infancy and toddlerhood to adequately document the rapid process of proliferation and pruning which occurs in the first few years of life and is one of the primary mechanisms of neural plasticity. The present study leverages data from a densely sampled longitudinal study to examine associations between brain development in infancy and early childhood (i.e., before age six) and executive function in mid-to-late childhood (age eight through twelve). Two primary aims guided the present study: 1) to examine patterns of cortical thickness change across all lobes of the brain over the first few years of life and 2) to explore how aspects of this change are associated with later cognitive function in order to contextualize the significance of early cortical development.

Methods. This project leveraged a multi-method, longitudinal design to characterize trajectories of early cortical development and assess how developmental patterns predicted differences in executive function in middle childhood in a sample of 50 children. Cortical thickness was assessed via magnetic resonance imaging scans that participants completed several times (mean number of scans = 7, range 3 11) between birth and six years of age. Structural brain scans were processed using the infant Brain Extraction and Analysis Toolbox (iBeat) to obtain thickness of the frontal, parietal, temporal, and occipital lobes of the brain. When they were between eight and twelve years old (M_{age} = 9.41), children returned to the lab and completed an n-back working memory task. Executive function was assessed via ‘ on 2-back trials, which corresponded to correct button presses indicating whether or not a stimulus matched one seen two trials previously.

Results. In line with animal research demonstrating early synaptic proliferation and pruning, we observed rapid initial increases in cortical thickness that peaked around 12 months of age. This increase was followed by an initially steep decrease in thickness between 12 and 18 months and a slow increase in thickness from 18 months to six years. Slopes of cortical thickness change differed significantly across all lobes of the brain (all *p*s <.001). With regard to later executive function, we found that 2-back ‘ was associated with peak levels of cortical thickness in the frontal lobe (b = -.09, SE = .04, *t* = -2.18, *p* = .04) but not in parietal, temporal, or occipital lobes.

Conclusion. Results demonstrate the capacity of neuroimaging to capture the rapid changes in cortical development that occur in infancy and early childhood. In addition, we demonstrate that these changes in cortical development in early postnatal life predict variability in cognitive function later in childhood. This highlights the possibility of observing brain development in vivo during sensitive periods as a means to understand how neural development may support the emergence of complex cognition across the lifespan.

3-H-74 - Social media exposure and distress among adolescents is associated with altered neural oscillatory dynamics serving emotion dysregulation and executive dysfunction

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Details

Objective: Adolescence is a critical period of neural development, and over the past decade, social media use has sharply increased among this age group. Deficits in executive function and emotion regulation typically emerge during adolescence, which can lead to downstream psychopathological symptoms such as depression and anxiety. Several studies have linked high social media use to internalizing symptoms such as depression and anxiety, illuminating the urgent need to elucidate how social media use alters the neural oscillatory dynamics serving cognitive function.

Methods: A total of 37 participants between the ages of 9-16-years underwent an emotional interference experiment during magnetoencephalography (MEG) and completed a battery of emotional and social media use assessments. MEG data were imaged in the time-frequency domain and oscillatory responses were imaged using a beamformer, which generated whole-brain oscillatory maps for each time-frequency bin per participant. Using the social media data, we derived two distinct continuous latent factors representing social media exposure and social media distress using exploratory factor analysis (EFA). Whole-brain correlations were conducted using the resulting social media indices for each oscillatory response, controlling for age.

Results: A latent factor depicting social media exposure was identified, which accounted for 57.24% of the variance. Similarly, a latent variable of social media distress was identified, which accounted for 69.13% of the variance. Continuous scores were extracted per participant for each latent factor identified in which higher values were indicative of greater social media exposure and social media distress. Whole-brain correlations using these metrics revealed that greater social media exposure was associated with blunted oscillatory gamma (62-90 Hz) power in the left dorsolateral prefrontal cortex (DLPFC; r = -.71, 95% CI: -1.30 - -.17) during the fearful face condition. In contrast, however, elevated social media distress was associated with stronger gamma power in the bilateral supramarginal gyri, controlling for age (left, *r*=.67, 95% CI: .39-1.04; right, *r*=.62, 95% CI: .23-.99) during the fearful face condition.

Conclusions: We found that greater social media exposure and social media distress were associated with alterations in oscillatory gamma activity in critical regions supporting attention and emotion

processing. Specifically, we identified blunted oscillatory gamma activity with greater social media exposure in the left DLPFC, which suggests that greater exposure to social media scales with greater desensitization to emotionally arousing stimuli. Conversely, however, elevated social media distress was associated with stronger oscillatory gamma activity in the bilateral supramarginal gyri, demonstrating that the social media exposure and social media detriment indices are differentially related to oscillatory gamma power in regions critical for attention and emotion processing.

3-H-75 - The first year of formal schooling improves working memory and academic abilities

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Details

Objective: Children between four and seven years of age undergo a dynamic shift in neurocognitive functions and academic abilities. It is unclear to what extent this shift represents the transition from a kindergarten environment to a formal school learning environment because it is simultaneously confounded by age-related developmental changes. Previous work employing school cut-off designs has demonstrated that exposure to formal schooling is associated with improvements in literacy and mathematics. However, there is limited evidence demonstrating the impact of schooling on executive sub-functions. The current study used a modified school cut-off design to tease apart schooling-related effects from age-related effects on visual working memory (VWM). Furthermore, the study examined the association between schooling-related changes in VWM and academic abilities.

Methods: We compared two groups of children with similar age, across two years: first- graders (FG), who were enrolled into primary school the year that they became eligible (37 FG (23 females, *Mage* = 53.7 months, *SD* = 1.4) and kindergarteners (KG), who were deferred school entry until the following year 37 KG (14 females, *Mage* = 53.3 months, *SD* = 1.2). In the first year of the study, both FG and KG were enrolled in kindergarten. In the second year of the study, FG were enrolled into primary school while KG remained in kindergarten. During both years, all children completed a colour change detection VWM task while brain activation was recorded using portable functional near-infrared spectroscopy (fNIRS), and a vocabulary assessment and numeracy screener as measures of academic ability. fNIRS data was analyzed using novel image reconstruction to transform channel-based data into voxel space. Behaviour and brain activation data were fitted with univariate latent change score models to investigate the effect of transition from kindergarten to primary school and later, to bivariate models to investigate the association between change across domains.

Results: Our results revealed that FG children showed greater improvement in VWM performance and greater engagement of left-lateralized inferior parietal lobule and inferior frontal gyrus compared to KG children. Thus, exposure to a disciplined schooling environment might enhance specialization in regions involved in integrating verbal, semantic, phonological processes with WM function. FG children also showed higher gains in vocabulary and non-symbolic numeracy scores suggesting that exposure to different types of interactions with teachers and peers (e.g., during group activities and recess) might lead to greater accumulation of rich word knowledge. Similarly, repeatedly performing magnitude comparisons and numerical operations in school could result in better performance in FG children. Finally, bivariate modelling revealed that VWM function predicted improvement in vocabulary following a year in

primary school. Our finding suggests that the quantity, persistence, and quality of rich visuo-haptic-verbal experiences relying on visual familiarity and working memory throughout early development can be critical for acquisition and development of word knowledge.

Conclusion: Our findings contribute to a growing body of literature examining the neurocognitive and academic benefits conferred to children following exposure to a structured formal schooling environment.

3-H-76 - Does Bilingual Exposure Protect against SES Disparities in Selective Auditory Attention? A fMRI Study in Young Children

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Details

Selective attentionâ€"the ability to focus on relevant signals and manage distractionâ€"is a foundational executive functioning (EF) skill important for academic and socioemotional developmental outcomes (Stevens & Bavelier, 2012; Veer et al., 2017; Garon et al., 2008), and it undergoes protracted development within the first few years of life (Blakey et al., 2016). While the neural basis of selective auditory attention has been extensively studied in adults (Hillyard et al., 1973; O'Connor et al., 2002; Astheimer & Sanders, 2009), less is known about its development in children. Studies have argued that growing up bi/multilingual may create mental confusion and 'slow downâ€ the development of crucial cognitive skills that allow for academic success in school (Hakuta, 1986; Peal & Lambert, 1962). In contradiction, there is research showing that speaking multiple languages in early years of life promotes EF skills of cognitive flexibility, working memory, and inhibition (Bialystok, 1999, 2011; Pliatsikas et al., 2020). However, studies of this so-called 'bilingual advantageâ€ tend to be in participants from higher socioeconomic status (SES) backgrounds. Thus, it remains unclear whether bilingualism may buffer against the negative effects of low SES on neurocognitive EF development.

In this pre-registered study (https://osf.io/sxkat), we use functional magnetic resonance imaging (fMRI) to examine children's selective attention during a dichotic listening task, and investigate relationships with family SES, language experience, and EF performance. Specifically, we address three hypotheses**:**

1. At the group level, participants will exhibit increased activation during dichotic listening in auditory/language areas (bilateral posterior superior temporal gyrus and left inferior frontal gyrus) and posterior attention areas (bilateral anterior and posterior cingulate, precuneus/cuneus, and superior parietal regions).
2. Both SES and bilingual exposure will be associated with performance on EF tasks and activation in language and attention regions during dichotic listening. Specifically, higher SES (controlling for bilingualism) and greater proportion of bilingual exposure (controlling for SES) will be associated with higher EF scores, but the direction of effect on dichotic activation is not hypothesized. Greater activation could indicate greater task engagement, or less activation could indicate neural efficiency.

3. Language status (bilingual/monolingual) will moderate the relationship between SES and EF scores/dichotic listening activation, such that greater bilingual exposure will reduce the correlation between SES and (a) the magnitude of activation during selective attention, and (b) performance on EF tasks.

Participants were 44 children (55% male) aged 4-7 years (M=5.82 years, sd=.64) from diverse socioeconomic, racial/ethnic, and linguistic backgrounds. N=12 were bilingual, though all were native and fluent English speakers. Children completed assessments of EF and English language skills, as well as a dichotic listening task during fMRI, in which they were instructed to attend to a story told by a female voice (played in one year) and ignore a story told by a male voice (played in the other ear), with visual reinforcements. Analyses will investigate main effects of SES and bilingual language status, as well as their interaction, on the magnitude of activation during dichotic selective attention (versus binaural story listening) and performance on EF tasks. Critically, we will examine whether bilingualism protects against the negative effects of low SES on neurocognitive EF development. Results have implications for reducing SES disparities in EF development, especially for children from demographically and linguistically diverse backgrounds.

As of the date of this submission, we have preprocessed the fMRI data and cleaned the behavioral data, but have not conducted any analyses central to the present study. This will be completed by Flux.

3-H-77 - Social learning across adolescence: A Bayesian neurocognitive perspective

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Details

Background

Adolescence is a period of social re-orientation in which we are generally more prone to peer influence and the updating of our beliefs based on social information, also called social learning, than in any other stage of our life. However, how do we know when to use social information and whose information to use and how does this ability develop across adolescence? I put forward a Bayesian reinforcement learning framework that incorporates social learning about value associated with particular behavior and uncertainty in our environment and experiences. I will discuss how this framework can inform us about developmental changes in social learning, including how the assessment of uncertainty and the ability to adaptively discriminate between information from different social sources change across adolescence. I will then substantiate this framework alongside recent results from a neuroimaging (fMRI) study in which we investigated individual differences in the assessment of uncertainty and how this leads to differences in social information use.

Study design

Participants play an estimation game while being fMRI scanned. In this game, participants can update their first estimate after seeing a peers estimate, which is shown alongside the peer's subjective confidence statement. Both the participants uncertainty and the peers reported confidence are manipulated.

Hypotheses

We expect that participants are more prone to use social information if they themselves are more uncertain and the peer reports to be more confident. We expect that individual differences in the processing of own uncertainty and peer confidence are mirrored in neural activity patterns in brain areas related to social, reward, and executive functioning. Moreover, we expect uncertainty to decrease, and the distinction between the reliability of peers to increase from adolescence into adulthood.

Analysis plan

Computational modelling will be used to determine how participants assess their own and their peer's estimate and confidence, and how they combine this information in a Bayesian fashion to arrive at a final decision. Univariate and representational similarity fMRI analyses will further probe which neural mechanisms are implicated in these computations. Data collection of an adult population (N=73) has been finished and analyses on this dataset will be finished before the conference. Data collection of an adolescent population (N = 120) will still be in progress.

3-H-78 - Relating socio-structural environment factors to adolescent inhibitory control neurodevelopment

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Details

Experiences are potent catalysts for developmental change. This is especially true for dimensions of cognitive control, including inhibitory control, which continue to develop into adolescence. The current study is an extension and replication of prior work demonstrating that neural focalization in brain regions related to inhibitory control track with task performance. Here, we describe methods and planned analyses for ongoing work utilizing the baseline sample from the Adolescent Brain Cognitive Development (ABCD) study (n=708; M_{age}=9.96 years, SD=0.63; 51% female) with usable data to examine relationships between neural focalization, Stop Signal Task (SST) performance, and aspects of adolescents' socioeconomic and home environments with three hypotheses.

Hypothesis 1. *Greater focalization in regions of interest (ROIs) tracks with better SST performance.* We previously demonstrated that neural focalization in regions of dorsolateral prefrontal cortex (DLPFC) and

parietal cortex related to better performance on a Flanker task. Here, we seek to replicate these results with a different inhibitory control task, the SST. With the SST, adolescents must withhold button presses on a small number of trials whenever a brief visual cue flashes on the screen, which conflicts with the prepotent response. Participants completed two runs of the SST (360 trials) while undergoing a functional MRI scan. Performance is benchmarked at 50% for stop signal trials. Task performance will be quantified using the Stop Signal Reaction Time (SSRT), which captures the response latency for stop trials. We will first examine relationships between SSRT and univariate activation from the successful stops unsuccessful stops contrast in our a-priori ROIs in cingulate, DLPFC, insula, and parietal cortex. A multilevel linear model (accounting for nested families and study sites) will estimate SSRT from univariate activation in each of the ROIs. We expect a positive relationship between cingulate activation and SSRT, given prior correlational studies. These preliminary findings will lay groundwork for future work examining focalization.

Hypothesis 2. *Socioeconomic status (SES) positively relates to performance and focalization*. Utilizing caregiver-reported income, education, and family demographic information, we will conduct a Principal Component Analysis to maximize the variance explained between participants along these dimensions of SES. Loading scores for the first component will be used to estimate SSRT and univariate activation in each ROI using separate multilevel linear models. We expect that *on average* individuals from lower socioeconomic backgrounds will have higher SSRTs, given prior literature on SES and cognitive control. Univariate results are expected to follow similar trends, although we do not have strong hypotheses regarding ROI-specific effects.

Hypothesis 3. *Home environments buffer associations between SES and focalization*. Prior work suggests that supportive home environments can mitigate adverse neurodevelopmental outcomes in youth. From the youth-report Parent Monitoring Survey and Parenting Behavior Inventory, we will compute a caregiver support principal component. This support score will be submitted as an interactive term alongside SES loading scores to estimate task-related univariate activity in a multilevel linear model. We expect to find that adolescents from lower socioeconomic backgrounds with more supportive caregivers will show greater task-related activity in our ROIs relative to similar adolescents with less caregiver support.

Implications. Together these results will provide insight into how experiences shape adolescent neurodevelopment. Importantly, the univariate results presented here will be used as comparison models for our planned analyses investigating the ways socioeconomic and home environment factors relate to task-related neural focalization, as well as future longitudinal models.

I- Language

3-I-79 - Bilingual and monolingual differences in basal ganglia reinforcement learning

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Details

Objective: Reinforcement learning (RL) theory states that individuals learn the value associated with choices by computing the discrepancy between reward and a previously estimated value, while

proportionally adjusting their estimate. RL lies at the core of successful goal-directed behavior and learning. Studies have implicated the Basal Ganglia (BG) in RL. Specifically, the Conditional Routing Model (Stocco et al., 2010; 2014) states that the BG's involvement in RL can be seen as a routing operation that defines which signals are being transferred between cortical regions through BG functional pathways. However, most RL studies have not considered bilingualism. Some studies show that bilingualism trains specific brain circuits involved in flexible rule selection and application, while other studies find no differences in cognitive performance between monolinguals and bilinguals. Thus, the current study will attempt to bridge the gap in the literature by examining RL differences between monolingual and bilingual language groups and within bilinguals. It is expected that 1) between language groups, bilinguals will outperform monolinguals in RL, and 2.1) within bilinguals, those with higher bilingual proficiency will outperform their counterparts, and 2.2) early bilinguals will outperform late bilinguals.

Method: English monolinguals and English-Spanish bilinguals will be recruited from the University of Houston. Handedness, demographic information, subjective language background (Language and Social Background Questionnaire), and objective language proficiency (Woodcock Language Proficiency Battery Revised) will be collected. A bilingual language proficiency score weighted for balance will be calculated. Participants will then complete an RL task paradigm adopted from Collins (2018). During the RL task, participants must learn correct associations based on feedback and be tested on the results later. For the learning phase, there will be 14 blocks in total with a new set of visual stimuli in each block. Blocks vary in numbers of stimuli (i.e., set sizes 3 or 6). Participants will also be given an n-back task between the learning and testing phase to prevent them from reciting what was learned. The testing phase will have 54 stimuli presented four times each, for a total of 216 trials. All stimuli will be pseudo-randomized. Accuracy and RT in learning and testing phase will be collected.

Analysis: We will explore RL performance, with separate analyses conducted for accuracy and reaction time. Analyses will first be conducted in the whole sample to explore the main effect and interaction of set size (3 vs. 6), phase (learning vs. testing), and language group (monolingual vs. bilingual). We hypothesize that bilinguals will outperform monolinguals. The second set of analyses will be conducted within bilinguals. We hypothesize that those with higher bilingual proficiency will outperform their counterparts, and early bilinguals will outperform late bilinguals. The analysis will explore the main effect and interaction of set size (3 vs. 6), phase (learning vs. testing), and language background (AoA and proficiency score). Data collection is in-progress and will continue being collected and analyzed in time to be presented at the Flux conference.

3-I-80 - Lateralization of activation in the superior temporal gyrus for speech processing in sleeping infants is predictive of their language skills in kindergarten: a task-based fMRI study.

Jin Wang [1], **Ted Turesky** [2], **Megan Loh** [1], **Ja'kala Barber** [1], **Victoria Hue** [1], **Escalante S. Elizabeth** [2], **Adrian Medina** [1], **Nadine Gaab** [1, 2]

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Details

Using functional magnetic neuroimaging (fMRI), prior studies have observed that infants already exhibit left-lateralized brain activation in the superior temporal gyrus (STG) for speech sentence processing even

during sleep. Using electroencephalogram (EEG), other studies have found that electrophysiological responses to oddball speech sounds in infancy are prospectively associated with language and literacy outcomes at preschool and school age. However, EEG does not provide spatial accuracy for brain function and the speech sounds in those studies were limited to a few syllables. Little is known about whether brain activity in STG localized by task-based fMRI for speech sentence processing, a more naturalistic task, in sleeping infants is associated with subsequent language outcomes. To address this gap, the current study involved 59 3-12-month-old infants who underwent fMRI while listening to forward- versus backward-speech during natural sleep. Of these, 25 were subsequently assessed on language skills in preschool/kindergarten. We observed that neither the amplitude of brain activation in the bilateral STG nor standardized behavioral measures were associated with subsequent language skills in kindergarten. However, the left-lateralization index of brain activation in STG consistently predicted various aspects of language skills, including expressive language, receptive language, and phonological awareness. Overall, our findings provide the first evidence suggesting that brain indices evoked by language tasks in sleeping babies during fMRI can be a useful tool and may be more sensitive than behavioral measures in predicting later language skills.

3-I-81 - Longitudinal associations between language network characteristics in infant brain and school-age reading abilities are mediated by early-developing phonological skills

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Details

Background: Reading acquisition is a prolonged learning process relying on sound and early language development starting in utero. Behavioral longitudinal studies have demonstrated that infant language abilities were prospectively associated with preschool/kindergarten language skills, which in turn related to school-age reading performance. The advances of pediatric neuroimaging techniques facilitate the characterization of the neural network mechanisms underlying language development in infancy. However, it is still unknown how the early-emerged language network scaffolds long-term reading acquisition.

Objective: To examine whether and how the FC characteristics of the language neural network in infancy are associated with individual differences in children's language and preliteracy skills in kindergarten and subsequent reading abilities.

