

Flux Congress Oral Presentations



Day 1 Friday, August 30

Science of Learning Symposium

Chair: **Bruce McCandliss** Stanford University, USA

Julia Moser fMEG-Center/Institute for Diabetes Research and Metabolic Diseases (IDM) of the Helmholtz Center Munich at the University of Tübingen, Germany

Magnetoencephalographic signatures of hierarchical rule learning in newborns

Fetal magnetoencephalography (fMEG) allows to non-invasively measure fetal and neonatal brain activity. With fMEG, auditory event-related responses to tones as well as auditory mismatch responses can be reliably recorded in the last trimester of pregnancy as well as shortly after birth, which demonstrates auditory discrimination on a neuronal level. To differentiate conscious perception and learning from automated sensory processing, a complex - hierarchical - oddball paradigm was used. The auditory "local-global" mismatch paradigm establishes a global rule, whose violation causes a global mismatch response, in addition to the mismatch response caused by a local oddball. After an initial rule-learning phase, this globally deviant sequence appears in one fourth of trials. Depending on the rule, the local oddball can be within either the standard or the deviant sequence. The sequence without oddball can be standard or global deviant respectively. All subjects were stimulated with both rules, resulting in four stimulus conditions. fMEG measurements were performed in 21 newborns between 13 and 55 days (M=31). Stimuli were sequences of 500Hz as well as 750Hz tones. Newborns showed mismatch responses towards local as well as global rule violations. The local oddball within the globally deviating sequence elicited the strongest mismatch response. A weaker mismatch response was observed for the oddball within the standard sequence. Comparison of both sequences with or without oddball (role of global standard or deviant) revealed in both cases an early and a late global mismatch response (peaking at 350ms & 1010ms; 380ms & 920ms respectively). These findings give a strong indication for learning of the presented rule. Within the framework of the "local-global" paradigm, learning of the global rule is seen as a neuronal correlate of conscious processing. Investigating this correlate can be a valuable contribution to the research on early cognitive development.

Rachel Romeo MIT & Boston Children's Hospital, USA

Cortical plasticity associated with a parent-implemented language intervention

Objective: Children's early language experiences, including high quality parent-child interactions, are related to their linguistic, cognitive, and academic development, as well as their brain structure and function (Romeo et al., 2018). On average, children from lower socioeconomic status (SES) backgrounds receive reduced language exposure, and several parent-implemented interventions have resulted in both improved home language environments as well as increases in children's language skills (e.g., Leech et al., 2018). However, the neuroplastic mechanisms underlying these changes are yet unknown.

Methods: One hundred lower-SES 4-to-6 year-old children and their primary caregivers were randomly assigned to either a 9-week family-based intervention focused on enhancing children's communication, executive functioning, and school readiness skills or a no-contact control group. Children completed pre and post assessments of verbal and nonverbal cognition, and subsets of each participant group additionally completed LENA home language recording and structural neuroimaging, from which longitudinal cortical thickness changes were calculated using Freesurfer. **Results:** Controlling for baseline

measures, families who completed the intervention exhibited significantly increased adult-child conversational turns. The magnitude of turn-taking change was positively correlated with increases in children's language scores, and was also positively correlated to cortical thickening in language-related left inferior frontal regions, as well as social-related right supramarginal regions. Conclusions: This is the first study to investigate neural mechanisms underlying perturbations to children's language environments. Results suggest that parent-implemented language interventions may improve children's language skills via cortical plasticity in canonical language and social regions during development. This has implications for social and educational policies for early intervention.

Stephanie DeCross Harvard University, USA

Dynamic neural correlates of fear conditioning in children exposed to trauma and associations with psychopathology