Methods: Our research question was addressed using a seven-year longitudinal dataset, spanning infancy to elementary school ages. Seventy infants (32 females) completed resting-state fMRI scanning during natural sleep (mean age = 9.4 ±3.6 months) and were followed until kindergarten (mean age = 5.7 ±0.7 years), where their oral language, phonological processing skills, and rapid automatized naming (RAN) abilities were assessed behaviorally. Of this larger cohort, thirty-nine (20 females; mean age = 7.7 ±0.8 years) were subsequently seen in second grade and assessed on their word reading abilities. The intrinsic functional organization of the infant language network was first probed using the hierarchical clustering. Correlation and mediation analyses were subsequently performed to evaluate prospective

associations between infant language network characteristics and school-age language and reading abilities.

Results:

4. A modular architecture (Q = 0.30) was identified for the infant language network, which included three modules: a) an inferior frontal (IFG) module comprising bilateral inferior frontal gyri and their orbital part; b) a middle frontal (MFG) module consisting of bilateral middle frontal gyri; and c) a temporoparietal (TPG) module involving bilateral middle temporal and angular gyri.
5. Longitudinal behavior analyses showed that phonological processing skills and RAN abilities at the kindergarten time point were significantly correlated with word reading abilities at the elementary school time point.
6. FC of the IFG module within the infant language network was positively associated with phonological processing skills at kindergarten age and word reading abilities at elementary school while controlling for infant scan age, head motion, nonverbal IQ, home literacy environment, and family socioeconomic status. Moreover, keeping the covariates consistent, mediation analyses further revealed a significant mediation role of kindergarten-age phonological processing skills on the relationship between the infant FC and school-age word reading abilities.

Conclusion: The current study demonstrates that the functional characteristics of the infant language network are linked to kindergarten-age phonological processing skills, and further support later reading development. Our findings shed light on the scaffolding role of the early-emerging language neural network in supporting the development of core language/preliteracy skills and laying the foundations for subsequent reading acquisition.

3-I-82 - Investigating the relationship between audiovisual integration and dyslexia with steady-state EEG

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Details

Objective

Automatic audiovisual (AV) integration of letters and speech sounds in the brain supports early reading development. This process is known to be impaired in developmental dyslexia, but few studies have explored AV integration in English, leading to a gap in understanding AV integration across languages and developmental populations. The present study presents a new steady-state evoked response (SS-EP) EEG paradigm to explore AV processing in an understudied population, neurotypical and dyslexic adolescents.

Methods

This pilot took place in an authentic school context through an existing research-practice partnership with a local school. Eight students (3 female, M = 13.17 years, SD = 1.42) participated in the paradigm. 4 students were diagnosed with dyslexia and 4 were neurotypical; all learned English from birth. During the sessions, participants indicated when identical stimuli appeared twice in a row while 128-channel EEG was recorded. We spatially filtered the EEG using RCA, which computes optimal linear weightings of electrodes to maximize covariance across trials. For each stimulus condition and participant group, we computed RCA across even harmonics of the response (2Hz-8Hz) to investigate stimulus-related activations. We visualize projected weight vectors on scalp maps, and present amplitudes of component-space data at each harmonic.

In the Letters condition, stimuli were six visual letters and natural speech sounds corresponding to the letters. In the Words condition, stimuli were six three-letter words and synthesized speech sounds corresponding to the words. All stimuli were presented in alternation at a rate of 2 Hz. When presented with letters, congruent letter-speech sound pairs (e.g., t and /t/) alternated with incongruent pairs (e.g., p and /d/). When presented with words, congruent word-sound pairs (e.g., bat and /bat/) alternated with incongruent pairs (e.g., bat and /zip/). Both conditions thus comprised a stimulus oscillation of 2 Hz as well as a congruence oscillation of 1 Hz.

Preliminary Results

We hypothesized that neural responses at even harmonics would indicate low-level effects related to sensory input from AV stimuli. In the neurotypical group, the maximally reliable component (RC1) topography for letters and words is consistent with a previously reported auditory RC1 (Kaneshiro et al., 2020). The second maximally reliable component (RC2) has an occipito-temporal topography, interpreted to be associated with visual processing. In the group of participants diagnosed with dyslexia, RCA recovered a unique RC1 topography for Letters and Words which is bilaterally symmetric through occipito-temporal and temporal areas.

Preliminary Conclusions and Future Directions

Using a steady-state paradigm together with a data-driven spatial filtering technique, we recovered modality-relevant topographies from neurotypical students and students diagnosed with dyslexia. The components recovered by RCA for neurotypical readers closely resemble RC1 and RC2 from a large sample of English-speaking adults run on the same Letters condition, suggesting this steady-state AV EEG paradigm is appropriate to run with participants of different ages. These preliminary RCA results also revealed a novel RC1 topography for participants with a dyslexia diagnosis. Finally, RC2 of the dyslexic group resembles RC1 of the neurotypical group, though from visual inspection, activation over occipital areas appears less left-lateralized for dyslexic than neurotypical participants. Moving forward, we plan to collect reading fluency data from current and future participants to be able to explore brain-behavior relationships in these populations and continue increasing our sample size to test the reliable components for significant differences and also complete analysis of the 1 Hz congruency effect. Taken together, these data sources could contribute to understanding AV processing differences in developmental populations with dyslexia.

3-I-83 - Pre-school children engage language areas of the brain to form predictions during sentence processing

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Details

Objectives: Changes in alpha power (9-12 Hz) have been observed when adults process sentences with different degrees of semantic predictability. Specifically, semantically constrained (high predictability) sentences are related to decreased alpha power compared to semantically unconstrained sentences (low predictability, Piai et al., 2017; Rommers et al., 2017; Terporten et al., 2019; Wang et al., 2018). The alpha effect is often found about 800 msecs prior to the onset of the target word, referred to as the predictability window. This is interpreted as alpha idling in highly constrained contexts. Although the alpha effect is well-known in adults, there is no evidence of this effect in young children. The goal of the present study was to investigate whether alpha idling is present during semantic prediction in a group of pre-school children. We hypothesize that children would also exhibit changes in neural oscillatory activity in the predictability window related to semantic predictability; however, due to developmental changes in language ability and neural oscillatory frequencies, those differences would likely occur at a lower frequency (~ 6-8 Hz).

Methods: Thirty-three 3â€“5-year-old children (M = 4.6, SD = 0.84, 11 females) with typical development participated in the study. Children were all in Spanish-dominate, Spanish-English bilingual households from a range of socioeconomical (SES) backgrounds. They listened to 100 sentences (50 with a high predictability final word [HP], and 50 with a low predictability [LP] final word). To ensure attention, after each trial children were asked to tap a picture that represented the last word of the sentence they just heard. Sentences were presented at 70 dB from a speaker centered one meter above the participant's head in a sound booth. A Neuroscan 64-electrode Quickcap was used to record EEG activity. Our analyses focused on alpha, (9-12 Hz); however, because alpha peaks at a lower frequency and shifts during development (Freschl et al., 2022), we explored differences between conditions at the predictability window at a wider frequency range (5-12Hz). We computed 5-12Hz over the predictability window per trial. Then, we compared LP and HP conditions using cluster-based Monte Carlo analyses within the EEGlab Toolbox to account for multiple comparisons (Oostenveld et al., 2011). Once we identified conditions differences in topography, we analyzed the timing of the effect during the predictability time window by selecting the most significant channel (Cz) and performing paired-sample t-tests between conditions using the same controls for multiple comparisons.

Results: We found that similarly to adults, highly constrained sentences elicited a significant decrease in power compared to semantically unconstrained sentences during the predictability window. This effect was strongest in the 5-9 Hz window indicating immature alpha responses in 3â€“5-year-olds. Importantly, these results suggest that children can predict upcoming words in a sentence when contextual cues are available, engaging language regions of the brain to form and assess predictions to maximize sentence comprehension (Rommers et al., 2017; Wang et al., 2018). Future analyses will include whether alpha idling is related to language skills in these children.

Conclusions: To our knowledge, this is the first study showing that semantic prediction can be assessed in preschool-aged children using neural oscillations of the EEG. Future studies could implement this methodology to assess semantic prediction in other contexts such as word learning or sentence processing in noise.

3-I-84 - Early brain connectivity patterns predict later language skills in preschoolers with autism spectrum disorder

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Details

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by social communication deficits and restricted and repetitive behaviors. Symptoms of ASD emerge in the first years of life and can be reliably identified during the second year. Although no longer required for an ASD diagnosis, speech delays or atypical emergence of language skills are common in children with ASD. Early language abilities affect later academic performance, social communication and relationships, and are among the best predictors of later functional outcomes in children and adults with ASD. However, little is known about early atypical brain organization in ASD and language abilities in young children with ASD. The present longitudinal study will examine links between brain connectivity patterns, especially between brain regions known to support language processing, estimated during toddler years, and language skills assessed in preschoolers with ASD during follow-up visits. We hypothesize that greater interhemispheric connectivity between language regions will be predictive of lower language skills assessed later in preschoolers with autism. This study will utilize functional MRI data acquired during natural sleep on a GE 3T MR750 scanner (two 6-minute runs, or 800 volumes), in combination with clinical and behavioral data collected from toddlers and preschoolers with ASD and typically developing (TD) young children participating in the longitudinal SDSU Toddler MRI Project examining early brain markers of ASD. The cohort with longitudinal data includes 24 children with ASD (7 female, 17 male) and 17 TD children (6 female, 11 male) who were between 16 and 51 months of age (mean age 28.7Â±8.8 months) at their first study visit, and between 36 and 68 months (mean age 49.8Â±11.4 months) at the second study visit (average 21 months between visits). The two groups are matched at group level on age, sex, socioeconomic status (e.g., household income-to-needs ratio) and fMRI data quality (in-scanner head motion estimated with RMSD). Developmental skills, including expressive and receptive language skills, were assessed in all (ASD and TD) participants with the Mullen Scales of Early Learning (MSEL). fMRI data will be preprocessed using SPM12 and the conn toolbox. Functional connectivity (at Visit 1) between canonical regions implicated in language processing (bilateral superior temporal gyrus [STG], posterior superior temporal sulcus [pSTS], inferior frontal gyrus [IFG], and middle temporal gyrus [MTG]) will be estimated with Fisher's z-transformed Pearson correlation coefficients calculated between the BOLD signal time courses from each region. Mean z scores (connectivity) between each pair of language regions will be submitted to Principal Component Analysis (PCA) for dimensionality reduction, to identify a principal language connectivity component (language PC), which will then serve as a predictor of language skills. Analyses of Covariance (ANCOVAs) will be employed to test for effects of diagnostic group (ASD, TD), language early connectivity, and connectivity by group interaction effect on later language skills (at Visit 2), with sex, age, socioeconomic variables (e.g., income-to-needs ratio), and head motion as covariates.

Considering the malleability of the brain during the first five years of life, gaining a better understanding of how early language develops in children with autism will help inform evidence-based early interventions, specifically current speech therapy models. This may lead to improved language and

social outcomes for children with autism who are showing atypical language development, contributing to improved quality of life for both children and their families.

J- Learning

3-J-85 - Neural synchrony during parent-child spatial problem-solving interaction: Role of parent verbal and gesture strategy

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Details

Synchronous interactions between parent and child are fundamental for children's development. Most prior work examined synchronous interactions focused on the relations to children's social cognition development (Nguyen et al., 2020) or emotional outcomes (Feldman, 2007a, Feldman, 2017). However, such interactions played a vital role in children's cognitive development as well (Casey et al., 2000; Mahy et al., 2014; Rueda et al., 2004; Hoeft et al., 2007; Redcay et al., 2008). The challenge of exploring how synchronization affects children's cognitive development lies in constructing a natural interaction scenario that requires the participation of cognitive abilities. fNIRS (functional near-infrared spectroscopy)-based hyperscanning, which measures neural data from all participants simultaneously using multiple devices, offers the opportunity of setting a natural interaction in the laboratory. In the current study, we apply fNIRS-based hyperscanning in a cooperative spatial task (tangram puzzle) and do the video recording for the whole session. Two main brain areas from both hemispheres, the dorsal lateral prefrontal cortex (dlPFC) which is relevant to problem-solving, and the temporoparietal junction (TPJ) area which is relevant to social mentalization, are covered using 8 by 8 fiber distribution through fNIRS. During the task, two participants are asked to cooperate with each other to solve a tangram puzzle together. Our goal in the current study is to explore how different parental strategies in this cooperative spatial task relate to different neural synchrony patterns. Therefore, we categorized parental strategies into two categories: verbal support and gesture support (Clingan-Siverly et al., 2021), and did the behavioral coding based on the videotape. After running the preprocessing to remove noise, we run the wavelet transform coherence (WTC) to represent the neural synchrony patterns underlying different conditions and strategies. We shuffled the dyads and ran WTC among random pairs (two participants coming from different families) as the control group. The results revealed higher WTC scores in regular pairs than in random pairs ($F(1, 287) = 99.2$, $p < 0.001$, Î·2 = .15ï¼‰ and the random pair is not related to the cooperation ($r = -.292$, $p = 239$). In other words, the elevated interpersonal neural synchrony came from real cooperation and interaction instead of doing the same task. Then, we aligned the behavioral data with the neural data to conduct strategy-based analysis. The effect of the strategy was significant and neural synchronization of the gesture strategy was significantly different from the no-strategy. When we zoomed into specific gesture strategy events, we found that the WTC score increased by comparing before, during, and after the gesture event, which meant the neural synchronization went up with the unfolding of the gesture strategy ($F(2, 26) = 0.001$, $p = 0.004$), controlling for overall WTC differences. From the spatial perspective of synchronous patterns, the highest levels of synchrony came from the channel pair based on dlPFC of the parent. This may reveal that during a cognitive relevant interaction, parent strategy plays a role and the child process information input given by the parents to help themselves develop cognitive abilities. Overall, from the current study, we explored the dynamic change of neural synchrony during a cooperation cognitive task

and the results showed that neural synchrony was higher in cooperation, went up with the unfolding of strategy, and showed up in a particular brain area.

3-J-87 - Convergent gain of function and cognitive inflexibility in mouse models of two autism risk genes

Juliana Chase [1], **Wan Chen Lin** [1], **Tory Benson** [2], **Linda Wilbrecht** [1]

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Details

Autism spectrum disorder (ASD) is a common neurodevelopmental disorder characterized by social differences and restricted and repetitive behavior. Over a hundred genes have been associated with ASD. Some of these genes have been reliably linked with larger syndromes that include a host of psychiatric, cognitive, and medical conditions including a behavioral diagnosis of autism. Two of these disorders, Tuberous Sclerosis Complex (TSC) and Phelan McDermid Syndrome (PMS) are caused by mutation to either *TSC1* or *TSC2* and *SHANK3*, respectively, and lead to an ASD diagnosis in over half of diagnosed individuals. We were interested in studying learning and cognitive flexibility in mice genetically engineered to model these genetic syndromes. We hypothesized that learning differences may be common to both syndromic genotypes and that these learning differences might explain core symptoms of restricted and repetitive behavior and social deficits. Another goal was to determine if learning differences were present when the reward schedule was deterministic or probabilistic, and to test for sex differences in phenotypes. Our overall goal was to look for convergent phenotypes across multiple risk genes that may help inform ASD etiology and aid in design of therapeutic interventions.

To test learning,we used an odor-based two-alternative forced choice task to assess learning and cognitive flexibility in *Tsc2+/-* or *Shank3B*+/-, -/- or WT mice. We focused on learning in adolescent mice, postnatal day (P)30-60. In our task, mice had to learn to discriminate between two odors and indicate which odor was presented by making either a left or right choice. After learning a series of ~5-7 odor pairs we tested flexibility using a reversal of the left/right contingency for the last odor pair learned. We found that in early learning with a deterministic schedule
both *Tsc2+/-* and *Shank3B+/-* male mice showed a significant gain of function in performance. This gain of function was not observed in females. T*sc2+/-* and *Shank3B+/-* male mice did not show this gain of function in early learning when we trained them using a probabilistic schedule. After repeated training to reach a criterion of 70% correct on an odor pair, *Tsc2+/-* and *Shank3B-/-* mice were slower to learn an odor-action rule reversal than WT littermates.

Together, our findings reveal behavioral convergence in a novel cognitive learning task that shows both gain of function early in learning and cognitive inflexibility in reversal learning. We interpret these findings in light of other observed gains of function in dorsal striatal dependent tests of motor learning that have been observed in multiple ASD risk gene mouse lines. We also will discuss the relevance of these data for designing behavioral interventions for restricted, repetitive behavior and inflexibility. Ongoing work will explore how differences in corticostriatal circuits in *Tsc2* and *Shank3B* mutant animals may underlie differences in learning and whether reinforcement learning models reveal common differences in trial by trial learning strategies across genotypes.

3-J-88 - Investigating the neural analog-to-symbolic shift in 5- to 7-year-old children's numerical cognition

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Details

Introduction. Number line estimation (NLE) is a major behavioral marker of cognitive development because it tracks the shift from perceptual (analog) to symbolic development in mathematics performance (Siegler & Opfer, 2003). Despite many advances in developmental neuroimaging (Cantlon, 2020), there is no work to date using fMRI to evaluate the neural mechanisms of the NLE task in children. This gap in developmental neuroimaging is important to fill because it will allow us to observe the neural events underlying a well-known analog-to-symbolic shift in children's cognition.

Methods. One key reason for the lack of fMRI research on NLE in children is task-related motion, as the traditional NLE task typically requires children to mark their response on the number line using a pencil or a computer mouse. To this end, we designed a novel NLE-comparison task to minimize task-related motion. In this task, children (n = 26; 5 7 years old) were presented with a number line bounded between 0 and 100, a target number (1-99, varied pseudo-randomly), and two vertical lines, marking possible spatial locations of the target number. Children used left and right response buttons to indicate which of two presented locations on the number line was closer to the target number's correct spatial location. Children also completed a matched control task in which children used left and right response buttons to indicate whether an item was presented on the left or right side of the screen. Following the fMRI session, children completed a behavioral session consisting of measures of formal math ability (WJ-Calculation; Woodcock, McGrew, & Mather, 2001), traditional NLE (Fazio et al., 2014), and general cognitive ability (KBIT-2; Kaufman, 1990).

Results. Whole-brain GLM contrasts were conducted to identify areas that showed greater activation during the NLE-comparison task than the control task. We found that bilateral intraparietal sulcus and inferior frontal gyrus exhibited significantly greater activation to the NLE-comparison task than the control task (p < .01; cluster-corrected at p < .05). NLE > Control activation in right inferior frontal gyrus and right intraparietal sulcus, was significantly correlated with children's performance on the traditional NLE task, outside of the scanner (p < .05). Furthermore, this effect was significant when controlling for children's scores on KBIT-2, suggesting that the involvement of right inferior frontal gyrus and right intraparietal sulcus during the NLE-comparison task cannot be attributed to general cognitive ability.

Conclusion. We found that children's NLE performance is supported by bilateral intraparietal sulcus and bilateral inferior frontal gyrus, replicating previous work on NLE in adults (Kanayet et al., 2017; Vogel et al., 2013). Moreover, the significant associations between right intraparietal sulcus and inferior frontal gyrus activation during our novel NLE-comparison task and out-of-scanner behavioral measures of NLE suggest that these regions may underlie the extensive developmental change in NLE performance over early childhood development. Lastly, these results provide initial validation of the use of the NLE-comparison task as both a behavioral and neural measure of number line estimation.

3-J-89 - Assessing white matter plasticity in a randomized controlled trial of reading training in preschoolers

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Details

Introduction: Reading is an evolutionary recent cognitive skill that requires our brain to go through a myriad of changes. While many studies have described how reading acquisition shapes children's brain function, less is known about the impact of reading on brain structure. Here we examined the causal effects of reading training on preschoolers' white matter structure.

Study's objective: We tested whether a two-week reading training in preschoolers causes changes in the diffusion properties of eighteen white matter pathways, including the left arcuate and the left inferior longitudinal fasciculus. Forty-eight English-speaking preschoolers (4y10m to 6y2m) participated in a randomized controlled trial. The pre-literate participants were randomly assigned to two training programs: the Reading training program focused on key skills for reading (e.g., phonological awareness, letter-sound decoding), while the Language training program strengthened oral language comprehension skills without text exposure (e.g., vocabulary, storytelling, syntax).

Methods: Behavioral and MRI measures were collected before and after the training programs. Participants' literacy skills were tested longitudinally with measures of letter knowledge and decoding. T1-weighted (T1w) images and diffusion-weighted magnetic resonance imaging (dMRI) data were acquired using a 3 T Phillips Achieva scanner at the University of Washington. MRI preprocessing and reconstruction were carried out using QSIprep. Eighteen white matter tracts were segmented using pyAFQ, and fractional anisotropy (FA) and mean diffusivity (MD) values were calculated along the trajectory of each tract (i.e., Tract Profile).

Results: Behavioral data showed that only the Letter Training group increased letter knowledge after the two-week training. DMRI measures showed high degrees of test-retest reliability between the two experimental sessions (FA: median r = 0.83, range 0.62-0.90; MD: median r = 0.87, range: 0.55-0.92). Linear mixed effects models testing changes in diffusion properties a) did not reveal any statistically significant changes for either intervention group and b) did not reveal any differences between the groups. Bayesian factors supported small-to-moderate evidence for the null effect (BFs<1).

Conclusions: These findings suggest that a two-week training reading training program causes behavioral changes in preschoolers' letter knowledge. However, this behavioral improvement is not accompanied by short-term changes in the structural properties of the major white matter pathways of the reading network. Future studies should examine whether behavioral changes precede white matter plasticity over a longer time scale. These findings highlight that fast white matter changes are not always observed in response to short-term training and point to the need of specifying the conditions under which white matter structure is plastic versus stable.

K – Mechanisms (hormones, neurotransmitters, physiology)

3-K-90 - Bidirectional associations between amygdala-striatal connectivity and oxytocin receptor gene DNA methylation in adolescent girls over time

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Details

Objective

Substantial developmental changes in puberty promote the expansion of skills necessary for greater independence and fostering peer relationships, while also increasing vulnerability to emotional and behavioral dysregulation. A commonly investigated pathway for heightened risk of psychopathology, which integrates biology and environment, is accelerated biological maturation. In this project, we will examine how epigenetic regulation of the oxytocinergic system, a key neuromodulator for social-emotional processes, impacts amygdala-striatal neural development and vice versa, in the second decade of life using a within subject design. Prior work has established that methylation along the promoter region of the oxytocin receptor (*OXTR*m) is dynamic in early life, strongly associated with several social phenotypes, and may be a useful marker of accelerated maturation. Additionally, amygdala-striatal development is posited as a central neurobiological mechanism that facilitates social learning. It has been suggested as a key mechanism modulating the pathway between early life stress, diminished affective and reward evaluation, and later internalizing illness. Collectively, this makes the investigation of how these two developmentally specific biological processes interact a promising mechanism of adolescent psychopathology. We predict that higher levels of *OXTR*m will be related to greater amygdala-striatal connectivity, and that *OXTR*m will be a stronger predictor of connectivity than chronological age.

Methods

Sample: The Transitions in Adolescent Girls (TAG) study includes 174 female adolescents aged 10.0 to 13.0 years at enrollment, recruited from Lane County, Oregon, USA. Participants follow a two visit protocol that includes hormone assessments, psychosocial functioning and neuroimaging measures approximately every 18 months for five waves.

Saliva Collection: At the neuroimaging visit of each wave, participants provide 2 ml of passive drool in OG-500 DNA Genotek saliva collection kits.

Neuroimaging: Participants are scanned on a Siemens Skyra 3.0 Tesla magnet and undergo two diffusion scans. See Study Protocol (Barendse et al, 2019) for sequence details.

Analysis Plan

Epigenotyping: DNA is isolated from passive drool and subjected to bisulfite treatment, which converts all non-methylated cytosines to uracil. A region of *OXTR* is then amplified via PCR, and remaining, non-converted cytosines are quantified via pyrosequencing. This results in a continuous measure of DNA methylation from 0-100% for each sample.

Diffusion Analysis: Images will be preprocessed using established methods to remove artifacts, the white matter fiber orientation distribution will be resolved using single-shell constrained spherical deconvolution. A whole brain connectome will be created using probabilistic tractography using the AAL atlas by assigning each terminal end of each tract to a corresponding nearest atlas region of interest. This results in a matrix in which all subjects provide the same number of total streamlines in the connectome and the number of tracts connecting any two regions can be inferred as a relatively stronger/weaker axonal connection between those regions compared to other individuals.

Statistical modeling: We will model linear and non-linear growth curves and will assess bidirectional influences by conducting random intercept cross-lagged panel models controlling for age, SES, race and ethnicity.

Timeline: Data collection is ongoing and the epigenotyping will not be conducted until all samples are collected in early 2024. Prior to the meeting, neuroimaging data will be pre-processed and analyzed to examine developmental changes with chronological age.

Implications

A longitudinal design is essential to expand our understanding of the core mechanisms of when and for whom mental health symptoms emerge in different contexts. This interdisciplinary project will provide a unique opportunity for novel mechanistic evidence of the impact of interactions between biological systems during a sensitive period of development that can only be understood with this type of longitudinal data.

3-K-91 - Early Life Stress Blunts the Neuroimmune Association of C-Reactive Protein and Nucleus Accumbens Activation During Adolescent Reward Processing

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Details

Early life stress (ELS) is associated with an increased risk of developing psychopathology in adolescence. Converging lines of evidence have demonstrated that ELS affects immune function and neural circuits underlying reward processing. Importantly, elevated levels of systemic inflammation have been found to be associated with blunted responses to reward in the ventral striatum, which includes the nucleus accumbens (NAcc), in both clinical and typically developing samples. It is unclear, however, if exposure to ELS exacerbates this association; and if these patterns are evident in adolescence. Here we tested whether exposure to ELS during childhood moderates the association between systemic inflammation and neural activation in adolescents as they completed a monetary reward processing task.

Our sample included 105 adolescents from the community who were participating in a longitudinal study of psychobiological mechanisms of exposure to ELS (mean age=16.01 years; SD=1.45 years; range=13.07-19.86 years; 59F/46M). ELS during childhood was assessed at the onset of the study when participants were a mean age of 11.5 years using the Traumatic Events Screening Inventory for Children (TESI-C), an interview that asks participants about their prior exposure to over 30 types of stressors.

Participants' responses were coded for objective severity and a cumulative score of ELS severity was calculated for each participant. Current levels of systemic inflammation were assessed using a dried blood spot protocol where participants provided a blood sample that was assayed for circulating levels of C-reactive protein (CRP). Participants also underwent a functional magnetic resonance imaging (fMRI) scan during which they completed a monetary incentive delay (MID) task, which probes neural responses during the anticipation and outcome of rewards and losses. We modeled participants' neural activation in the NAcc during two phases of the task: anticipation of reward > neutral and outcome of reward > neutral. Parameter estimates of activation were extracted using a bilateral anatomical NAcc mask derived from the Harvard-Oxford atlas (50% threshold). We tested whether participants' exposure to ELS significantly moderated the association of CRP levels with NAcc activation during the contrasts, controlling for assay batch, BMI, age, sex, race, MRI scanner upgrade, and previous Covid infection. Significance was set to a multiple comparisons-corrected a=0.025 for each contrast.

We found a significant interaction between participants' cumulative exposure to ELS and their CRP levels on NAcc activation during the outcome of reward contrast (*B*=-0.31; 95% CI=[-0.53,-0.09]; *t*(87)=-2.82, *p*=0.006). Specifically, in youth with lower ELS exposure, higher levels of CRP were associated with higher levels of NAcc activation during outcome of reward. Conversely, in youth with higher ELS exposure, higher levels of CRP were associated with lower levels of NAcc activation during outcome of reward. The interaction effect of ELS and CRP on NAcc activation during the anticipation of reward was not significant.

We found that exposure to ELS in childhood significantly moderated the association of inflammation with NAcc activation during outcome of monetary reward. Adolescents with low ELS exposure had a positive neuroimmune association, suggesting that in typically developing adolescents, higher levels of systemic inflammation are associated with activation of reward processing regions. Conversely, high ELS exposure was associated with a blunted relation between inflammation and activation in reward regions. This negative association is consistent with previous neuroimmune findings in both typically developing and clinical populations. Our findings highlight the importance of considering environmental influences during sensitive periods of development and suggest that maladaptive outcomes associated with exposure to ELS are due, at least in part, to altered immune function.

3-K-92 - Salivary DHEA moderates the regulation of amygdala reactivity to valenced stimuli in adolescents

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Details

Objective: Emotion *dys*regulation is a transdiagnostic risk factor for the development of several psychiatric disorders and increases in such dysregulation are a hallmark of adolescence. Emotion dysregulation has been shown to be temporally linked with *puberty* rather than age alone, which suggests that pubertal hormones may play an important role in emotion regulation trajectories. Dehydroepiandrosterone (DHEA) is one such hormone that plays a critical role in the onset of puberty, and recent studies have revealed a link between DHEA and emotion dysregulation-related psychopathology. However, no studies to date have directly examined the link between DHEA and

emotion regulation. Given this, it was the aim of the present study to investigate DHEA as a potential moderator of amygdala reactivity during an emotion regulation task.

Methods: Sixty-nine community adolescents (M_{age}=12.3; 50.7% male) were recruited as part of a larger study. Levels of DHEA were acquired via passive drool saliva collection at awakening. Given sex differences in DHEA, these values were z-scored within sex. Amygdala activation was measured during an fMRI emotion regulation task that required the participant to either regulate or react naturally (i.e., focus level) in response to either negative or neutral stimuli (i.e., stimulus valence). A series of repeated measures analyses were utilized to examine whether DHEA moderated amygdala activation in the context of the focus level x stimulus valence interaction.

Results: A significant three-way interaction between focus level (regulate v. react), stimulus valence (negative v. neutral), and DHEA was observed (p = .044). We probed this interaction by first looking within each focus level, which revealed a significant interaction between DHEA and stimulus valence for the regulation condition (p = .046) but not for the react condition (p = .474). Within the regulation condition, partial correlations revealed that DHEA was significantly associated with higher amygdala reactivity only within the neutral condition (p = .040).

Conclusion: Among adolescents in the regulation condition, those with higher relative DHEA were hyperresponsive to neutral stimuli, whereas participants' amygdala reactivity to negative stimuli were similar regardless of DHEA levels. In particular, adolescents with high DHEA responded to both negative and neutral stimuli with the same level of reactivity, whereas those with low DHEA demonstrated the expected pattern of amygdala response in which reactivity to negative stimuli was greater than for neutral stimuli. These findings have significant implications for understanding the relationship between pubertal hormone levels and differential activation of brain regions involved in emotion regulation. Given that emotion dysregulation and generalization of threat-evaluations to typically â€˜neutral' stimuli are common features of fear- and anxiety-based psychopathology, this knowledge may aid in the identification of adolescents at heightened risk for these disorders.

3-K-93 - Investigating Sleep as a Risk Mechanism for Anxiety in Adolescents with ACEs

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Details

BACKGROUND: Sleep problems prevalent in children exposed to adverse childhood experiences (ACEs) are recognized as a transdiagnostic risk factor for developing psychopathology. However, this notion relies mainly on subjective reports that are inconsistently associated with objective sleep disturbances. Few studies have utilized objective measures, such as actigraphy or polysomnography (PSG), to examine sleep problems in adolescents with ACEs, especially in a clinical population. Given the phenotypic overlap between ACEs and anxiety in negative emotions and sleep disruptions, examining sleep in a clinical sample has the potential to divulge transdiagnostic psychophysiological mechanisms. This is particularly relevant during a neurodevelopmentally sensitive period, like peri-adolescence (ages 10-13), which precedes the escalation of sleep problems and emotion-related disorders in mid-late adolescence. Current theories suggest that trauma-related sleep disturbance might stem from the aberrant stress-

regulatory system, such as chronic HPA axis activation, leading to increased attention and vigilance. Hyperarousal, including somatic (e.g., heightened nocturnal activity), cortical (e.g., increased beta-frequency activity), and cognitive (e.g., pre-sleep rumination), may also contribute to sleep problems. Additionally, research on adult PTSD and emotional processing has implicated reduced theta-frequency activity and other abnormal REM sleep parameters. Building on these theories, we aim to investigate disturbances in sleep continuity and architecture as a potential risk mechanism to prevent the development of psychopathology in children exposed to ACEs.

OBJECTIVE: Incorporate feedback from Flux to 1) assess sleep disturbances and examine cross-method correspondence in a large clinical sample of adolescents with a history of ACEs; 2) explore the mediating role of sleep disturbances between ACEs and anxiety.

PROPOSED METHOD: Our sample comes from an ongoing R01 (#MH100451-01) examining sleep-dependent negative overgeneralization in anxious peripubertal youth. Participants (N=200, aged 10-13 years), on a continuum of anxiety symptoms (assessed via Pediatric Anxiety Rating Scale), completed Child and Adolescent Trauma Screen (CATS) to assess ACEs history and posttraumatic stress symptoms (PTSS). To evaluate sleep, participants completed rating scales, a daily diary, 14 consecutive days of actigraphic monitoring, and one overnight of ambulatory polysomnographic (PSG) recording. We will use a cumulative risk (i.e., the number of adverse experiences) approach to study the association between ACEs and sleep, an established method in early life adversity and health outcomes studies.

HYPOTHESIS: ACEs history will be associated with decreased total sleep time, sleep efficiency, slow wave sleep, and theta-frequency during REM, and increased sleep onset latency, wake after sleep onset, number of awakenings, Stage 1, beta-frequency during REM, REM fragmentation and density. Furthermore, the sleep problems will 1) be correlated across methods, 2) be associated with anxiety, and 3) mediate the relationship between ACEs and anxiety.

PROPOSED ANALYSIS: Correlations will be run for 1) subjective and objective sleep disturbances and 2) ACEs, sleep disturbance, and anxiety. The mediation model will be run for indirect (i.e., ACEs to anxiety via sleep disturbances) and direct pathways (i.e., ACEs to anxiety). Sensitivity analysis will include elevated PTSS and type of ACE.

L- Memory

3-L-94 - Intergenerational transmission of emotional memories from parent to adolescent child

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Details

Intergenerational transmission describes the persistence of characteristics such as memories, experiences, and psychopathology in successive generations. Past research has investigated the nature of such transmission in the context of memories for public events, passing down of knowledge, etc., often within parent-child dyads. Although the events examined are often highly salient, the emotional qualities of these event memories are typically not the focus of the research. The emotional features of memories may be particularly important for transmission during adolescence, when individuals show

heightened sensitivity to emotional information and are establishing independence from their caregivers. Additionally, prior research has found that children's knowledge of family stories is related to emotional wellbeing, which in turn influences how we remember our pasts and guides our future decision-making. The current research examines within family transmission of highly *emotional* personal memories, focusing on the salient dimensions (e.g., valence, arousal) of emotional memories and how they might influence memory transmission in parent-adolescent child dyads. Furthermore, this study aims to understand how emotional memory concordance across generations relates to the quality of memory transmission. Through this work we aim to bridge the gaps in our understanding of emotional memory transmission, intergenerational emotional memory concordance, and relations to dimensions of psychopathology. To this end, we propose an online study of healthy parent-child dyads where children are adolescents aged 13-18 (n = 125). The sample size was determined through a multiple regression power calculation in R to provide 90% power to detect a medium effect size. First, the parents will be presented with 20 events cues and asked to briefly describe highly emotional personal memories associated with these event cues that are well-known to their family. Then, they will complete a modified Autobiographical Memory Questionnaire (AMQ) to rate the mnemonic and emotional properties of the event memories. They will also be asked to rate their motivations to transmit event memories, parent-child interactions, and perceived social desirability of the event; participants will also complete dimensional measures of depression, anxiety, and traumatic stress. Afterwards, the child will complete the same narrative reports and questionnaires about their parent's memories. We predict that high emotional memory ratings and high emotional memory concordance across generations will be associated with stronger intergenerational transmission of emotional memories. We also predict that emotional memory transmission is correlated with transmission of psychopathology. To test these predictions, we will assess memory concordance across parent and child recollections of the parent's highly emotional personal memories in two ways. Memory concordance will be calculated subjectivelyâ€"as the difference of parent and child composite scores of self-reported vividness and distinctiveness of the memories describedâ€"and objectivelyâ€"based on the content overlap between the parent and child memory descriptions. We will examine relations between emotion ratings (the parent's and parent-child emotion rating difference score) for the event memories and these memory concordance measures. We will then investigate whether memory concordance for positive and negative memories within subjects predicts measures of psychopathology. That is, we will assess the extent to which the transmission of emotional memories relates to indices of psychopathology. This investigation of the emotional dimensions of transmitted memories has the potential to help us better understand how intergenerational transmission of emotional memories contributes to wellbeing and healthy development.

We anticipate enrolling 50% of the sample by the Flux congress.

3-L-95 - Buffering the long-term effects of prenatal drug exposure: Early caregiving emotional environment is associated with memory performance and hippocampal volume in adolescents with a history of prenatal drug exposure

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Details

Background: Prenatal drug exposure has been associated with long-term adverse outcomes in multiple developmental domains (Buckingham-Howes et al., 2013). For example, a previous study from our lab reported associations between prenatal drug exposure (PDE), poorer memory performance, and altered hippocampal volume during adolescence.

However, not all children with a history of PDE are impacted to the same extent. Research suggests that the early caregiving environment may attenuate the impact of PDE on developmental outcomes (Conradt et al.,2018); however, in previous studies of neurocognitive outcomes, the relative impact of PDE and the caregiving environment are difficult to disentangle. We sought to explore this by examining relations between early caregiver emotional environment, adolescent memory, and hippocampal volume.

Methods: Phase 1 (Prenatal-24 months). Data were drawn from a randomized, controlled trial of an intervention for substance-abusing women and their infants. Parent-child dyads enrolled at delivery from a University Hospital (Schuler et al.,2000). Eligibility included gestational age>32 weeks, birth weight>1,750g, no neonatal intensive care unit admission, and positive (cocaine/heroin) maternal/infant urine toxicology or maternal self-report of cocaine/heroin use during pregnancy. Mothers completed the Center for Epidemiological Studies Depression Scale (CES-D), the Parenting Stress Index (PSI), and the Child Abuse Potential Inventory (CAPI) between 18-24 weeks post-partum.

Phase 2 (14 years). Participants were re-contacted during adolescence (*N*=69, *M*age=14.24Â±1.14, 52.17% female). Adolescents completed the California Verbal Learning Test-Child Version (CVLT-C), Child Memory Scales (CMS), the Rey-Osterrieth Complex Figure (ROCF), and the Wechsler Abbreviated Scale of Intelligence (WASI-II). A subset of adolescents completed a Siemens 3.0T MRI scan (*n*=26, *M*age=14.51Â±1.18, 54.85% female). Volumetric hippocampal segmentation was performed using AFNI (Analysis of Functional Neuro-Imaging; Cox, 1996) and FreeSurfer v5.2.

Confirmatory Factor Analysis (CFA) was used to construct a latent variable of caregiver emotional environment (CEE), composed of three dimensions from measures collected in Phase 1: maternal depression (CES-D, *M*=14.28Â±10.67), maternal stress (PSI: Parent Score, *M*=130.91Â±19.2), and caregiver distress (CAPI: Distress Score, *M*=82.52Â±70.63). Higher scores represent a more negative environment. CFA was also used to construct a latent variable of episodic memory, consisting of three different delayed free-recall tasks from three separate Phase 2 measures, CVLT-C (*M*=10.38Â±2.38), CMS (*M*=26.18Â±14.04), and ROCF (*M*=11.64Â±6.15). Higher scores represent better memory. All variables were standardized. All models were saturated. Standardized factor loadings were above .51 ($p<.001$). Hippocampal volume was adjusted for intracranial volume, age, and sex following methods detailed by Keresztes et al., 2017.

Two separate regression analyses explored whether CEE predicted episodic memory or hippocampal volume. A third regression model explored associations between episodic memory and hippocampal volume.

Results: CEE significantly predicted adolescent episodic memory, controlling for IQ, $t(64)=-.18$, $p= .04$, and left hippocampal volume, $F(1,24)=5.55$, $p=.03$. Episodic memory did not predict hippocampal volume in adolescence, $t(23)=.89$, $p=.38$.

Conclusion: Our results show significant associations between early caregiving emotional environment, memory, and hippocampal volume within a sample of adolescents with a history of PDE. This association highlights the interaction between prenatal and postnatal environments, suggesting a more negative caregiver emotional environment may accentuate the effects of PDE on neurocognitive development. Future analyses will assess the impact of CEE on additional memory domains (e.g., semantic, prospective) and consider the effects of concurrent CEE and primary caregiver changes across childhood.

3-L-96 - Hippocampal Function and Memory in the Second Year of Life

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Details

Prior research has demonstrated that the hippocampus is recruited in response to previously learned information during sleep in adults and children as young as 24-months of age. However, based on non-human models of hippocampal development, it is not clear whether its function and association with episodic-like memory may documented earlier in development. The present study aims to investigate younger children, aged 18 to 22 months, and their hippocampal recruitment in response to different types of learned stimuli (songs, words. etc.) learned across different learning contexts. Data collection is ongoing but, to date, 12 children have participated, and 35 participants are expected by September 2023.