Objective: One potential mechanism linking childhood trauma (CT) exposure to psychopathology is fear learning, a phenomenon that is well understood in adult but not developmental populations. This study aims to describe how the neural correlates of fear learning unfold over time in children, as well as how CT may disrupt patterns of neural response in ways that contribute to psychopathology. Methods: 147 children (aged 8-16 years) with and without exposure to CT underwent a differential fear conditioning procedure during an fMRI scan. Dynamic patterns of learning were examined in voxel-wise parametric modulation analyses and region-of-interest analyses, and functional connectivity was assessed with whole-brain task-based connectivity analyses. Multiple regression was used to examine associations with psychopathology symptoms. Results: In children, canonical salience network regions (including amygdala, insula, anterior cingulate cortex) were active to the CS+ relative to CS- and exhibited habituation across learning blocks. Default mode network regions (including hippocampus, frontal pole, vmPFC, and posterior cingulate cortex) were active to CS- relative to CS+, and increased activation across learning blocks. Children with CT display blunted habituation to CS+>CS- in right amygdala and insula and smaller increases in right hippocampus and frontal pole to CS->CS+. Additionally, children with CT showed greater functional connectivity of amygdala with fronto-parietal regions associated with attention direction and initiation of defensive responses to CS+>CS-, and less amygdala-hippocampus connectivity. Patterns of altered dynamic neural response were associated with depression, generalized anxiety, and externalizing symptoms. Conclusions: Alterations in fear learning processes and the dynamic communication between salience network and default mode network regions may be a key mechanism underlying the link between CT and psychopathology.

Local Symposium: NeuroConstruction & the self-organizing brain

Chair: **Nim Tottenham** Columbia University, USA

Catia Teixeira Nathan Kline Institute, USA

Perinatal interference with the serotonergic system affects VTA function in the adult via glutamatergic co-release

Serotonin and dopamine are neurotransmitters associated with multiple psychiatric disorders. However, how they interact during development to affect subsequent behavior remains relatively unknown. Here I will present work from my laboratory showing how changes in serotonin levels during early-life, induced by exposure to antidepressants, alter dopaminergic function and behavior later in life.

Christina Alberini New York University, USA

Molecular mechanisms of episodic learning and memory in early development

Infantile episodic experiences are rapidly forgotten; nonetheless, they profoundly affect the brain's functions and physiology throughout life. In agreement, recent studies in rodents showed that memories formed in infancy are not lost, but instead are stored long-term in latent forms. Molecular and behavioral characterization of hippocampus-dependent memories in rats and mice led us to suggest that they undergo a developmental critical period. I will discuss new findings revealing that, during this period, learning produces a significant maturation at the cellular, synaptic and behavioral levels. This maturation appears to be selective for the type of experience encountered.

Sean Froudish-Walsh New York University, USA

Brain injury at birth disrupts the development of dopamine and working memory networks in humans

Working memory requires dopamine. In rodents, damage to the hippocampus at birth affects dopamine function and working memory in later life. Similar studies in humans have been lacking. I first present results from a longitudinal study of people who had brain injury at birth. Their hippocampal damage correlates with reduced presynaptic dopamine function in adulthood. However, compensatory cortical activity may reduce working memory deficits. Next, I present a new large-scale computational model. We find that increases in cortical dopamine in development can lead to less distractible working memory. Together, this shows how specific developmental changes can impact working memory ability.

Chris Baldessano Columbia University, USA

Learning how to remember

Building memories of realistic experiences in our everyday lives is a daunting task, requiring us to break down the continuous world in meaningful events that can be understood, stored, and communicated. My recent projects have explored the ways in which our knowledge about the schematic structure of the world changes how we build these event representations. I will discuss the new experimental and analytic methods I have developed to study this question in naturalistic stimuli, and current work in my lab in which we have applied these approaches to study developmental changes in event perception.

Trainee Dissertation Award Presentation

Chair: **Bea Luna** University of Pittsburgh, USA

Katie Insel Harvard University, USA

Brain and behavioral asymmetries for gain and loss learning emerge with age during adolescence

Adolescence is a period of the lifespan accompanied by normative shifts in motivated behavior, and the ability to learn from gain and loss incentives matures with age. However, it remains unclear whether adolescents exhibit value prioritization during gain and loss learning, a process that allows individuals to enhance learning for high-value outcomes in a goal-directed fashion. To test this question, N=84 participants age 13-20 completed a value-modulated probabilistic reinforcement learning task with low and high stakes gain and loss learning contexts during functional neuroimaging. Value prioritization was indexed by comparing learning performance, as measured by proportion optimal choice, between high and low stakes conditions when participants learned to approach gains or avoid losses. Older adolescents exhibited value prioritization in the gain domain, a behavioral profile that emerged with age during late adolescence. In contrast, younger adolescents exhibited value prioritization in the loss domain, and this effect attenuated with age. These age-related differences in learning could not be explained by differences in self-reported subjective value of the monetary incentives. Age-related asymmetries in value-prioritization were mirrored in functional recruitment of the ventral striatum during feedback. Younger adolescents exhibited value-based differentiation in the striatum during loss learning. However, with age, individuals were more likely to increase ventral striatal activity for high

relative to low value gain outcomes. Moreover, gain value-tracking in the ventral striatum was associated with enhanced value prioritization during gain learning. Together, these findings reveal age-related asymmetries in brain and behavioral signatures of value-prioritization during gain and loss learning.

Huttenlocher Lecture

Chair: **Deanna Barch** Washington University, USA

BJ Casey Yale University, USA

Developmental cognitive neuroscience: We've come a long way, baby, or have we?

With advances in imaging technology, we have significantly improved our ability to examine the developing brain in vivo. The rise in large scale, longitudinal data collection now allows us to examine developmental trajectories in dynamic brain systems across and within individuals to make predictions about long term outcomes. But what impact has developmental science had on the quality of life for our youth or for our society to date? How can developmental science better inform the treatment of the developing brain in medicine, law and society? This lecture will discuss these issues from a historical perspective and consider future opportunities.

Local Session:

Chair: **Francis Lee** New York Presbyterian/Weill Cornell Medical Center, USA

Jordan Marrocco The Rockefeller University, USA

Epigenetic Signature in CA3 Neurons Associated with Altered Stress Reactivity in Mice Subjected to Early-Life Stress

Epigenetic control of gene expression by early-life adversities affects discrete brain regions involved in mood regulation and response to stress, such as the hippocampus. Using a protocol of chronic early-life stress (ELS) in mice followed by acute-swim stress in adulthood, we showed that ELS induced persistent changes in histone methylation in CA3 region that differed from those observed in control mice. RNA-sequencing of TRAP-isolated CA3 neurons revealed that ELS programs a restricted transcriptional response to stress in adulthood, inducing unique gene pathways. This sheds light on novel biomarkers for diagnostic prevention of psychiatric disorders in populations at risk.

Conor Liston Cornell Medical, USA

Info to come

David Pagliaccio Columbia University, USA

Subcortical brain structure and function in youth with depression or familial risk

Research probing subcortical structural and functional deficits in youth depression has often relied on small sample sizes, which limits generalizability. Toward addressing this gap, data from the Adolescent Brain Cognition Development Study (n=4,521 9-10-year-olds) showed that maternal depressive history related to smaller right nucleus accumbens volume. Building on this, data from the Human Connectomes Related to Anxiety and Depression in Adolescents Project (n=170 14-16-year-olds) indicated that reduced accumbens volume and reactivity to incentive cues in depressive-anxious adolescents relative to healthy adolescents. Collectively, smaller accumbens volume and altered accumbens functioning may play a key role in depression onset and maintenance.

Flash Talks

Chair: **Cate Hartley** New York University, USA

Suzanne van de Groep Leiden University, The Netherlands

The neural correlates of giving under different social contexts in adolescence

Giving is essential for forming and maintaining social relationships, which is an important challenge for adolescents. This behavior is often characterized by the conflicting decision whether to forego self-interest to benefit others, and as such is highly context-dependent. There is currently little understanding of the mechanisms that drive context-dependent giving and how they develop in adolescence. Understanding the neural components of giving in different social contexts may shed light on these mechanisms. In this preregistered study, we studied giving and its neural correlates in different social contexts across adolescence. Specifically, we manipulated the extent to which self-interest outweighed benefits for others (i.e., donations were small instead of large), whether adolescents gave to a friend or unfamiliar other, and whether they were being observed by others or made anonymous choices. Participants (N = 140, ages 9 - 18) performed a novel giving fMRI paradigm, in which they divided coins between themselves and someone else in the aforementioned different social contexts. In line with our expectations, results showed that regardless of age, adolescents gave more i. when self-interest outweighed benefits for others, ii. when the beneficiary was a friend, and iii. when being observed. On a neural level, we found medial prefrontal cortex activity for small compared to large donations, and bilateral postcentral gyrus activation for the reverse contrast. Playing for a friend compared to an unfamiliar other elicited activity in the lateral and medial prefrontal cortex, as well as the right precentral gyrus, and the right inferior and left superior parietal lobules. These findings provide insights into the modulation of neural processes that underlie giving decisions as a function of the social context, highlighting the role of prefrontal areas and social brain regions.