Twelve toddlers, aged 18-22 months (*M* = 20.7, *SD* = 1.8; 7 males) learned two novel songs in association with cartoon faces and four novel words in association with novel objects across two contexts. Toddlers learned these associations during two sessions and, following each encoding phase, they were presented with the images of two previously learned objects (faces or objects), while the auditory sound associated with one of the objects/images played. Eye movements data were collected during this phase. Subsequently, toddlers underwent a nighttime scanning session in which we obtained both structural and functional scans during natural, nocturnal sleep. Functional imaging data consisted of a targeted memory reactivation (TMR) functional task with the previously learned auditory stimuli, as well as novel auditory stimuli the child had not yet been exposed to.

Toddlers looked longer at the image corresponding the face learned in association with the song compared to the face associated with the other song (Match: *M* = 3.1 sec., *SD* = 1.6 sec.; Mismatch: *M* = 2.5 sec., *SD* = 1.1 sec.) on the first testing trial, but looked longer at the mismatched (*M* = 2.8 sec., *SD* = 1.7 sec.) compared to matched (*M* = 2.2 sec., *SD* = 1.5 sec.) stimuli on their second testing trial. Preliminary fMRI results show that hippocampal activation for both learned songs compared to two never heard before songs, was significantly correlated with the percentage of time spent looking at the matching stimulus paired with the auditory song relative to the total looking time, r(10) = .78.

Future analyses will examine the persistence of this pattern of results across the entire sample. Moreover, we will use Representation Similarity Analysis to establish whether patterns of activation will be more similar for stimuli (songs and words) learned in the same context (i.e., same room) compared to a different room indicating contextually integrated memory representations. Our study uniquely investigates hippocampal recruitment for memory for complex memory associations in very young children.

3-L-97 - Exploring Memory Functioning in Children with Asthma: Insight from the ABCD Study

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Details

Objective

Asthma is a common pediatric disease characterized by systemic inflammation antecedent to respiratory symptoms such as shortness of breath, coughing, and wheezing. Non-human animal models of asthma have provided evidence of hippocampal injury and memory deficits, but little research has assessed neurocognitive functioning in humans. Initial studies in children showed that those who suffer from asthma treated with higher doses of corticosteroids exhibited reduced verbal memory compared to children receiving lower doses (Kollasch et al., 1988), but the absence of a comparison group of children without asthma precludes any conclusions about associations between asthma and memory. Other studies have reported difficulties in executive function (Hajek et al., 2014; Zhao et al., 2021) and working memory (Hajek et al., 2014), however these studies did not account for confounding effects of common demographic variables that might affect both the probability of developing asthma and cognitive difficulties. To address these limitations, we leveraged the Adolescent Brain and Cognitive Development (ABCD) Study (Volkow et al., 2018) to assess whether children who suffer from asthma exhibit different trajectories of developmental change in memory abilities compared to a matched comparison group of healthy children.

Methods

Participants were recruited via the ABCD Study, forming a diverse initial baseline population (N=~11,800; Ages 9-10 years; Garvan et al., 2018). Demographic, health, and cognitive variables were assessed at multiple timepoints following a longitudinal design. Memory abilities were examined using the NIH Toolbox Picture Sequence Memory Test (NIH-PSMT). In this subtest, participants see picture sequences of objects and activities, and after a delay, must reproduce the order of each picture sequence.

Children were included in the asthma group if their parents/guardians reported seeking medical attention or treatment for asthma at all timepoints. We then generated a healthy comparison group of children without asthma from the remaining ABCD Study population using *Matchit* implemented in *R* (Ho et al., 2011). Specifically, groups were matched at baseline on demographic variables such as age, sex, socioeconomic status (i.e., combined parental income), and other health indicators including allergies, bronchitis, diabetes, lead poisoning, and heart conditions. Measures that change over time

were allowed to vary. This sampling process produced a baseline group of children with asthma (n=150) and preliminary analyses were conducted using a matched group of healthy controls of equal size (n=150) to examine longitudinally. Given the large sample size in the ABCD, we will conduct additional analyses using a larger comparison sample matched on the same variables to increase generalizability.

Results

Using a multilevel model, we predicted memory performance on the NIH-PSMT as a function of group membership (asthma versus comparison group), change in age, and their interaction accounting for baseline performance, and all covariates used in the matching procedure. We found a significant interaction between group membership and time ($b = -2.06$, $p < 0.01$), such that children with asthma showed reduced developmental improvement in memory compared to children without asthma.

Conclusions

The results from this study provide preliminary evidence for divergent developmental trajectories of memory in children with and without asthma. Additional analyses will seek to identify the neural underpinnings of these behavioral results to provide a more nuanced understanding of how asthma might affect neurocognitive development.

3-L-98 - Association between slow oscillation-spindle coupling and declarative memory in early childhood

Eunsol Noh [1], **Sanna Lokhandwala** [1], **Tracy Riggins** [2], **Rebecca Spencer** [1]

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Details

INTRODUCTION: Naps are beneficial for memory in early childhood (3-5 years) even as children transition from biphasic to monophasic sleep. This memory benefit is thought to reflect sleep-dependent memory consolidation, a process orchestrated by three oscillations in the sleep EEG - neocortical slow oscillations (SO), thalamo-cortical sleep spindles (SP), and hippocampal sharp-wave ripples. Recent findings indicate that SO-SP coupling in children's (5-6 years old) overnight sleep may be related to improved memory function. However, SO-SP coupling patterns in naps at this age have not been explored and whether these patterns are associated with declarative memory in early childhood remains to be examined.

HYPOTHESIS: Coupling strength will increase with development. This increase will coincide with greater memory consolidation. Alternatively, it may be that naps are not sufficient enough to demonstrate significant differences in coupling and thus we may not observe coupling changes.

METHODS: Data was collected as part of a larger study which included PSG-recorded naps, memory performance, and MRI collected at baseline (W1), ~6 months later (W2), and ~1 year after baseline (W3). . Memory performance was assessed before and after a nap and wake. Participants in the analysis will be a sample of 3 to 5 year olds. Event detection for SOs will be performed by first filtering the PSG signals in 0.16-1.25 Hz using two-pass FIR bandpass filter (order = 3 cycles of the low frequency cut-off). Then, artifact-free SOs will be extracted into 5 s-long segments (Â± 2.5 s around slow troughs) from the raw

unfiltered signals. To avoid filter edge artifacts, we will use Â± 2 s of SO segments for phase-amplitude coupling. The mean direction of coupling (phase) and amount of coupling (strength) will be measured. To assess memory performance across the nap and wake session, each subject completed a memory task by encoding image locations on a grid. They were then tested on the image locations before (recall 1) and after (recall 2) a nap and equivalent wake period (within-subject). Wake and sleep difference scores were calculated as follows (recall 2 - recall 1)/ recall 2. Nap benefit score was calculated as sleep difference score - wake difference score. We will use circular-linear correlation to examine associations between coupling phase and memory performance and Pearson's correlation to examine relations between coupling strength and memory performance.

All parts of data analysis are in progress and will be completed by Flux.

3-L-99 - Investigating the local representation quality differences underlying pattern separation processes during a mnemonic discrimination fMRI task

Jade Dunstan [1], **Jeremy Purcell** [1], **Daniel Callow** [1], **Tracy Riggins** [1]

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Details

Pattern separation is a computational process by which patterns of neuronal activation underlying similar memories are made distinct to counteract interference during retrieval (Norman & O'Reilly, 2003). This process is essential to distinguish similar memories but cannot be measured directly; however, mnemonic similarity tasks (MST) where participants discriminate similar stimuli can serve as an index (e.g., Lacy et al., 2011). During these tasks, participants encode pictures and then must discriminate between those they saw during encoding (Targets); new pictures (Foils); and pictures that are similar, but not the same as the previously seen pictures (Lures). Previous research in young children has shown that hippocampal structure shows dramatic changes, and these *structural* changes relate to age-related improvements in children's ability to form precise memories through pattern separation. However, we have yet to establish 1) whether there are *functional* hippocampal changes during early childhood and 2) whether functional changes relate to pattern separation development. To address these gaps, we developed a passive viewing, block design, MST where participants encode 60 pictures outside of the scanner, passively view 30 in the scanner (10 Targets, 10 Lures, 10 Foils), and complete an active retrieval of 30 pictures (yes/no judgment about whether they saw the pictures during encoding) after the scan. From the active retrieval we calculated the Lure Discrimination Index (LDI) to assess how well participants distinguish Targets and Lures. Preliminary univariate results using anterior/posterior hippocampal ROIs from this work in an adult pilot sample revealed marginal differential activation for Targets relative to Lures in right posterior hippocampus (t = 2.05, $p_{corrected}$ = 0.094) and, in left anterior hippocampus, the differential activation for Targets relative to Lures, was marginally predictive of LDI (B = 0.34, t = 1.86, p = .0728). For the proposed analyses we build off of our previous findings by going beyond traditional univariate analysis, using local heterogeneity regression (Purcell & Rapp, 2018), to quantify representation quality differences between Targets, Lures, and Foils in our sample of 34 adults. We will also use hippocampal subfield ROIs to improve our sensitivity to detect these differences as prior research has specifically implicated DG/CA3 in pattern separation processes (e.g., Lacy et al., 2011). Finally, we will also analyze data from a sample of 13 3-4-year-old children. We will investigate: 1) local heterogeneity of the neural representation quality between Targets, Lures, and Foils during passing viewing and 2) whether these measures of local differentiation

relate to out-of-scanner performance. We predict greater heterogeneity in CA3/DG for Targets relative to Foils. We predict this difference to be greater in adults. Additionally, we predict that the individual variability in behavioral LDI to be related to the Target>Lure heterogeneity across all ages.

M- Methods

3-M-100 - Leveraging Data Integration (Not Only Harmonization) in Developmental Cognitive Neuroscience

Kelsey Canada [1], **Ana Daugherty** [1], **Noa Ofen** [1]

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Details

In the field of developmental cognitive neuroscience, multi-site data collection is increasingly relevant, but Big Data methods that presume identical or harmonized methodologies are often not feasible. A potential path toward overcoming the requirement of harmonized data is the latent modeling method Integrative Data Analysis (IDA). IDA is a technique to test hypotheses by combining data of the same construct from similar, but not identical, measurements. IDA can overcome the challenges of integrating multi-site neuroimaging data collected on different scanners and different study-specific protocols. As long as portions of measurement overlap across sites, datasets with measurements that are related, but not identical, can be stitched together. The key is the latent modeling that can account for site- and measurement-specific differences separate from hypothesis tests with latent constructs. IDA is more than a summary technique, it creates means to test new hypotheses about individual differences that cannot be tested in any single study, while improving statistical power and external validity. Moreover, IDA facilitates team-focused collaborative science to answer new questions about health disparities in brain and cognitive development using diverse samples.

We are developing an application of IDA to test hypotheses of hippocampal subfield development in a combined large sample that is geographically- and demographically-diverse, taking a wholly unique approach with neuroimaging data. Participants in this ongoing work include 678 4- to 25-year-olds, who were recruited to four existing independent studies of healthy cognitive and brain development funded by the National Institutes of Health. Each study collected high-resolution images of the medial temporal lobe allowing for accurate delineation of hippocampal subfields using published protocols that differed between studies. Because of consensus from histologists regarding the boundaries of subfields within the hippocampal body, but continued disagreement about definitions within the hippocampal head, as well as challenges to visualization of subfields boundaries in the head and tail with MRI, we will focus on subfields in hippocampal body. All studies used comparable anatomical landmarks to determine the start and end of the hippocampal body and delineations in each study-specific protocol share overlapping information, making the application of IDA to this sample a feasible and powerful approach. Completed preliminary cross-sectional model results suggest integration of volumetric hippocampal subfield measures is tenable. A detailed description of the IDA method applied to neuroimaging data, preliminary cross-sectional findings, and planned analyses incorporating longitudinal data and measures of socioeconomic status on hippocampal development will be presented at Flux 2023.

Successful implementation of IDA to structural brain measures can serve as a blueprint for future combined analyses of existing developmental neuroimaging datasets that vary in the specific methods and measures used.

3-M-101 - CABINET: an application for containing and linking standardized modular neuroimaging pipelines

Audrey Houghton [1], **Greg Conan** [2], **Eric Feczko** [1], **Timothy Hendrickson** [1], **Julia Moser** [1], **Dimitrios Alexopoulos** [3], **Mathias Goncalves** [4], **Sanju Koirala** [1], **Aidan Latham** [3], **Erik Lee** [1], **Jacob Lundquist** [1], **Thomas Madison** [1], **Christopher J. Markiewcz** [4], **Lucille Moore** [1], **Paul Reiners** [1], **Amanda Rueter** [1], **Damien Fair** [1], **Barry Tikalsky** [1]

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Details

CABINET[1] is a robust novel open-source software application that bridges multiple modular, containerized neuroimaging processing pipelines designed to enhance accessibility, reproducibility, and sustainability in the neuroimaging field. CABINET's modular architecture allows for easy customization by selecting and connecting different processing modules to suit the specific needs of researchers. Its containerization ensures reproducibility and compatibility across different computing systems and environments. Each module can be modified or replaced with alternative implementations, making the pipeline adaptable to changes in standards and best practices in the field.

The current version of CABINET is optimized for infant anatomical and functional MRI processing. Due to the lack of popular standardized neuroimaging packages that process resting-state functional MRI infant data to completion, we chose infant anatomical and functional MRI processing as the first use case. In addition to guaranteeing reproducibility and decreasing compute time, this version of CABINET improves the quality of outputs, increasing the number of participants whose MRI data can be successfully pre-processed to be included in analyses.

Each module follows the Brain Imaging Data Structure (BIDS) designed to standardize file formatting and naming conventions to foster reproducibility. The current implementation includes several processing modules, such as BIBSNet[2], NiBabies[3], and XCP-D[4]. BIBSNet uses deep neural networks to quickly and accurately segment anatomical images, producing a segmentation and brainmask in native space that are then fed into the Nibabies module to perform anatomical and functional preprocessing. The outputs of Nibabies are then fed into XCP-D to perform functional connectivity preprocessing and produce an executive summary with which to perform quality assessment. CABINET therefore is a comprehensive processing pipeline that generates a diverse set of standardized outputs essential for conducting quantitative analysis. We demonstrate the current functionality and capabilities of the pipeline through a use case example for infants within the Baby Connectome Project dataset.

The flexible software can easily extend to other neuroimaging domains, such as monkey and adult MRI processing. The usability of CABINET makes it accessible to researchers of various backgrounds and skill

sets. CABINET is open source and available to the community for free, with the hope that it will be a valuable tool for neuroimaging researchers, particularly those working with infant fMRI data.

[1] Houghton, Audrey, Conan, Greg, Hendrickson, Timothy J., Alexopoulos, Dimitrios, Goncalves, Mathias, Koirala, Sanju, Latham, Aidan, Lee, Erik, Lundquist, Jacob, Madison, Thomas J., Markiewicz, Christopher J., Moore, Lucille A., Moser, Julia, Reiners, Paul, Rueter, Amanda, Fair, Damien A., & Feczko, Eric. (2023). CABINET (2.4.1). Zenodo. https://doi.org/10.5281/zenodo.7843888

[2]Hendrickson, Timothy J., Reiners, Paul, Alexopoulos, Dimitrios, Conan, Greg, Goncalves, Mathias, Houghton, Audrey, Koirala, Sanju, Latham, Aidan, Lee, Erik, Lundquist, Jacob, Madison, Thomas J., Markiewicz, Christopher J., Moore, Lucille A., Moser, Julia, Rueter, Amanda, Fair, Damien A., & Feczko, Eric. (2022). BIBSnet (v1.0.0). Zenodo. https://doi.org/10.5281/zenodo.7106148

[3]Goncalves, Mathias, Markiewicz, Christopher J., Esteban, Oscar, Feczko, Eric, Poldrack, Russell A., & Fair, Damien A. (2023). NiBabies: a robust preprocessing pipeline for infant functional MRI (23.0.0). Zenodo. https://doi.org/10.5281/zenodo.7562647

[4]Adebimpe, Azeez, Bertolero, Maxwell, Mehta, Kahini, Salo, Taylor, Murtha, Kristin, Cieslak, Matthew, Meisler, Steven, Madison, Thomas, Sydnor, Valerie, Covitz, Sydney, Fair, Damien, & Satterthwaite, Theodore. (2023). XCP-D : A Robust Postprocessing Pipeline of fMRI data (0.4.0rc2). Zenodo. https://doi.org/10.5281/zenodo.7717239

3-M-102 - Characterization of the maturing metastable dynamics in the term neonatal brain at rest

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Details

Objective

Adults can execute a wide range of behavioural and cognitive functions through brain networks transiently segregating and integrating on a spatial and temporal scale [1,2]. We can model these metastable brain dynamics using neural microstates, which are transiently stable electrical topographies derived from spatio-temporal patterning of electroencephalography (EEG) recordings [3]. In a mature brain, four microstates reliably explain ~75% of resting brain activity [4], however we do not know whether this is the case in neonates when the brain is rapidly developing. To assess this, we tested whether neonatal functional brain activity can also be described by a distinct set of microstates and explored how this relates to age.

Methods

We studied 20-channel EEG recordings from 57 healthy term (37.14-42.86 postmenstrual weeks, 54% female) neonates at rest and included a mix of vigilance states (active sleep, quiet sleep and awake) and recording positions (cot, skin-to-skin, held with clothes). Microstates were inferred from 120-150s EEG epochs (bandpass filtered with cut-off frequencies at 0.1 and 70Hz and down sampled to 128Hz) using an agglomerative hierarchical clustering algorithm [5] at subject and group level. Clustering was performed across all samples of the time series to extract topographies that accounted for most of the variance in the data. Topographies with opposite polarity were considered as separate microstates.

Results

At a subject level, 7-25 microstates accounted for 70% of the EEG signal, with the number significantly increased with postmenstrual age (PMA) (r=0.32, p=0.01). Following further clustering, 7 dominant microstates explained 60% of the signal across subjects. Adult microstates A, B and D were visually identifiable in neonatal microstates 7, 6 and 3 respectively. The remaining 4 were denoted as neonatal specific microstates.

Conclusions

Our results indicate that as in adults, neonatal brain activity is organised in metastable states which are already capable of transient segregation and integration. This metastable organisation, reflecting the functional status of cortical neural networks, evolves between 37- and 43-weeks PMA. The maturational changes in brain structure and function such as synaptogenesis, myelination and the growth of long intra- and interhemispheric cortico-cortical connections could explain the development of metastability observed during this short time span [6]. As these processes are disrupted by conditions like preterm birth, characterising microstates could provide new insight into the pathophysiology of the associated adverse neurodevelopmental outcomes.

1. Tognoli, E. & Kelso, J. A. S. The Metastable Brain. *Neuron* **81**, 35 (2014).

2. Iraji, A. *et al.* The spatial chronnectome reveals a dynamic interplay between functional segregation and integration. *Hum Brain Mapp* **40**, 3058 (2019).

3. Pascual-Marqui, R., Michel, C. & Lehmann, D. Segmentation of brain electrical activity into microstates: model estimation and validation. *IEEE Trans Biomed Eng* **42**, 658â€“665 (1995).

4. Michel, C. M. & Koenig, T. EEG microstates as a tool for studying the temporal dynamics of whole-brain neuronal networks: A review. *Neuroimage* **180**, 577â€“593 (2018).

5. Rupawala, M. *et al.* A developmental shift in habituation to pain in human neonates. *Current Biology* **33**, 1397-1406.e5 (2023).

6. KostoviÄ‡, I., Sedmak, G. & JudaÅ¡, M. Neural histology and neurogenesis of the human fetal and infant brain. *Neuroimage* **188**, 743â€“773 (2019).

3-M-103 - Healthy Brain Network (HBN): A quality controlled and reproducible data repository enriched for clinical mental health measures

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Details

Background: Recent neuroimaging studies highlight the need for large sample sizes to estimate accurate associations between brain and clinically relevant mental health outcomes. In response, researchers formed large data consortiums comprising neuroimaging, clinical, and behavioral data to measure the 'trueâ€ effect sizes of such associations. However, many large consortia data, such as the Adolescent Brain Cognitive Development (ABCD) or UK Biobank, collected datasets sampled from the general population. As a result, such datasets are not enriched for clinical measures, making it difficult to test the generalizability of brain-behavior findings in clinical populations. Prior datasets like the autism brain imaging data exchange (ABIDE) are enriched for clinical samples, but such data have been acquired across decades, making comparison to modern samples like ABCD difficult. The Healthy Brain Network (HBN) comprises a large dataset, enriched for clinical mental health measures and acquired using modern neuroimaging protocols. Such data are publicly available, but have not undergone modern, surface-based ABCD-BIDS style data processing, due to the need for extensive data infrastructure required to perform such processing.

Objective/Implications: This project will leverage the HBN dataset and develop a data repository that will be made available to the broader neuroimaging community. This dataset will augment already available datasets, so that researchers can answer neuroimaging questions with clinically enriched and relevant data. The usage of citizen scientists will amplify the decisions of the standard experts and allow for wide-scale quality control of the HBN dataset (Keshavan, Yeatman, and Rokem, 2019).

Methods/Analysis: The HBN dataset comprises over 3,000 children and young adults between the ages of five and 21 years in the New York area with clinical mental health, behavioral phenotypic, and MRI data. Critically, individuals were recruited if seeking help for psychological/psychiatric symptoms, providing a sample enriched for clinical mental health measures (Alexander et. al 2017). The data processing of the Healthy Brain Network dataset is currently occurring in multiple phases. The first phase which has been completed involves the conversion of the raw structural and functional MRI data into the Brain Imaging Data Structure (BIDS) format, a standardized format for organizing and describing outputs of neuroimaging experiments (Gorgolewski et. al 2016). Secondly, the BIDS-formatted HBN data will then be processed using the standardized ABCD-BIDS MRI pipelines developed within the DCAN Labs. The data will be housed at the Minnesota Supercomputing Institute (MSI), and provided through a data platform, where researchers will have access to both the data and analytical tools. Finally, the processed outputs will then be reviewed for quality control (QC) through crowdsourcing the neuroimaging community. The ABCD-BIDS pipeline will produce a series of summaries for each HBN participant, which will be ingested into an online platform called Swipes For Science. Swipes for Science enables phone/tablet/computer-based quality assurance across the neuroimaging community, where users can"swipe left" or "swipe right" to determine if an MRI image is usable for further analysis. Swipes enables us to leverage the "wisdom of the crowds" and develop a large pool of ratings. Further analysis with gold standard experts can enable

us to filter the ratings pool to generate reliable and valid users. Swipes will then be aggregated into three distinct categories of "pass", "questionable" , and "fail" QC which will then be uploaded into the data repository.

3-M-104 - Reliability and spatial specificity of ALFF in neonates and adults

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Details

Background: Amplitude of low frequency fluctuations (ALFF) is a measure of the power of spontaneous low-frequency fluctuations in the BOLD signal detected with fMRI and may be an indicator of regional plasticity. Early in development, spontaneous activity is large and synchronous. As inhibitory inputs increase with the maturation of inhibitory interneurons, intracortical myelination, and perineural nets and sensitive periods close, spontaneous activity becomes more sparse, potentially resulting in a decrease of the ALFF in the BOLD signal. Recent work in human adults demonstrates that ALFF increases in a regionally specific manner following a limb disuse intervention, potentially indicating changing plasticity and inhibitory tone. While the ALFF of spontaneous activity has promise as a marker of plasticity in both adults and developing samples, further work is required to measure the reliability and the regional brain patterns of ALFF in individuals across various stages of development. Uncovering these properties is required before ALFF can be used as a tool in developmental samples. **Objective:** In this study we will utilize precision functional mapping (PFM) to 1) characterize the within-subject reliability of ALFF, and 2) characterize regional patterns (topography) of ALFF in neonates and in adults. **Method:** Our PFM dataset will consist of 10 adults, each with 300 minutes of resting-state fMRI data and 6 neonates, each with at least 90 minutes of resting-state fMRI data. ALFF will be calculated as the averaged square root of the Fast Fourier Transformation (FFT) across the 0.01-0.08 Hz frequency band of the BOLD time series. This will be done by first bandpass filtering the preprocessed fMRI data and then performing a FFT to obtain the power spectrum. We will then take the averaged square root across 0.01 0.08 Hz at each vertex to obtain the ALFF for each vertex. Then, we will quantify the reliability of ALFF within each individual for both datasets. To do this, each individual's dataset will be split in half for testing and training datasets before calculating ALFF as previously described. The reliability of ALFF will be defined as the correlation of ALFF across all vertices on the cortical surface for varying amounts of data in the testing dataset. To compute regional patterns (topography) of ALFF in neonates and in adults, we will first compute regional ALFF within individuals in both the adult and neonatal samples. Then, we will average ALFF across each network, using adult networks. Finally, we will compare the magnitude of ALFF in each network between adults and neonates using t-tests. **Prediction:** We hypothesize that the reliability of ALFF will increase with increasing amounts of data in both adult and neonatal dataset. Further, greater amounts of data will be required for a reliable ALFF signal in neonates compared to adults. We also hypothesize that functional brain networks with the highest ALFF in adults will consist of networks responsible for higher cognitive functioning, like the default mode network (DMN), dorsal attention network (DAN), and ventral attention network (VAN), whereas sensory systems (somatomotor network (SMN), Visual, and Auditory networks) will show the highest ALFF in neonates. **Discussion:** Understanding the reliability of ALFF in different age groups, as well as how development affects the magnitude of ALFF in various brain regions is important for interpreting individual differences

in brain function and for informing the use of ALFF for identifying biomarkers of brain function in health and disease.

3-M-106 - A comparison of standard single echo MRI sequences and state-of-the-art multi echo MRI sequences for precision functional mapping in children

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Details

Precision functional mapping (PFM) is a promising tool for studying functional brain organization in individuals. However, PFM relies on collecting hours of fMRI data over multiple scan sessions, which is not simple to obtain, especially in child populations. Given recent advances in fMRI sequences with improved signal-to-noise ratio and denoising capabilities, it is possible that use of these sequences will allow PFM methods to be employed with less data per individual. In this study, we will compare resting-state functional connectivity MRI measures computed from densely sampled individual child participants scanned using either standard single echo (SE) MRI sequences or newer multi echo (ME) MRI sequences. Our goal is to examine whether a PFM approach is more feasible with less data per individual child using ME sequences. We have densely sampled resting-state fMRI data from ten children using a standard SE MRI sequence and from three children using a state-of-the-art ME MRI sequence. To test the hypothesis that ME sequences advance PFM potential, we plan to conduct the following analyses. First, we will test the within-subject reliability of functional connectivity metrics for each child. Specifically, each individual's functional data will be split into two subsets, one consisting of 60 minutes of motion-censored data to serve as the comparison data, and the remaining data to serve as the test data. Increasing amounts of data will be randomly selected from the test data in 5-minute increments. Functional connectivity correlation matrices will be created for the comparison data and for each increasing increment of the test data, using a set of 333 cortical parcels. Reliability will be estimated by computing the correlation between the upper triangles of the parcel-to-parcel matrices from the comparison and test data. We will also create functional connectivity matrices using 15 minutes, 30 minutes, 45 minutes, and 1 hour of data to examine the strength of functional connectivity with increasing amounts of data. We will then compare reliability and functional connectivity strength for the individual children collected with ME sequences to those collected with SE sequences. We predict that high reliability (e.g., r=0.9) and stronger within-network functional connectivity will be reached with less data for the ME sequences than for the standard SE sequences. Such a result would be promising for applying PFM methods to developmental and clinical populations in which collecting extensive amounts of data is more challenging.

N- Networks

3-N-106 - Characterizing individualized TMS Efield spatial specificity in the adolescent brain

Cristian Morales-Carrasco [1], **Oscar Miranda-Dominguez** [1], **Amal Adeen** [1], **Alana Lieske** [1], **Mia Kellman** [1], **Timothy Hendrickson** [1], **Robert Hermosillo** [1], **Christine Conelea** [1], **Steve Nelson** [1], **Damien Fair** [1]

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Details

Transcranial Magnetic Stimulation (TMS) is a non-invasive neuromodulation technique used to treat mental health disorders. TMS induces a transient Electric Field (Efield) in the cortex that modulates neural activity in the target area. Its effectiveness, however, varies across individuals. One reason could be that current methods identify the target using canonical scalp landmarks, which do not account for intersubject variability of the function and anatomy of the brain. A recent clinical trial conducted in adults showed an increased efficacy when using individualized anatomical and functional information of the brain organization in the treatment of major depressive disorder, which reinforces the relevance of spatial accuracy when applying a TMS. The spatial specificity is affected by individualized brain structure and the spatial dispersion of the TMS pulses. Functional and anatomical brain organization is a dynamic process during the lifespan, going through dramatic changes from early childhood to adulthood and Precision Non-invasive neuromodulation has emerged particularly as an important treatment in the developing population as invasive alternative treatments effects are not fully understood.

With the current advances of functional MRI we can now identify the functional brain structure, but little is known about how TMS induced Efiled distributes across the individual functional structure and how variable it is across participants. To estimate how selective TMS interventions can be in terms of the amount of energy that is retained within the target network we implemented a workflow to quantify the magnitude of the simulated electric field (Efield) (using Simnibs, Saturnino et al 2019) on each personalized functional brain network in healthy adults. We performed simulations targeting >60k different cortical areas (grayordinates) and identified the coil position that induces the highest Efield magnitude on the target regions. This results in an Efield distribution map that informs the relative energy distributed across networks per individual.

We observed that when a TMS pulse is delivered the Efield reaches high values in non target networks, which can lead to unintended outcomes. We found that the energy distribution is subject specific, dependent on subject brain anatomy and functional organization. For instance, in targets that are within the salience network there is low variability of total distributed energy within network across participants, a low percentage (< 20%) of the applied energy remains in the network. In targets within the frontoparietal network, distributed energy variability remains low across participants, preserving between 20% and 60% of the applied energy within the target network. These findings account for the variability observed in healthy adults. We aim to explore the spatial variability of TMS at a critical period of development where the brain undergoes dramatic changes. In particular we plan to apply the above described framework to quantify Efield variability in the young children (9 to 10 years old participants from the ABCD dataset) and additionally create a probabilistic Atlas of the energy distribution to use as further reference when fMR is not available. First we will select a small but diverse sample (10 - 20 participants) and obtain their functional brain networks using template matching, a method that assigns networks to each grayordinate based on its connectivity information and a reference network. We will calculate the energy distribution maps using Efield modeling. Finally we will generate an Atlas that will inform how likely a given network is to preserve a given amount of total energy. This will allow us to quantify the variability in Efield distribution per network observed at this age span and compare it against adults. We aim for this Atlas to be accessible by the clinical and research community.

3-N-107 - Individual Differences in Delay Discounting are Associated with Dorsal Prefrontal Cortex Connectivity in Youth

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Details

Delay discounting is a measure of impulsive choice relevant in adolescence as it predicts many real-life outcomes, including substance use disorders, obesity, and academic achievement. However, the functional networks underlying individual differences in delay discounting during youth remain incompletely described. Here we investigate the association between multivariate patterns of functional connectivity and individual differences in impulsive choice in a large sample of youth. A total of 293 youth (9-23 years) completed a delay discounting task and underwent resting-state fMRI at 3T. A connectome-wide analysis using multivariate distance-based matrix regression was used to examine whole-brain relationships between delay discounting and functional connectivity was then performed. These analyses revealed that individual differences in delay discounting were associated with patterns of connectivity emanating from the left dorsal prefrontal cortex, a hub of the default mode network. Delay discounting was associated with greater functional connectivity between the dorsal prefrontal cortex and other parts of the default mode network, and reduced connectivity with regions in the dorsal and ventral attention networks. These results suggest that delay discounting in youth is associated with individual differences in relationships both within the default mode network and between the default mode and networks involved in attentional and cognitive control.

3-N-108 - Transdiagnostic polygenic risk, general psychopathology, and personalized functional brain networks in the Adolescent Brain Cognitive Development cohort

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Details

Objective:

A critical question in developmental neuroscience is how genetic risk influences functional brain networks and psychopathology in preadolescence. A recent multivariate genome-wide association study found two genetic factors, F1 and F2, that capture the majority of genetic variability associated with transdiagnostic psychopathology. Additionally, emerging evidence has suggested the importance of a latent overall factor, or p-factor, that quantifies an individual's generalized vulnerability to psychiatric symptoms. However, it is unclear how F1 and F2 are related to p-factor, and how these variables are reflected in functional brain networks. The present study uses personalized functional networks (PFNs)â€"which capture individual variation in functional network topography that is otherwise ignored

by standard analyses based on group atlasesâ€”to elucidate the associations among polygenic risk, functional brain networks, and p-factor in preadolescence.

Methods:

MRI data from the Adolescent Brain Cognitive Development Cohort (ABCD) baseline (9-10-year-olds) were used to derive PFNs. Each participant's fMRI time series was decomposed through spatially constrained non-negative matrix factorization, resulting in a PFN loading matrix of 17 networks across 59,412 cortical vertices. A bifactor model of 93 mental health indicators collected at the 1-year follow-up was used to derive p-factor scores (N=7,045). Polygenic risk scores (PRS) of F1 and F2 were derived in a European ancestry subsample (N=3,858) using continuous shrinkage priors (PRS-CS).

Linear mixed-effects models were used to investigate correlations between PRS-F1, PRS-F2, and p-factor. Ridge regression models trained on PFN loading matrices were used to associate PFN topography with PRS-F1, PRS-F2, and p-factor scores. Two-fold cross-validation was performed across matched discovery and replication samples; statistical significance was evaluated using permutation testing and stability was evaluated using 100 random splits across the data.

Results:

If polygenic risk was associated with the development of psychopathology, we would expect correlations between PRS-F1/PRS-F2 and p-factor in preadolescence. PRS-F1 was indeed found to be correlated to p-factor (standardized Î²=0.11, $p<0.001$), whereas PRS-F2 was not (Î²=0.03, $p=0.059$).

Furthermore, there was a moderate association between PFN topography and p-factor (discovery: $r=0.17$, $p<0.001$; replication: $r=0.15$, $p<0.001$). Repeated random cross-validation returned consistent results (mean $r=0.16$, range=0.14-0.18).

PFN topography was also found to be significantly associated with PRS-F1 (discovery: $r=0.074$, $p=0.0013$; replication: $r=0.051$, $p=0.025$) and PRS-F2 (discovery: $r=0.082$, $p<0.001$; replication: $r=0.080$, $p<0.001$). Results were shown to be stable for PRS-F1 (mean $r=0.042$, range=0.00-0.082) and PRS-F2 (mean $r=0.076$, range=0.044-0.10).

Conclusions:

This study revealed new insights into genetic risk and functional brain networks in preadolescent psychopathology. First, the F1 polygenic risk score was found to be significantly correlated to p-factor, whereas the F2 polygenic risk score was not. In a prior study, F1 was associated with more common psychiatric symptoms, and F2 with rarer, more severe disease. As the average age of onset in mental disorders occurs during adolescence, it is possible that F2 genetic risk has yet to clinically manifest at ages 10-11.

Second, personalized measures of functional network topography were robustly related to interindividual differences in F1, F2, and p-factor. Notably, prediction accuracy of p-factor was consistent with prior findings from the Philadelphia Neurodevelopmental Cohort (N=790, ages 8-23). The association of PFN topography with F2 implies that although F2 risk has yet to clinically manifest in

preadolescence, it is captured by functional brain network topography. Future studies could investigate how F2's associations with p-factor and PFNs change across later time points in ABCD.

3-N-109 - Short-term trajectories of functional brain network integration in children during motor learning and working memory tasks

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Details

Prior work has demonstrated opposing trajectories of network integration (between-network connectivity) during motor learning and working memory training spanning several weeks. Specifically, integration decreases with motor learning, whereas integration increases with working memory gains. At shorter timescales of minutes, behavioral gains during motor learning and working memory performance have been demonstrated in children, yet, the trajectories of network integration supporting these behavioral gains have not been characterized. Thus, the proposed study examined how functional brain networkorganization reconfigured in children aged 8-12 years during motor learning across blocks of a serial reaction time (SRT) task(n=33) and during working memory across blocks of an n-back task (n=23). Each task was divided into four one minute blocks to assess both behavioral trajectories (i.e., learning) and neural trajectories (i.e., brain network reconfiguration). For the SRT task, participants practiced a 12-item repeating pattern for the sequence condition, and responded to items in a pseudorandom order for the random condition. For the n-back task, participants indicated whether the current stimulus was a match or non-match to the stimulus seen *two* previously for the 2-back condition, and whether the current stimulus was the letter â€˜X' (match) or another letter (non-match) for the 0-back condition. Behaviorally, motor learning was operationalized as change inresponse times (RT) across blocks of the sequence condition, and working memory was operationalized as change in ' (difference between the z-transform of hit and false alarm rates) across blocks of the high working memory load condition, or 2-back condition. Brain data were processed with fMRIPrep, and timeseries were extracted from 228 regions of a functional brainatlas across five task-relevant networks: visual (VIS), somatomotor (SM), salience (SAL), frontoparietal (FP), and default mode (DM) networks. Network integration was measured with the graph metric participation coefficient (PC), which quantifies between-network connectivity, on each block per task. Multilevel models (MLMs) were used to separately model behavioral gains and network reconfiguration across eachtask, controlling for age, sex, and IQ. Brain-behavior relationships were examined by introducing PC as a time-varying covariate to the MLMs of behavior. For motor learning, decreased RT was observed across sequence and random blocks ($p<0.001$), and children were generally faster on the sequence condition ($p=0.001$). Neurally, decreased SM PC was observed across sequence blocks ($p=0.025$), and decreased VIS-SM PCpredicted faster motor sequence RT and slower random RT as a time-varying covariate ($p=0.049$). For working memory, a block by condition interaction revealed that increased ' was observed across 2-back blocks, but not across 0-back blocks ($p=0.026$). Neurally, SM-SAL PC increased across 2-back blocks ($p=0.042$), whereas DM PC decreased across 2-back blocks ($p=0.044$). However, PC did not predict 2-back ' as a time-varying covariate ($p>0.755$). These findings suggest that decreased SM integration subserved motor learning in children, whereas increased task-relevant (SM-SAL) and decreased task-irrelevant (DM) integration were observed with working memory gains in children. Critically, opposing trajectories of network integration for motor learning and working memory demonstrated here across shorter timescales of minutes are

consistent with trajectories demonstrated over weeks, and may indicate that these network integration trajectories accumulate across multiple timescales.

3-N-110 - Ontogeny of the Ascending Arousal Networks

Roxane Licandro [1], **Mark Olchanyi** [2], **Luiz F. Ferraz Da Silva** [3], **Andre Van Der Kouwe** [2], **Camilo Jaimes** [4], **Nathan Xi Ngo** [2], **William Kelley** [2], **Richard D. Goldstein** [4], **Robin Haynes** [4], **Brian L. Edlow** [2], **Hannah C. Kinney** [4], **Lilla Zollei** [2]

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Details

Objectives

Arousal, also referred to as wakefulness, is an essential element of consciousness. Human wakefulness is mediated by the ascending arousal network (AAN) and its connections from the brainstem tegmentum to the diencephalon, basal forebrain, and cerebral cortex. In this work, we are closing the gap with the more extensively studied adult population by analyzing seven timepoints (19, 21, 22 weeks of gestation, 1 and 2 months, 60 and 61 years) of the perinatal and adult population to advance our understanding of the ontogeny of subcortical arousal networks in the human brain. We hypothesize that graph theoretic measures can assess developmental patterns of the AAN by quantitatively characterizing the complex configuration of developing brain networks. As a corollary, we also test the hypothesis that the structural connectome of the AAN becomes increasingly complex and progressively reaches rostral brain sites during the first year of development.

Methods

Here, we investigate the ontogenic development of subcortical arousal networks by imaging 7 whole human brain samples, all reported with no developmental abnormalities after neuropathologic assessment. We acquire high-resolution *ex-vivo* MRI after brain fixation of 24hrs (fetuses), 30-50 days (neonates), and > 90 days (adults). Subsequently, we perform probabilistic diffusion tractography incorporating 27 manually annotated seed regions of the AAN and additionally computing atlas-based segmentations of 58 cortical regions. To quantify network connectivity properties, we use graph theoretical analysis, including hub region determination by combining degree, clustering coefficient, and betweenness centrality ranks and estimating short- and long-range structural connectivity. For visual assessment, three-dimension tracts are derived by deterministic tractography.