Sarah Tashjian University of California, Los Angeles, USA

Perseverance in adolescents and young adults is related to neural response to performance feedback

Although performance feedback itself has no extrinsic value, it can produce subjective feelings similar to rewards and punishments (Eisenberger, 2012). When perceived as motivational, performance feedback provides valuable information that can help guide learning (Tricomi et al., 2016). The present study examines whether neural response to feedback is related to intrinsic motivation to engage in an effortful cognitive task despite prior failure (i.e., perseverance). Adolescents and young adults were tested to examine age-related development in neural response and behavioral perseverance. During functional magnetic resonance imaging, 100 adolescents and young adults ages 13-30 (61 female; Mage=18.33) completed a novel perseverance task. Participants first completed a series of mental rotations during which they received quasi-manipulated feedback that their responses were either correct or incorrect (40% of trials received incorrect feedback regardless of performance, 60% received accurate feedback). Participants then made decisions to continue on a path requiring more mental rotations (persevere) or quit for an easier path. Perseverance decisions increased with age, $t(98)=-2.27$ $p=.026$. Negative feedback (manipulated and accurate collapsed) elicited activation of anterior insula (AI) and dorsal anterior cingulate whereas positive feedback elicited activation in ventral striatum and medial prefrontal cortex, $Z>3.1$ $p<.05$ corrected. Individuals who persevered exhibited reduced AI activation to negative feedback and lower behavioral inhibition scores (BIS scale, Carver & White, 1994), measuring tendency to avoid aversive experiences, compared to individuals who quit. Results expand understanding of the neural systems associated with motivation and perseverance during adolescence and early adulthood. Additional results controlling for prediction error during manipulated feedback and examining how feedback relates to subsequent performance will be presented.

Hyesung Grace Hwang University of Chicago, USA

Neighborhood racial demographics predict infants' motor system activation toward racial out-group individuals

Objective: The human tendency to view the social world in terms of "us" and "them" emerges early in ontogeny yet the mechanism behind this tendency remains unclear. One candidate mechanism for this tendency is the action processing and mirroring mechanism. This study examined whether infants' perception of others' actions as reflected in neural motor activation is affected by the racial demographics of the neighborhood they live in. Methods: Forty-three 8- to 12-month-old White infants' EEG data across three studies were combined for secondary analyses. In all studies, infants observed either a White or Asian female actor grasp an object. Baseline-corrected mu power (6-9 Hz for infants) averaged across the C3 and C4 electrode clusters was extracted locked to the observed reach-to-grasp movement. This neural correlate of motor activity was examined in relation to neighborhood demographics based on zip code using a mixed model approach. Results: There was a significant interaction of mu power between the proportion of non-White population in the zip code and the racial group (White vs. Asian) of the presenter, $= -7.965$, $SE = 2.348$, $t = -3.392$, $p = .002$. Specifically, when White infants viewed an Asian presenter ($n = 24$), those from a neighborhood with greater proportion of non-White population showed greater mu desynchronization (i.e., greater motor activity), adjusting for variety of racial groups, proportion of Asian population, median income, and population density of the neighborhood, $= -5.757$, $SE = 2.047$, $t = -2.812$, $p = .012$. However, when White infants viewed a White presenter ($n = 19$), none of the neighborhood demographic variables predicted mu desynchronization. Conclusions: White infants showed greater motor activation toward a racial out-group individual if they have more exposure to racial out-group individuals in their neighborhood, suggesting motor system activation related to action understanding and mirroring is sensitive to neighborhood context.

Zaixu Cui University of Pennsylvania, USA

Individual variation in fronto-parietal control network topography supports executive function in youth

Recent evidence has established that the spatial topography of functional brain networks differs markedly among individuals, with the frontoparietal control network (FPN) being the most variable. However, it remains unknown how this topography evolves during youth or relates to individual differences in executive function. Here, we capitalized upon a sample of 713 participants ages 8-22 who were imaged as part of the Philadelphia Neurodevelopmental Cohort and had over 27 minutes of high-quality fMRI data. We used a recently developed single-subject brain parcellation method based on non-negative matrix factorization to identify 17 individualized networks for each participant. Consistent with prior reports, we found that across-subject variability of network topography was highest in FPN and lower in visual and motor networks. Notably, the proportion of cortex devoted to the FPN increased with development ($P(FDR) = 0.01$) and was positively associated with executive functioning ($P(FDR) < 0.001$) while controlling for age. Using machine learning techniques, we found that this individualized functional topography could accurately predict both an individual's age ($r = 0.72$, $p < 0.001$) and executive performance ($r = 0.45$, $p < 0.001$) in unseen data. Critically, elements of the FPN were the most important features for predicting both age and executive performance. Finally, the spatial distribution of these predictive features within the FPN aligned with fundamental properties of brain organization, including evolutionary expansion, areal scaling, myelin content, functional role, and cerebral blood flow. Together, these results delineate a process whereby specific functional network topography in the FPN matures during youth to support executive function.