Results

The AAN structural connectivity pattern analysis focuses on the hub rank since it provides information about the presumed functional importance of a region within a defined network. A key finding is that the dorsal raphe nucleus (DR) (serotonergic system) as an AAN connectivity hub beginning in the fetal period. We also observe that the ventral tegmental area (VTA) (dopaminergic system) shows the highest hub ranks for every age group within the AAN as well as within the whole brain network, including cortical

regions. We show that the structural connectome of the AAN becomes increasingly integrated and progressively reaches rostral sites during the first year of development, highly correlating with myelination patterns. Short- and long-range connectivity analysis revealed that highly probable connections of long-range connectivity are evolving postnatally, while short-range connections are present over the entire observed period. Specifically, DR demonstrated to be a hub of short-range connectivities, while VTA to be a hub of evolving long-range connectivities.

Conclusions

We demonstrated that graph-based analysis could be used to assess the ontogeny of structural connectivity in the AAN. This study is limited by the number of observed subjects, thus resulting AAN connectivity maps should be considered as a case study to advance the understanding of human brain development. For future work we will use the established references to provide new insights into how arousal networks may fail in disorders of wakefulness, such as coma, seizures, and sudden infant death syndrome.

3-N-111 - Developmental associations between DNA methylation bioclocks and the white matter connectome in adolescence

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Details

Social stress “weathers” the body and accelerates the pace of biological aging, which is reflected in epigenetic processes such as DNA methylation (DNAm) bioclocks. However, it is unknown how biological aging changes the development of white matter structural networks, preventing understanding of how pace of aging impacts the organizational development of the brain. Bioclocks, including GrimAge, which predict aging-related outcomes and early mortality, reliably estimate biological aging. Network neuroscience metrics quantify segregation (e.g. modularity, transitivity) and integration (e.g. global efficiency) and can be applied to describe properties of white matter. These metrics index brain development with increased network integration and decreased network segregation being associated with maturation. Our central hypothesis is that acceleration in bioclocks will be associated with greater maturation of brain networks.

181 adolescents from the Study in Adolescent Neural Development (SAND) were included in the analyses. SAND is a subset of participants from the Future of Families and Child Wellbeing Study, a population-based longitudinal cohort study with substantial representation of marginalized youths. Participants provided DNAm via saliva samples at ages 9 and 15 as well as participated in multimodal MRI scans at age 15. Data collection was completed prior to analysis. Four bioclocks were used to estimate biological age from DNAm (Grimage, Horvath, Phenoage, and Pace of Aging) and were age-residualized to derive a measure of biological age acceleration. Measures of white matter connectivity organization (global efficiency, transitivity, and modularity) were estimated from structural MRI scans. These four bioclocks were used to predict connectivity metrics using multiple regressions controlling for self-identified race, socioeconomic status at birth, maternal education at birth, maternal marital status at birth, and birth city. All results were adjusted for multiple comparisons using false discovery rate (FDR) correction.

At age 15**,** GrimAge acceleration was associated with reduced modularity (β = -.218, q = 0.084). These associations were FDR-corrected for 12 comparisons across the four biological age acceleration-based variables and three WMC metrics. There were no significant associations when conducting sensitivity analyses using a prior time point of DNAm age acceleration at age 9 and modularity at age 15, although associations were in the same direction (βPaceofAging = -.113, q=0.581; βPhenoage = -.175, q = 0.423; βGrimAge = -.145, q = 0.488, FDR-corrected).

Current findings highlight that biological age acceleration, as assessed with GrimAge, is associated with decreased white matter modularity, a measure of segregation. This provides potential evidence for accelerated neural development since modularity (a metric that measures the extent to which the structural connectome can be divided into specialized subnetworks) decreases with age as long-range white matter fiber pathways white matter fiber structures become more specialized during adolescent development. Thus, accelerated GrimAge may be a biomarker for greater maturation of the structural connectome. Future analyses will investigate whether bioclock acceleration is differentially associated with specific white matter tracts during adolescent neural development, as well as if they are associated with adolescent behaviors, such as internalizing and externalizing symptoms. These findings may contribute to a better understanding of the associations among the methylation of genes, brain development, and mental health.

3-N-112 - Highly Reproducible Normative Representation of Functional Brain Network Organization in Childhood: An ABCD study

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Details

Understanding the functional network organization of the developing brain can provide insights into the differential maturation of cognitive, sensorimotor, and social functions. While there has been extensive research on the organization of functional networks in adults, there has been less focus on organization of functional brain networks during childhood. The current study aims to describe a detailed view of the functional organization of brain networks using resting state functional connectivity (RSFC) MRI data from a large sample of children age 9-10 years, collected via the Adolescent Brain Cognitive Development (ABCD) Study.

This project used RSFC data released through the ABCD fast track portal. Our final dataset was created by dividing the full baseline sample (N = 11,572) into discovery (N = 5,786) and replication (N = 5,786) sets, which were demographically matched across 9 variables using the ABCD 2.0 data release. Participants were included if they had at least 600 frames (8 minutes) of low-motion (framewise displacement < 0.2) RSFC data, resulting in a final dataset of 7,303 9-10 year old children across the discovery (N = 3,615) and replication (N = 3,688) sets. We calculated the Pearson correlation matrix of timecourses from all cortical vertices, and averaged those matrices across participants. Each cortical vertex was then assigned to a functional network using an adaptive version of the graph theoretical community detection algorithm, Infomap. Functional connectivity, as measured by the z-transformed

correlations, and network assignments were then compared between the discovery and replication datasets.

Across the cortex, 9-10 yr olds demonstrated functional network organization that reflects similar broad organizational properties observed in adult canonical networks: default mode, visual, fronto-parietal, dorsal-attention, etc. This functional organization was highly reproducible across the discovery and replication datasets, as shown by high similarity of parcel-to-parcel correlation matrices (r = 0.99) and network assignments (Normalized Mutual Information = 0.88).

In this study, we leveraged the largest available collection of RSFC in children to provide a baseline representation of childhood functional network organization. Developmental research often relies on adult network templates, as a child template has not yet been well-established. Here, we provide this needed representation of childhood functional networks. Furthermore, given the large sample size, we were able to demonstrate high replicability between independent discovery and replication sets. Thus, this work establishes a stable baseline template of functional brain networks in childhood that can be used in future developmental cognitive neuroscience research.

3-N-113 - Examining individual variability in functional network topography over development

Sanju Koirala [1], **Julia Moser** [1], **Robert Hermosillo** [1], **Lucille Moore** [1], **Thomas Madison** [1], **Oscar Miranda-Dominguez** [1], **Eric Feczko** [1], **Alyssa Labonte** [2], **M. Catalina Camacho** [2], **Michael Myers** [2], **Kimberly Weldon** [1], **Alice Graham** [3], **Nico Dosenbach** [4], **Steve Nelson** [1], **Theodore Satterthwaite** [5], **Jed Elison** [1], **Chad Sylvester** [4], **Damien Fair** [1]

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Details

Objective: A longstanding objective in neurocognitive research has been to subdivide the human brain into a mosaic of anatomically and functionally distinct areas to understand how the brain segregates and integrates information. The discovery of resting state functional MRI (rsfMRI) has led to the characterization of human brain organization based on the co-activation patterns of brain areas. However, such network organization is created by spatially coregistering data across multiple individuals which assumes homogeneity in brain organization and obscures meaningful subject-specific features. Recent work using Precision Functional Mapping (PFM) techniques have rendered unique insights into individual functional brain network architecture, revealing idiosyncratic network topography such as individual variation in functional network size (i.e., how much cortical real estate is taken by each network). Such variation in individual topography has been shown to relate to individual differences in behavior such as cognition and motor skills. However, it is not known when individual variation emerges over development.

Methods: In this study, we aim to examine whether the surface area of functional networks differs between three different age groups: neonates, adolescents, and adults. We utilized functional neuroimaging data from the Adolescent Brain and Cognitive Development study (n=6000) and the Midnight Scan Club precision imaging study (n=10) to derive adolescent and adults individual network

maps using Template Matching. For neonates, we derived individual network maps from extended acquisitions of neonatal resting state fMRI data (n=8, duration: 80-200 minutes).

Analysis: In our analyses, we will calculate the mean total surface area for each group. As neonates have less gyrification than the other two groups, we hypothesize that the mean total surface area will be smaller for neonates compared to adolescents and adults. We will also calculate the proportional surface area for each individualized network in each age group. Using the large sample from ABCD, we will create a distribution of proportional surface area for each network and examine potential age effects based on where the network size for neonates and adults fall within this distribution. We hypothesize that the relative proportion of the cortex devoted to each network at different age points will vary.

Implications: Taken together, our study will provide important insights into age-related changes in individual-level functional network topography, and open opportunities to investigate how such changes in functional network topography relate to emergence of various behaviors in health and disease.

3-N-114 - Individual-specific sensory brain networks in children are more similar than control and attention networks to canonical adult networks

Matthew Feigelis [1], **Damion Demeter** [1], **Sana Ali** [1], **Deanna Greene** [1]

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Details

Characterizing an individual's functional brain network organization holds promise for understanding individual differences in behavior, cognition, and psychopathology. Functional brain networks in individual young adults have been reliably characterized using precision functional mapping (PFM) through the collection of large amounts of data per individual. In this study, we used PFM to investigate individual-specific network organization in children. Densely sampled resting-state functional connectivity fMRI data were collected from 12 children (age 8-11, mean = 9.91) across 3-12 scan sessions. After rigorous preprocessing and motion censoring, we obtained 56.7-293.4 (mean = 140.1) minutes of high-quality, low motion fMRI data per participant. We used InfoMap community detection to identify whole-brain communities (functional networks) at the individual-child level. Then, we tested the similarity of each network in each individual child to canonical group-level networks previously characterized in 120 adults. By calculating the dice coefficient between the individual-specific networks and the group-level network templates, we tested which networks in the children are most similar to the canonical functional networks well described in adults. Our results show that sensory networks in each of the 12 children closely resembled the canonical group-level sensory networks, as demonstrated by a large dice coefficient for the visual, somatomotor-mouth, and somatomotor-body networks. In contrast, control and attention networks (salience, ventral attention, frontoparietal, cingulo-opercular, dorsal attention) had a smaller dice coefficient on average, indicating less similarity to the canonical functional networks. Greater similarity of child sensory networks to group-level adult networks compared to that of control and attention networks may be due to earlier maturation or less individual variability of sensory systems than control and attention systems. Future research will aim to differentiate the contributions of potential developmental effects versus individual variability.

O- Other

3-O-114 - Developmental changes in the serial position function for different visual elements

Grace Adebogun [1], **Jason Yeatman** [1], **Mahalakshmi Ramamurthy** [1]

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Details

Background: The multi-element processing task measures how the visual system encodes a brief presentation of a string of letters/numbers/symbols. Interestingly, previous studies have shown that element recognition varies as a function of position within a string. This relationship is called the serial position function (SPF) and has been shown to differ for letters in comparison to other visual categories such as pseudo-fonts, symbols, and numbers. An empirical observation from these studies is that letters and numbers display similar serial position functions (W-shaped) whereas symbols display a different function (inverted U-shaped). The similarities in the serial position functions for letters and numbers have been interpreted to indicate the conjoint influence of two factors: (a) the drop in visual acuity as a function of distance from fixation and (b) the amount of lateral interference (crowding) determined by the number of flanking letters. However, the inverted U-shape for symbols goes against the crowding interpretation, and researchers have argued a top-down bias in the interpretation of why symbols show a different shape. Importantly, many studies show that children with reading disabilities do not exhibit a deficit in processing symbols and numbers but do with letters. In the present study, we asked, does the serial position function vary across different visual categories as reported in previous literature, and do the shapes of these functions change with age and reading ability?

Methods: To investigate this, we tested two groups of participants, beginning readers (BR) (children ages 7-12 yrs; n=18) and skilled readers (SR) (adults ages 18-35 yrs; n=14), to understand the relationship between reading experience and the ability to simultaneously process a string of visual elements (letters, numbers, nameable symbols: objects, and unnameable symbols: pseudo-fonts). Participants completed the partial report version of the multi-element processing task. All stimuli were calibrated to ensure that the perimetric complexity of all elements matched, and eyes were tracked to ensure fixation. During the task, participants fixated on a central cross while a string of six elements (3 on the left and right of fixation) briefly flashed for 240 ms. Participants were then asked to report the element in the post-cued position from a set of ten choices.

Results: Overall, accuracy in the multi-number trials was greater, followed by the multi-letter, multi-object, and multi-pseudo-font trials [SR mean accuracy (‘): letters = 2.20; pseudo-fonts = 1.50; numbers = 2.62; and objects = 1.77; BR mean accuracy (‘): letters = 1.55; pseudo-fonts = 1.10; numbers = 1.89; and objects = 1.15]. The SR group showed higher recognition accuracy compared to the BR group across all visual categories. Both groups exhibited a W-shaped SPF for letters and numbers and an inverted U-shaped SPF for nameable symbols, as previous studies have shown. The SPF for pseudo-fonts (unnameable symbols) appears to be an inverted U-shape for the SR group and a W-shape for the BR group, suggesting that beginning readers process pseudo-fonts more like letters. We observe that task performance (in all visual categories) correlates with age [Letters: r = 0.45, p= 0.0096; Pseudo-fonts: r = 0.41, p= 0.02; Numbers: r = 0.46, p = 0.0088; Objects: r = 0.6, p = 0.00032]. After adjusting for the effect of age on task performance,

we found a significant correlation between reading ability and performance on the multi-letter (r = 0.39; p = 0.03), multi-pseudo-font (r = 0.4; p = 0.03), multi-number (r = 0.4; p = 0.03), and multi-object (r = 0.36; p = 0.05) processing trials. Our findings indicate that processing a myriad of different visual categories is related to reading ability. Based on our findings, we hypothesize that children with dyslexia should exhibit a deficit in processing all visual categories.

P – Rewards/Motivation

3-P-115 - Leveraging novel music to examine age-related reward responses across development

Nick Kathios [1], **Kelsie Lopez** [1], **Juliet Davidow** [1], **Psyche Loui** [1], **Laurel Gabard-Durnam** [1]

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Details

While music listening is a pleasurable experience throughout life, adults show a lifelong preference for, and heightened autobiographical memories associated with, music from their adolescence (i.e. the 'reminiscence bumpâ€ effect). This effect may be linked to fluctuations in experience-dependent neural plasticity, especially in reward-system circuitry that supports motivated behavior throughout the lifespan. An open question concerns the developmental processes that produce the reminiscence bump. One theory suggests heightened reward learning capacities during adolescence could lead to this preference for adolescent music. Recent empirical evidence in adults indicates that music acquires implicit reward value through exploiting reward-prediction mechanisms: listeners tend to prefer music for which the prediction error for acoustic and structural features is minimized. At the same time, adolescents show heightened sensitivity to reward-predictive cues. Though the functional development of reward circuitry in adolescence is hypothesized to overlap with that which is involved in pleasurable music listening experiences, little is known about adolescents' reward responses to music. Thus, it remains unclear whether adults' lifelong musical preferences result from an adolescent period of neuroplasticity supporting reward responses, and how music reward valuation changes across development. To address this, we propose a cross-sectional comparison of reward responses to music from childhood through adulthood. We will test the relationship between participants' liking of melodies that they are exposed to with variable frequencies during an exposure phase across a cross-sectional cohort of individuals ages 5-24, using a novel paradigm developed in our lab. In a post-exposure test phase, participants will rate their liking and familiarity for both the previously exposed melodies and versions of those melodies which begin the same, but end differently (a manipulation of prediction error). To ensure that listeners' predictions are learned from exposure within the lab, rather than lifetime experiences of music within their culture, these melodies will be written in the Bohlen-Pierce (BP) scale, a musical system acoustically different from any existing scales across cultures. We hypothesize that the age-related trajectory of the strength of the linear relationship between exposure and liking ratings will be best characterized by an inverse-U curve, peaking in adolescence, and that the effect of prediction error on liking ratings will greatest for adolescents (i.e. they will dislike the melodies that contain a prediction error the most compared to children and adults). Participants will also complete a music-listening functional magnetic resonance imaging (fMRI) task developed in our lab, which involves listening to self-selected music and previously-heard BP melodies. I hypothesize that fronto-striatal connectivity will peak in adolescence while listening to both self-selected music and BP melodies presented more often during an outside-scanner exposure phase. These results would indicate that both novel and familiar musical experiences exploit functionally developing circuitry in adolescence.

This would also offer evidence that the brain is most sensitive to the rewarding properties of music in adolescence and highlight a potential neuroscientific mechanism supporting adults' lifelong preference for music from this time period. Overall, this project highlights the powerful, yet relatively underutilized, perspective music provides into the neurocognitive developmental trajectory of reward responses.

3-P-116 - Early childhood reward-related neural reactivity concurrently and prospectively associates with depressive symptom severity

Nicolas Camacho [1], **Michael Gaffrey** [1]

[1] Duke University

Details

Depressive symptoms during the early childhood period have been associated with, and predictive of, a variety of behavioral and emotional problems later in life. Recent functional Magnetic Resonance Imaging (fMRI) reward processing data indicates that left amygdala reactivity to salient (i.e., reward and loss) versus neutral outcomes (RLvN) is associated with acute depressive symptom severity in young children (Gaffrey et al., 2018). Given the recognized need to replicate novel brain imaging findings in new samples, and for follow-up data to inform fMRI findings as potential biomarkers of future symptom course, we investigated the concurrent and longitudinal relationships between left amygdala reactivity to salient outcomes and depressive symptom severity in a community-based sample of 4â€"8-year-old children (N = 115; M_{age} = 6.12, SD_{age} = 0.94; 55% female, 74% white). Based on our prior work on depression (Gaffrey et al., 2018) and emotion regulation (Gaffrey et al., 2021) in young children, we also explored associations between depressive symptom severity and bilateral caudate and right medial prefrontal cortex (mPFC) reactivity to reward versus neutral (RvN) outcomes. During two separate visits (T1 and T2) approximately 13-months apart (M = 13.79; SD = 2.04; range = 11.03 22.63), caregivers reported on their chil's depressive symptom severity using the Preschool Feelings Checklist Scale Version. At T1, children underwent fMRI while completing a simple guessing task in which they chose between two doors and received pseudorandom feedback (i.e., no learning involved) in the form of reward (i.e., gain M&M's), loss (i.e., lose M&M's), and neutral (i.e., no gain or loss). Based on our prior work and that of others, we hypothesized that depressive symptom severity would show concurrent and longitudinal associations with both bilateral (1) caudate and (2) right mPFC RvN reactivity and negative associations with left amygdala RLvN reactivity. Given the directionality in our hypothesis based on prior findings, a one-tailed approach to statistical significance was used for left amygdala analyses. Model-based statistical outliers that were considered highly influential to changes in the slope of the relationship between neural reactivity and depressive symptom severity scores were removed prior to each analysis. Concurrently (controlling for parent depressive symptom severity and child age), T1 child depressive symptom severity was negatively associated with left amygdala RLvN reactivity (Î² = -.17, p = .041 [one-tailed], Cohen's f^2 = 0.04), right caudate RvN reactivity (Î² = -.29, p = .003 [two-tailed], Cohen's f^2 = 0.09), and right mPFC RvN reactivity (Î² = -.21, p = .027 [two-tailed], Cohen's f^2 = 0.05). Prospectively (controlling for T2 parent depressive symptom severity and child age, T1 child depressive symptom severity, and the time between timepoints), results showed that T2 child depressive symptom severity was negatively associated with T1 right caudate RvN reactivity (Î² = -.15, p = .029 [two-tailed], Cohen's f^2 = 0.08). Using a new young child sample, we replicated our prior finding of a negative concurrent association between left amygdala reactivity to salient outcomes and depressive symptom levels. We extend this work by showing concurrent negative associations between depressive symptom

severity and reactivity to reward outcomes in right mPFC and caudate regions. Finally, we show that only attenuated right caudate reactivity to reward outcomes was associated with depressive symptom severity scores one year later. These results suggest that state levels of depression may be related to reward processing in frontal, subcortical, and striatal regions, while trait levels may be distinctly linked with striatal reactivity to rewards. The current study furthers our developmental neurobiological understanding of depression by elucidating brain-behavior relationships during the early childhood period both concurrently and longitudinally.

3-P-117 - Neural response to monetary incentives in acquired adolescent depression

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Details

Depression is a common consequence of adolescent traumatic brain injury (TBI). Separately, developmental depressionâ€”i.e., not acquired after a TBIâ€”has been linked to aberrant responses to the anticipation or receipt of rewards in motivational neural circuitry, which can be normalized following treatment. Previous studies have looked at the effectiveness of antidepressant treatments for adolescent TBI sequelae, but it is unclear if there are different neural bases for developmental and acquired depression. To support evidence-based treatment in adolescents with acquired depression after TBI and identify neural markers of acquired depression in adolescence, this study will use the Adolescent Brain Cognitive Development (ABCD) dataset to examine the relationship between disruption in functional neural responses to rewards and acquired depression after TBI. The study will compare N=42 adolescents who have experienced mild TBI with N=42 control participants, and will test the hypothesis that mTBI is associated with depressive symptoms and blunted recruitment of motivational neural circuitry during reward processing. The study will also examine if aberrant neural recruitment during reward processing is related to post-TBI depression, providing insight into the shared vs. distinct mechanisms underlying neurodevelopmental and acquired depression. Regardless of the results, the study will provide evidence regarding the current standard of care for depression after mild TBI in adolescents.

3-P-118 - Exploring the relationship between intrinsic dopamine-related neurophysiology and risk-taking during pubertal development

Tehya Drummond [1], **Arianna Cascone** [1], **Ashley Parr** [2], **Finnegan Calabro** [2], **Will Foran** [2], **Beatriz Luna** [2], **Jessica Cohen** [1]

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Details

Puberty is a developmental period often marked by a significant increase in risky behaviors. Previous research has found that more advanced pubertal status is linked to increased risk-taking, which can be attributed to dopaminergic function. However, research on the relationship between pubertal status,

intrinsic dopamine (DA) availability, and risk-taking behaviors is lacking. To examine this relationship, the proposed analyses will use data from an ongoing longitudinal study, using a single timepoint for each subject. In this study, typically developing adolescents ages 10-14 undergo an fMRI scan and complete a series of questionnaires and behavioral tasks. The Pubertal Development Scale (PDS) is administered in order to calculate a continuous pubertal score for each participant. To assess risk-taking behavior, the Balloon Analogue Risk Task (BART) is administered. Risk-taking measures calculated from this task include the average number of balloon pumps on trials in which participants cashed out and total number of exploded balloons. Intrinsic DA availability will be indirectly assessed by extracting brain tissue iron content in the basal ganglia using normalized T2* weighted (nT2*w) signal from resting state scans. Analyses will quantify nT2*w signal in the whole basal ganglia, as well as separately in basal ganglia subregions (i.e., caudate, putamen, globus pallidus, and accumbens). Linear regression models will be used to investigate the potential interactions between nT2*w signal, pubertal status, and BART performance scores, covarying for age and sex. We will correct analyses using false discovery rate for 2 comparisons for the whole basal ganglia analyses (1 ROI x 2 behavioral measures) and 8 comparisons for the basal ganglia subregion analyses (4 ROIs x 2 behavioral measures). Secondary analyses will assess for sex differences. We hypothesize that participants with lower nT2*w signal, reflecting greater tissue iron levels and therefore more intrinsic DA, will have higher risk-taking scores on the BART. Additionally, we hypothesize that pubertal status will moderate the relationship between DA availability and risk-taking. Specifically, a stronger relationship between DA availability and risk-taking will be associated with more advanced pubertal status. The proposed analyses will contribute to understanding the underlying neurophysiological mechanisms of risk-taking during pubertal development.

3-P-119 - Examining Associations between Neural Sensitivity to Social Feedback with Trait and State Loneliness in Adolescents

Victoire Alleluia Shenge [1], **Junaid Merchant** [2], **Hua Xie** [3], **Paige Munshell** [2], **Elizabeth Redcay** [2]

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Details

Examining Associations between Neural Sensitivity to Social Feedback with Trait and State Loneliness in Adolescents

Authors: Victoire Alleluia Shenge, Junaid S. Merchant, Hua Xie, Paige Munshell & Elizabeth Redcay

Loneliness, or perceived social isolation, can be defined as the negative emotional response to an experience of discrepancy between the desired and actual quality or quantity of one's relationships (Brennan, 1982) and is associated with multiple negative outcomes (Hedley et al., 2018). Further, loneliness tends to increase in adolescence (Heinrich & Gullone, 2006; Vanhalst et al., 2013) and in the wake of the global COVID-19 pandemic, loneliness has been shown to increase across all 50 states in the US (Killgore, 2020).

Theoretical models of loneliness based on research with nonautistic adults (Cacioppo and Hawkley, 2015) highlight the effect that perceived social isolation can have on both social cognitive and social reward systems. Specifically, loneliness leads to an increase in the detection and perception of social threats. Thus, neutral or mildly negative social stimuli (e.g., a thumbs down) may be seen as more negative or a social threat which serves to further reduce social interaction and consequently the feeling of loneliness is increased. Similarity, loneliness affects the reward system by making social experiences less enjoyable which similarly serves to reduce seeking out of social experiences and increase feelings of loneliness. Therefore, it is crucial to understand the effect of social isolation on social reward systems.

This pre-registered study aims at leveraging real-world peers in ecologically valid paradigm for our fMRI task alongside real-world experience sampling to assess state loneliness within adolescence, which is a critical time in the development of loneliness. Our sample will include 50 adolescents (11â€“14-year-olds) from a larger longitudinal study (data collection in progress).

To assess neural sensitivity to social feedback (positive and negative), our fMRI task consists of the teens learning about whether peers in the study share similar likes and dislikes to them. The positive social feedback (thumbs up appears on the screen) occurs when participant and peer agree and negative social feedback (thumbs down appears on the screen) is given when they disagree. A nonsocial control includes positive and negative nonsocial feedback. Trait Loneliness will be assessed using an adapted version of the Loneliness Rating Scale (Asher et al., 1984) while State Loneliness will be assessed using ecologically momentary assessment (EMA) text prompts across 10 days following the MRI visit.

Our fMRI analyses will include two contrasts of interest 1) positive social feedback (Peer positive vs Computer positive) and 2) negative social feedback (Peer negative vs Computer negative). We will extract the beta values from each contrast from within a priori defined ROIs encompassing regions associated with reward and salience systems. Lastly, we will look at how our measure of neural sensitivity to social feedback from the above task is associated with State Loneliness (mean daily EMA text prompts) and Trait Loneliness (adapted Asher questionnaire).

We hypothesize that loneliness will be related to greater neural sensitivity to negative social feedback (due to perceived social threat observed through greater neural activation to thumbs down vs. X within "salience" regions like anterior cingulate cortex and bilateral insula). Further, we hypothesize that loneliness will also be related to reduced neural sensitivity to positive social feedback (due to reduced social reward observed through lower activation in reward sensitive regions like ventral striatum to thumbs up vs. check).

Taken together, this study is important because they will be the first to look at ecologically-valid neural factors associated with the development of loneliness in adolescents.

Q – Socioemotional Processing

3-Q-120 - Neural meaning making of early caregiving experiences: the developmental neurobiology of affective semantic memory

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Details

Background: Developmental science has long posited that affective semantic knowledge of early relationships (aka attachment schemas), which generates expectations about future affective outcomes, is abstracted from regularities in caregiver-child experiences. Yet, how this process unfolds in the brain is unknown. Causal evidence from rodent research suggests that medial prefrontal cortex-amygdala circuitry is preferentially modulated by parental cues during development; these alterations, in turn, have been linked to differences in emotional memory. At the same time, experimental studies in cognitive neuroscience find that midline corticolimbic circuitry, comprised of the midcingulo-insular 'salienceâ€ network and posterior-medial 'default modeâ€ network, has a broader functional role in semantic social and affective knowledge. Might the stimulus-evoked neural patterns in this circuitry, in part, reflect the affective semantic knowledge acquired from caregiving experiences?

Study Objective: We tested the hypothesis that midline corticolimbic circuitry represents affective semantic knowledge related to the caregiver-child relationship.

Methods: The sample comprised 98 adolescents (10-17 years-old; 43F/55M; 12% Asian, 23% Black, 42% White, 17% Multi-Racial, 6% Other; 21% Hispanic/Latine), most of whom had exposure to early caregiving adversity (72%). We measured (a) adolescents' attachment with the Child Attachment Strategy Questionnaire (Finnegan et al., 1996); and (b) adolescents' responses to abstract animated shape stimuli designed to evoke attachment schemas (including BOLD signal during an fMRI scan and verbal content during recollection of the video stimuli). The Linguistic Inquiry and Word Count software (Boyd et al., 2022) coded the affective semantic content of transcribed responses. Additionally, indices of psychologically-close language, such as first-person singular pronouns (social closeness) and present-tense verbs (temporal closeness), were coded because this narrative style is used when recalling schema-consistent memories (Trope & Liberman, 2010). Subcortical ROIs were anatomically-defined (Amunts et al., 1999) and cortical ROIs were defined with functional connectivity-derived parcels (Schaefer et al., 2018). All ROI analyses adjusted for age, household income-to-needs ratio, verbal IQ, total word count, and mean framewise displacement.

Results: Greater activity in the ventromedial prefrontal cortex during the insecure (vs. secure) schema condition was associated with higher levels of insecure attachment. Further, stronger engagement of the ventromedial prefrontal cortex and anterior insula during the insecure (vs. secure) schema condition was associated with higher levels of negative affective semantic content inferred from the insecure schema. By contrast, the secure (vs. insecure) schema stimuli evoked robust amygdala and posterior superior temporal sulcus (pSTS) responses when they were described with more psychologically-distant language (suggesting recall of schema-inconsistent memories), which indicates that the amygdala and pSTS may elicit affective prediction errors. Consistent with prior work on event schemas, activity in other midline corticolimbic regions (e.g., precuneus, hippocampus) was observed across both affective schema conditions (vs. implicit baseline). However, these neural activity patterns did not differentiate between the insecure and secure semantic content, supporting a role for these regions in representing non-affective aspects of event schemas. Additional planned analyses include searchlight representational similarity analysis and brain-based predictive modeling, which will be completed before the conference.

Conclusions: Midline cortico-amygdala circuitry may represent affective schemas that embody the content of caregiving experiences and support schema-based affective meaning-making during development.

3-Q-121 - From Literal to Implicit: Neurocognitive Development of Communicative Reasoning during Adolescence

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Details

Objective

Decoding what is and is not being said from a communicative signal in context is fundamental to successful communication. Recent neurocomputational evidence suggests that recovering others' unstated intents may require a listener to inhibit the literal interpretation of a received communicative signal and to mentally simulate the choice process by which a cooperative speaker selects an appropriate expression for best delivering an intended meaning. It remains largely unknown, however, when humans acquire this ability, and how the development of relevant neural and cognitive functions supports the maturation of communicative reasoning ability. By combining ideas and methods from developmental psychology, decision neuroscience, and computational pragmatics, we investigate the trajectories of neural and cognitive changes during the transition from childhood to adulthood, using cross-sectional and longitudinal neurobehavioral data.

Methods

A total of 316 typically developing children, adolescents, and adults (ages 8-24, 157 females; fMRI = 141, behavior = 175) participated in a well-established Referential Communication Game, where they acted as listeners who need to recover the target item in context based on a referring expression received from a speaker. Among participants, 53 fMRI subjects participated in the experiment twice (ages 8-17 at baseline, 25 females), spanning 20 months.

Results

Both cross-sectional and longitudinal data show that the overt behavioral performance, as measured by the rate of successfully recovering the speakers' intended referent for each participant, increases continuously from childhood into early adulthood. Leveraging a well-established computational model previously used for quantifying the underlying neural processing of intentional communication in adults, we show that, in cross-sectional data, the overall age-related improvements are supported by changes in two basic cognitive operations and their related neural processing. These include (i) an adolescent-nonspecific increase in the engagement of mental simulation of what a speaker would say given a communicative goal and context, subserved by functional changes in the ventromedial prefrontal cortex (VMPFC), and (ii) an adolescent-specific development in the egocentric processing of contextual saliency, subserved by functional changes in association areas in the visual cortex. Importantly, the relative contribution of the two cognitive operations is associated with the extent to which the frontoparietal

areas engaged during communicative interpretation, which explains the developmental differences in communicative performance. The longitudinal data show consistent developmental patterns and further indicate that the activation of frontoparietal areas at baseline is predictive of the strength of the VMPFC encoding the probabilistic inference about the speaker's choices 20 months later.

Conclusions

These results suggest separate, yet intertwining neurocognitive developmental trajectories of egocentric context processing and mental simulation of others, which underlie the maturation of communicative reasoning ability from childhood through adolescence to adulthood. These findings also provide novel insights into how the neural systems related to self- and other-oriented processes interact with one another during development, enabling our ability to understand communicative, and more generally, social signals.

3-Q-122 - Mindful attention can support emerging adults to reduce alcohol cravings in the moment and consumption in daily life

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Details

Alcohol use in college is highly normative the majority of college students report drinking in the past month, and 25% of students report academic difficulties due to drinking and even minimal alcohol consumption is associated with negative health outcomes. Since late adolescents and emerging adults are at risk for developing alcohol-related problems, identifying scalable strategies to encourage the development of healthy alcohol use behaviors is critical. Combining multivariate neuroimaging, experience sampling methodologies, and experimental intervention, we tested the degree to which mindful attention the directed and nonjudgmental awareness of the present moment reduces both momentary alcohol cravings in the laboratory and alcohol consumption in daily life. Specifically, we used multivoxel pattern analysis to create a neural signature of mindful attention and used it to evaluate how a mindful attention intervention alters alcohol-related responses and behavior from three angles: 1) *efficacy* - performance under controlled conditions, 2) *effectiveness* - performance under 'real-world conditions, and 3) *individual differences* - identification of for whom the intervention works most successfully.

College students (N=38) from two universities completed a mindful attention and alcohol cue-reactivity task while in the fMRI scanner followed by a 28-day, smartphone-based experience sampling intervention. We used a within-person intervention design. During intervention weeks, participants received daily reminders to respond mindfully to alcohol, whereas during control weeks, they were prompted to respond naturally. This design allowed us to examine within-person changes in alcohol craving and consumption as a function of the intervention, and test underlying mechanisms.

To overcome potential biases with self-reported mindful attention and investigate dynamic relationships between fluctuations in mindful attention and craving, we adopted a '*neural signature*' approach to create a sensitive and specific index of mindful attention. Using machine learning, we developed a neural signature of mindful attention that accurately predicted whether a person was mindfully attending to or reacting naturally to alcohol.

Efficacy. We applied this neural signature to trial-level data to examine dynamic relationships between mindful attention and self-reported cravings. We found that greater expression of the mindful attention signature was associated with decreased craving for alcohol in the laboratory. This finding highlights that mindful attention is an effective approach (requiring minimal training) for regulating alcohol craving in controlled settings.

Effectiveness. We found that the mindful attention intervention increased self-reported mindful responses to alcohol, which in turn were associated with decreased alcohol consumption in daily life. This finding underscores the potential use of mindful attention as a preventative intervention in emerging adults to reduce alcohol consumption.

Individual differences. Individual differences in how strongly individuals expressed the mindful attention signature in the brain during the laboratory session moderated both intervention-related increases in mindful responses to alcohol and the negative relationship between mindful responses and alcohol consumption. Individuals who more strongly expressed the mindful attention signature benefited the most from the intervention, responding more mindfully on intervention compared to control weeks and a stronger negative relationship between mindful responses and alcohol consumption.

Together, our findings demonstrate the promise of a scalable, smartphone-based intervention to reduce alcohol consumption in late adolescents and emerging adults who could benefit from strategies that help them develop healthy habits with alcohol. We use a neural signature approach to identify possible mechanisms underlying mindful attention and individual differences in intervention success.

3-Q-123 - Facial Masking, ADHD Symptoms, and Prefrontal Cortex Activation in Early Childhood

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Details

Facial masking is known as the ability to conceal one's genuine affect to produce facial expressions that display an emotion that is incongruent to the emotion that is felt (e.g., smiling during times of frustration). Researchers have theorized that children engage in masking during negative emotional challenges to conform to social norms which can reflect better emotion regulation (Cole, 1986; Saarni, 1984). However, few studies have sought to examine masking in early childhood, its relation to early ADHD symptoms, and its neural correlates. ADHD is a neurodevelopmental disorder that is impacted by the prefrontal cortex (PFC) which is central to adaptive self- and emotion-regulation. Emotion-related difficulties, such as mood lability and emotion recognition, are strongly associated with attention-deficit/hyperactivity disorder (ADHD). Additionally, studies have identified that children with ADHD experience deficits in complex emotion-related tasks, specifically their ability to mask negative emotions

(Walcott & Landau, 2004). This study examined the relation between masking during frustration and ADHD symptoms in preschool-aged children, as well as whether prefrontal cortex (PFC) activation moderates this relation. We hypothesized PFC activation will moderate the relationship between masking and ADHD symptoms. We predict that children with lower PFC activation who produce more complex and simple masking during frustration will have higher ADHD symptoms than children with higher PFC activation who produce more complex and simple masking during frustration.

Preschoolers (N = 77, *M*age = 4.57 years, *SD* = 0.73) completed a frustration inducing task called 'Incredible Cake Kids' (Grabell et al., 2019) on a touchscreen computer in which children were told to choose the most delicious cake for virtual customers. The customers then provided the child with predetermined feedback (unbeknownst to the child) that was either positive (e.g., yummy!) or negative (e.g., yuck!). This task was video recorded to code the chil's facial expressions, and prefrontal cortex activation was also recorded during the task via functional near-infrared spectroscopy (fNIRS). The Facial Action Coding System (FACS; Ekman & Friesen, 1977) was used to categorize children's facial expressions as simple and complex masking during negative feedback. Complex masking was defined as a 'lip corner puller'(AU 12) with a co-occurring negative emotion AU such as 'brow lowerer' (AU 4), 'nose wrinkler/upper lip raiser' (AU 9 and/or 10), or a 'lip corner depressor' (AU 15). Simple masking was defined as an AU 12 without a co-occurring negative AU. Parents completed the Barkley ADHD Rating scale about their chil's inattentive and hyperactive symptoms.

Linear regression analysis were conducted to test how facial masking, PFC activation, and the masking*PFC interaction predicted ADHD inattentive and hyperactive symptoms for simple and complex masking respectively. None of these models were statistically significant. Exploratory analyses yielded a marginally significant interaction in which right PFC activation buffers the relationship between inattentive symptoms and partial incongruent smiling during negative feedback (*b* = -.0037, SE = .0020, *p* = .068). We had no a priori hypothesis about the lateralization of the PFC activation; however, lateralization has been shown to be a potential factor in the study of adaptive attention in young children in EEG studies of frontal symmetry (Fox et al 2003). Further exploratory effects and intended future directions will be discussed.

3-Q-124 - Examining the unique contribution of parental anxiety on adolescent neural responses during an emotion regulation task

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Details

Introduction: Anxiety sensitivity and emotion dysregulation are transdiagnostic risk factors for the development of anxiety pathology and are shown to be particularly salient during adolescence. Theoretical frameworks on youth anxiety highlight the role of parents' own anxiety on their children's capacity for emotion regulation, which may be driven by genetic and environmental mechanisms. Yet, relatively few studies to date have explored the impact of parental anxiety sensitivity on chil's neural activation related to emotion regulation. To address this gap, we tested whether parent anxiety sensitivity uniquely moderated adolescent emotion regulation-related neural activation, after

accounting for child anxiety sensitivity. Given its role in emotion regulation, we focused on regions of the orbitofrontal cortex (OFC) for the current study.

Methods: Participants were 91 adolescent-parent dyads (youth: M/SD_{age}= 12.24/.95; 52.7% female; 92% biological mothers). Parents and children completed measures of the Anxiety Sensitivity Index (ASI), which measures sensitivity to anxiety-related physiological sensations. Adolescents also completed an fMRI emotion regulation task that required youth to either regulate or react (focus factor) to negative or neutral trials (valence factor). Analyses examined whether parent ASI moderated adolescent neural activation related to the interaction between focus demands and stimuli valence, above and beyond adolescent anxiety sensitivity.

Results: Analyses revealed a significant 3-way parent ASI x focus x valence interaction. Parent ASI moderated adolescent neural responses in regions within the OFC, specifically the bilateral frontal medial cortex (*p=.03)* and the bilateral subcallosal cortex (*p=.01)*. Importantly, this effect remained significant with the inclusion of child anxiety sensitivity, indicating that parental anxiety sensitivity was uniquely associated with child emotion regulation-related neural circuitry. We first decomposed the 3-way interaction by examining effects within each level of the focus factor. Results showed parent ASI moderated adolescent neural responses to regulation (but not react) demands in both regions, such that greater parental ASI was associated with greater OFC recruitment to negative vs. neutral stimuli (during regulation condition). Next, we split by valence levels and partial correlations revealed that activation was not significantly correlated with either negative or neutral images (within the regulate level) in isolation. This suggests it is the difference in activation between negative and neutral stimuli driving this significant finding when regulation is required.

Discussion: Our results provide novel insight into the role of parental anxiety sensitivity on child neural activation related to emotion regulation, over and above child anxiety sensitivity. Specifically, parent anxiety sensitivity was shown to influence child neural activation when emotion *regulation* was required, extending previous work linking children's own anxiety sensitivity and emotion regulation processes. One potential interpretation of these findings may be that parental anxiety sensitivity impacts children's emotional learning, particularly as it relates to emotion regulation, and these effects can be observed at a neurobiological level. Together, this work contributes to empirical models of youth anxiety by elucidating links between parental pathology and neural circuitry involved in emotion regulation.

3-Q-125 - Distressing social media use is associated with developmental sex differences in hippocampal and amygdala subregions

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Details

Social media use (SMU) is highly prevalent among youth, with nearly 95% having access to a smart phone and 45% reporting online use 'near constantlyâ€. Despite these high rates of accessibility and use, the effects of SMU are poorly understood, with some emerging evidence of detrimental effects on youth's mental health. Prior behavioral work suggests that detrimental effects can range from feelings

of stress and negative affect due to a fear of missing out, to outright traumatic experiences due to online bullying. Aside from general screen time exposure, very few studies have examined SMU effects on neurodevelopment, including brain structure. Regions that are particularly rich with glucocorticoid receptors, such as the amygdala and hippocampus, may be especially sensitive to the effects of social media distress. Indeed, prior work has linked amygdala and hippocampal volume to more general forms of stress and risk for psychopathology in developmental samples. Therefore, hippocampal and amygdala volumes may be an early indicator of stressful and traumatic experiences due to SMU. In the current study, we used exploratory factor analysis to compute a latent variable that we termed social media distress (SMD), which reflected negative aspects of social media use (e.g., bullying, pathological use, etc.), and then examined how variance in this composite score was related to hippocampal and amygdala subregions in a sample of 68 youth (7â€“16 years). All youth completed high-resolution T_1- and sub-millimeter T_2-weighted structural MRI scans, as well as social media assessments. Using multiple linear regression, corrected for total intracranial volume and general social media exposure, we found significant sex-by-age-by-SMD interaction effects on several subregions. These effects, seen in the left amygdala basolateral complex and left CA1 of the hippocampus, showed relatively flat trajectories for adolescent males and females (11 16-years), while young males (7 10-years) showed decreases in volume and young females showed increases in volume in both regions, as function of SMD. The current data suggests that females and males may be differentially impacted by SMU. Our observation that this sex interaction was only present in younger youth may indicate a sensitive period during which social media-related stress acutely influences stress sensitive neural circuitry. While these subregions are expected to be increasing in volume throughout development, negative SMU may be accelerating this trajectory in females while having the opposite effect in males. In summary, the current results provide novel insights into the possible negative effects of social media on brain development in brain regions critical for memory and emotional processing.

3-Q-127 - Examining the link between neural mechanisms of emotion regulation and callous-unemotional behaviors in young children: An fMRI study

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Details

Background*: Callous-unemotional (CU)* traits [or behaviors when studying young children] refer to low levels of guilt, empathy, and caring for others, and are important characteristics for identifying a subgroup of children who display a more pervasive, severe, and aggressive pattern of antisocial behavior/conduct problems (CP). In prior work, we examined the uncinate fasciculus (UF), a bidirectional fiber pathway connecting anterior temporal lobe with medial, ventrolateral, and orbital prefrontal cortex, with connectivity through amygdala. We found associations between UF fractional anisotropy (FA) and callous-unemotional behaviors in young children diagnosed with ADHD, and in typically developing children (Graziano et al., 2022). Objective: Building on this work and to further explore the neural mechanisms of emotion regulation present among children displaying callous-unemotional behaviors, the current study examined brain activity in these medial, ventrolateral, and orbital prefrontal cortex regions and amygdala during an emotion regulation task during fMRI. Method: In this task children watched (without sound) 30 s film clips taken from Disney/Pixar movies. These clips were designed to elicit four emotions: Anger, Fear, Happy, Sad. Children were asked to imagine what the

main character was feeling, but to refrain from making a face, thereby attempting to suppress the emotional response. A block design (30 s ON; 20 s OFF), with 6 epochs (2 for each emotion, counterbalanced across subjects) was used in the scanner. The final participating sample consisted of 58 4-7-year-old children diagnosed with ADHD (dual clinician diagnosed) and 88 typically developing children (Mean age = 5.66, SD = 0.87, 69% male; 81% Hispanic/Latinx). All children were scanned in an MRI (3T Siemens Prisma; whole-brain EPI T_2* BOLD scan, TR/TE = 1000/30 ms; FOV = 216 x 216; FA = 52; 2.4 x 2.4 x 2.4 mm; 60 slices no gap). Standard image post-processing corrected for movement (FD = .9 mm) and a voxelwise GLM analysis was applied. Results: First, it is important to note that we did not find any association between CU behaviors and amygdala activation. On the other hand, we did find significant CU x emotion task condition interactions in predicting activation in right lateral inferior frontal gyrus ($p < .001$) and left orbital frontal cortex ($p < .001$). Upon examining these interactions, it appears that even after controlling ADHD symptom severity and demographic variables (age, sex), higher levels of CU behaviors were associated with less or blunted activation during the happy and sad conditions. On the other hand, higher levels of CU behaviors were associated with greater activation during the fear and angry conditions. Conclusions: When viewed in conjunction with the null amygdala finding, it appears that the some of the underlying emotional processing deficits related to children with high levels of CU behaviors may be more confined to the brain regions involved in the top-down regulation of emotions. Furthermore, this study is unique in terms of further highlighting how emotional valence may differentially impact top-down neural processing among children with high levels of CU.

3-Q-128 - Maternal Depression Impacts Children's Responses to Mothers' Voices: An fNIRS Study

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Details

Background and Objective: Major depressive disorder (MDD) is among the most prevalent psychiatric disorder (Kessler & Bromet, 2013). Maternal MDD casts transdiagnostic psychiatric risk in offspring (Goodman, 2007), creating great public health concerns worldwide. Depressed mothers show blunted emotional expressions during social interactions (Girard et al., 2014). Findings from our group indicate that mothers with a history of MDD had a slower and more monotonous voice when speaking in happy tones (Ilyaz et al., in prep). Repeated exposures to aberrant maternal emotional expressions may gradually fine-tune children's perceptual and neural sensitivity to symptom-relevant stimuli (Leppanen & Nelson, 2009). The present study aimed to examine the impact of maternal depression history on young children's neural responses to emotionally-varied voices spoken by their own mothers and mothers of other children (i.e. stranger females).

Methods: Participants were 52 children (24 girls, M_{age}=4.02, *SD*=0.15) and their mothers. High-risk (HR) children had mothers who met the criteria for MDD during the children's lifetime (*N*=25, 15 girls), and mothers of low-risk (LR) children had no history of mood disorders. Children completed a Localizer task and an Emotion Recognition task while undergoing fNIRS recording. In the LC task, children heard human and environmental sounds (20s) following a period of silence (8-12s). In the ER task, children were presented with emotionally-varied natural speech stimuli (Angry, Happy, or Neutral) from a female

speaker (Mother or Stranger) for 17.5s after a period of silence (10s). One challenge of fNIRS data analysis is that the scalp-based measurement does not directly provide information on scalp-location-to-anatomy or scalp-location-to-function correspondence. That is, the same scalp channel location may measure different brain regions that support different functions across participants. To address this challenge, we implemented a functional channel of interest (fCOI) analysis approach (Powell, Dean, & Saxe, 2018) in addition to the standard analysis approach. The fCOI analysis identified a channel in the left and right temporal lobe of each child that showed the strongest response to human voices in the Localizer task and then independently examined the extent to which responses in these channels were modulated by speaker identity in the Emotion Recognition Task.

Results: The standard fixed-array analysis revealed a significant interaction effect of Group (HR, LR) and Speaker (Mother, Stranger) on oxygenated hemoglobin (HbO) responses to the voices at a left (#4), $F(1, 42)=6.06$, $p=.02$, and a right temporal channel (#14), $F(1, 44)=4.10$, $p=.05$. However, the effect was not robust against correction for multiple comparisons (6 statistical tests). The fCOI analysis (2 statistical tests) revealed a significant Group-by-Speaker interaction effect on the HbO responses to the voices at the left, $F(1, 37)=5.16$, $p=.03$, and right temporal lobe, $F(1, 37)=8.13$, $p=.01$. Specifically, HR children displayed greater HbO responses to their mothers' compared to strangers' voices at the right temporal lobe, $B=0.63$, $t=2.34$, $p=.02$.

Conclusions: Both the fixed-array and fCOI analysis indicated group differences in children's neural responses to mothers' versus strangers' voices. Given mothers with a history of MDD had more monotonous happy voices, the greater right temporal activations in response to mothers' than strangers' voices among HR children might be linked to their enhanced efforts in emotion recognition.

3-Q-129 - Coordination of social attention, mentalizing language and mentalizing network connectivity during a naturalistic social interaction between emerging adulthood friends

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Details

Social interactions are foundational for social behavior and social brain development (Carpendale & Lewis, 2004; Johnson, 2011). Two mechanisms that may support social interactions include social attention, attending to social interaction partners, and mentalizing, interpreting the intentions and feelings of others (Frith & Frith, 2003). Social attention and mentalizing may coordinate in real time, enabling people to navigate social interaction dynamics (Capozzi & Ristic, 2020). However, most tasks have assessed social attention or mentalizing separately and outside of the interaction context, limiting inferences about how these processes may coordinate in real time. Emerging adulthood is an important developmental period for building the skills and support systems necessary to thrive during adulthood (Silvers & Peris, 2023). Socializing with friends likely plays an important role in how emerging adults learn to navigate the adult social world. Here, we designed a novel method to assess the coordination of social attention, mentalizing language, and mentalizing network neural connectivity during a naturalistic social interaction between emerging adulthood friends. We anticipate that moments of social attention

(dwelling on a social interaction partner) will be associated with use of mentalizing language and greater positive connectivity in the mentalizing network.

Data collection ended in April 2023. 32 platonic, same gender identity dyads (N = 64; 38 Women, 79.7% White, M_{age} = 19.76, SD_{age} = 1.27) participated. Participants visited the lab in friend pairs and engaged in a social interaction designed to elicit both positive and negative affect. Participants wore a mobile eye-tracking system that collected eye-tracking metrics and videos of their individual perspectives of the social interaction. Participants self-reported on how well they felt the social interaction went. Videos from each participant's perspective of the social interaction were extracted. Participants then viewed these videos from their perspective (self run) and their frien's perspective (friend run) while fMRI data were collected. The social interaction is coded offline for mentalizing language using an adapted version of the conversational Theory of Mind coding scheme (Alkire et al., 2021). Mobile eye-tracking data are processed using Yolo v7 (Wang et al., 2022), a modern computer vision object detection model. fMRI data are preprocessed using fmriprep 22.0.0. Level 1 analyses are conducted in FSL using fmri.factory (Hallquist, 2022). To-date, whole-brain analyses suggest the task elicits robust signal throughout the mentalizing network. The deconvolved time series during the self run for mentalizing regions (identified using neurosynth) will be extracted for data analysis.

We will analyze the data using two multilevel structural equation models. The behavioral model will assess relations between moment-to-moment social attention and moment-to-moment mentalizing language. The neural model will assess moment-to-moment social attention and moment-to-moment mentalizing network connectivity. We will also conduct sensitivity analyses to assess if observed relations are specific to mentalizing. For the behavioral model, we will assess moment-to-moment relations between social attention and talking-with-hands. For the neural model, we will assess moment-to-moment relations between social attention and visual network connectivity. Finally, we can use participant's self-reported feelings about the social interaction to assess if coordination between social attention and mentalizing was related to more successful social interactions.

This novel project assesses how social attention and mentalizing may coordinate in real time to support social interactions. These data can lay the foundation for future work assessing individual differences that may influence the coordination of social attention and mentalizing, such as social anxiety.

3-Q-131 - Neural and Behavioral Responses to Others' Struggles in 1-year-old Infants

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Details

Prosocial behavior, in the forms of both helping and expressing empathy, emerges in the first few years of life (Vaish et al., 2009; Warneken & Tomasello, 2006). Individual differences in these early helping behaviors persist through childhood into adulthood, indicating that these early expressions of compassion truly represent the origins of human prosociality (Eisenberg et al., 1999; Roth-Hanania et al., 2011). In adults, two complementary brain networks support empathic and compassionate responding. One, sometimes called the mentalizing network, supports thinking about others' thoughts and

emotions, while another, the pain network, is comprised of regions responsive to the sensory, motor, and affective significance of stimuli (Jacoby et al., 2016; Singer & Klimecki, 2014). Here we aim to test the role of these two brain networks in infants' early prosocial responses.

This study involves two phases. In the neuroimaging phase, 14- to 20-month-old infants wear a functional near-infrared spectroscopy (fNIRS) cap covering bilateral regions of frontopolar cortex, premotor cortex, temporal cortex and anterior parietal cortex, while watching two types of video stimuli. 'Successâ€ videos show an actor successfully performing an instrumental action (e.g. stacking blocks or drinking from a cup), while matched 'struggleâ€ videos show an actor either failing to perform the same actions or sustaining a minor injury (e.g. stubbing a toe or pinching a finger) in the process of executing them. The videos feature two different actors who each succeed or struggle an equal number of times. All videos are 14 seconds in length and each is preceded by a 4 second attention getting video. Each participant sees up to 16 unique videos, presented in pseudorandom order and separated by interstimulus periods (slowly moving geometric shapes on a black background) that vary from 6 to 12 seconds in length.

In the behavioral phase, half of which occurs before the fNIRS phase and half after, an experimenter engages the participant in several different activities that provide the participant with a chance to help or empathize with the experimenter. This includes picking up spilled blocks, moving the top of a container so the experimenter can put blocks inside, pointing out a 'lostâ€ object that is clearly visible to the participant but not the experimenter, handing back a dropped marker, and expressing concern for or attempting to help clean water spilled on the experimenter's drawing. In each case, we measure whether or not the participant helped or expressed empathy, and their latency to offer help or comfort.

We will use an individual functional channel of interest approach (Powell et al., 2018) to analyze the fNIRS data, testing for higher activation to struggle than success videos in each of four regions of interest (medial prefrontal, premotor cortex, somatosensory cortex, and temporo-parietal junction). The fNIRS data will allow us to ask if videos of others struggling primarily activate infant mentalizing network regions (medial prefrontal cortex, temporoparietal junction), pain network regions (premotor cortex, somatosensory cortex), both, or neither. We will also then ask if differential activation to struggle videos in any of these regions positively correlates with a composite helping score or negatively correlates with latency to help. Over half of the intended sample (26/50) have been tested. We anticipate completing data collection by mid-July and analyzing data by the end of August.

3-Q-132 - Relating emotional lability to brain activation differences in perception of emotional faces in preschool-aged children with familial risk for ADHD

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Details

ADHD is a prevalent disorder that often onsets in early childhood and is associated with negative outcomes spanning multiple domains of life. ADHD is defined by inattention and/or hyperactivity, but emotional dysregulation is also common and is associated with greater functional impairment. Further, ADHD is highly heritable, and it has been estimated that approximately half of children with a parent

with ADHD will also develop the diagnosis themselves. However, nearly all studies have examined individuals who already have the diagnosis of ADHD. Longitudinally studying children at familial risk for developing ADHD could help to disentangle the *causes* vs. *consequences* of ADHD. Early identification of traits that predispose children toward ADHD could enable prevention or early intervention.

As part of a larger longitudinal study, we are presently recruiting preschool-aged children (ages 4-6) with at least one parent diagnosed with ADHD (familial risk group) or whose parents do not have ADHD (control group). Families attend an initial screening visit with the clinical team to determine their chil's group. Parents complete the NIH Toolbox Parent Proxy Emotional Battery about their child, including measures of anger, fear, sadness, and social distress, to assess their chil's emotional wellbeing. Following the initial visit, children return for a separate MRI scanning visit for neuroimaging; researchers are blinded to the chil's group status. During the visit, children complete three runs of a block-design emotional face matching fMRI task to measure brain responses while viewing emotional expressions. In each trial, children are presented with a target face in the top center of the screen and indicate via button press which of two faces at the bottom of the screen is identical to the target. The faces, drawn from the NimStim and Radboud databases, display happy, sad, angry, or neutral expressions (30 total trials per condition). The order of the blocks is counterbalanced across participants. Data collection is ongoing, and we expect a sample size of approximately n=30 by the time of the conference.

We hypothesize that children with familial risk for ADHD will exhibit greater activation in the amygdala and insula while viewing negative facial expressions relative to children in the control group. In addition, we hypothesize that emotional dysfunction as reported by parents will be positively associated with elevated activation in these regions in the ADHD group. We will use a general linear modeling approach to extract activation from these structurally defined ROIs in the negative > neutral contrast for each of the negative facial expressions (i.e., sad and angry). We operationalize emotional dysfunction as a composite score of the negative NIH Toolbox measures. All analyses will control for child age and sex.

This research will fill a gap in the current literature by better characterizing emotional well-being in children at familial risk for ADHD and elucidating underlying neural mechanisms. Characterizing emotional dysregulation in this pre-clinical sample has the unique potential to serve as a behavioral and brain marker of risk for conversion to an ADHD diagnosis, which is a promising future direction for the longitudinal component of this larger project. Although understudied relative to executive functioning deficits, deficits in emotional functioning warrant further study as they may be mechanistically involved in the emergence and maintenance of ADHD symptoms.

3-Q-133 - Understanding the development of self-processing and depression in adolescence: Is brain function where it starts?

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Details

Background:

Adolescence is characterized by neural and cognitive changes in self-development and vulnerability to depression--particularly among girls. Self-evaluation is altered in girls with depression. Yet, the *directional* associations between self-evaluation and depressive symptoms across adolescence has not been robustly delineated. Does increased negative self-evaluation predict elevated depressive symptoms or is it the other way around?

In addition to a current lack of clarity regarding these longitudinal trajectories, clinical scientists have struggled with early detection of depression prior to disorder onset. Brain function, such as vmPFC activity which has been robustly associated with *both* self-evaluative processing *and* depression, may increase our chances of early detection and offers a potential avenue for prediction of *prospective* depression.

Aim:

We will assess longitudinal associations between neural and behavioral indices of self-evaluation and depressive symptoms, allowing us to parse directional associations. Through a mediation model, we will test our hypothesis that brain function during self-evaluative processing predicts future behavioral indices of self-evaluation which then predict depressive symptoms.

Method:

A unique opportunity to advance this essential research is provided by the Transitions in Adolescent Girls (TAG) study, which has now at least four waves of neural indices of self-evaluation and depressive symptoms (N=174, initial ages 10.0-13.0, 18 months between waves). Depressive symptoms will be assessed via the Center for Epidemiological Studies Depression Scale for Children (CES-DC) and disorders via clinician-administered interviews following the Kiddie Schedule for Affectives Disorders and Schizophrenia (KSADS). Participants complete a self-evaluation fMRI task where they decide whether traits from three domains (prosocial, antisocial, and social status) describe them. The behavioral metric of self-evaluation will be the proportion of self-evaluations that are negative (negative adjective endorsed and positive adjectives rejected). Univariate analyses of vmPFC activity during the self-evaluative condition (contrasted against a high-level control during which participants describe whether the same traits are malleable for people in general) will serve as the neural marker.

Preliminary Findings:

In order to control for trait-like variability, I conducted a four-wave Random Intercept Cross-Lagged Panel Model (RI-CLPM) in the TAG study which revealed transactional associations between the behavioral index of self-evaluation and depressive symptoms across adolescence (age range: 9 - 16 years old). In addition, linear regression models have shown that vmPFC activity at wave 1 predicts *future* depressive symptoms at wave 2 *above and beyond* depressive symptoms at wave 1. Moreover, brain function and depressive symptoms were not cross-sectionally associated. Combined with existing research, these preliminary findings suggest the possibility, reflected in our hypothesis, that aberrant brain function may predict future behavioral indices of self-evaluation which, in turn, predict depressive diagnoses during adolescence.

Proposed Analyses:

To test this theory, we will conduct a multilevel mediation model whereby self-evaluative behavior mediates the relationship between brain function during self-evaluation and subsequent depressive diagnoses. We will use a minimum of four waves of data, which have already been collected, for this multilevel mediation model. To minimize researcher degrees of freedom and follow rigorous open and reproducible science practices, we have not yet run these analyses but will present them at the 2023 Flux conference.