Marjolein Barendse University of Melbourne / University of Oregon, USA

Neural correlates of self-evaluation during puberty

Forming a clear and multifaceted concept of the self is an important life challenge in adolescence. Previous studies have shown that self-concept changes during adolescence and that underlying neural correlates also change, for example in the medial prefrontal cortex (PFC). Very few studies have examined the change in self-evaluations/-concept and its neural correlates in relation to puberty, and whether pubertal processes relate to self-evaluative neural processes over and above age. The current study uses data from 174 girls aged 10.0 to 13.0 years to examine this. The girls completed a functional MRI paradigm in which they decided whether or not an adjective describes them, including positive and negative adjectives grouped into three factors: 'prosociality', 'antisociality/aggressiveness', 'urgency/detachment'. Participants also completed the Pubertal Development Scale and morning saliva samples to measure DHEA, testosterone and estradiol levels. We expect that (1) activation in the ventromedial PFC (vmPFC) and pregenual anterior cingulate (pgACC) during self-evaluation (relative to the control condition) increases with age; (2) pubertal development, both hormonal changes and self-reports of physical changes, will explain activation in areas subserving self-referential, affective and reward processes over and above age. This effect of pubertal development on neural activation will depend on adjective type/factor; (3) activation in vmPFC, pgACC and ventral striatum will be higher for positive adjectives compared to negative. In addition, on a trial-by-trial-level, negatively valenced adjectives that are endorsed as self-descriptive will engage the vmPFC and pgACC more than those that are rejected. This project is preregistered here: <https://osf.io/g94h8/>.

Tzipi Horowitz-Kraus Technion and Cincinnati Children's Hospital, USA

Executive functions in reading: impairment and plasticity in children with and without dyslexia

Approximately 15% of children in the western world have reading disabilities, a neurodevelopmental disorder known to impact academic achievements as well as social and emotional wellbeing. Identification of the underlying factors contributing to RD is crucial for proper classification and planning of remedial interventions. Current strategies rely exclusively on behavioral measures and are of limited precision. Here, we aimed to study the role of cognitive control in reading among children from birth to age 12 years using a multimodal approach utilizing several MRI methodologies as well as EEG data. Results provided potential biomarkers for reading difficulties in children: EEG data suggested decreased event related potentials evoked from the anterior cingulate cortex (ACC) and functional MRI data showed decreased functional connectivity of cognitive control networks. Using MRI, we then demonstrated the effect of an executive-function based intervention on these functional connections during both reading and resting-state conditions. Greater attention- and inhibition-related ERPs were observed following training. The advantages of using neuroimaging methods in evaluation of neurodevelopmental disorders in children and the challenges the field of developmental neuroimaging is facing will be discussed.

Ashley Nielsen Washington University in St. Louis, USA

Two patterns of atypical development involving distinct functional networks in Tourette syndrome

Tourette syndrome (TS) is a complex disorder with symptoms that involve sensorimotor and top-down control processes that fluctuate over the course of development. Understanding the neural substrates supporting the range and time course of symptoms in TS may require a whole-brain description of large-scale circuitry and examination of these substrates across development. Here, we used functional connectivity MRI to examine, in TS, the diverse functional networks across the brain that support cognitive functions. We considered the connections within each functional network and between each pair of functional networks separately. We then compared the development (here, cross-sectional

differences between children and adults) of these connections in TS to that in healthy controls. We found evidence for two patterns of atypical development in TS that involved different within-network and cross-network connections. Developmental differences that were greater in TS than in controls were among control and processing networks. These connections did not differ between control children and adults, but were stronger in adulthood TS. By contrast, developmental differences that were smaller in TS than in controls involved functional connections between subcortical structures and control and processing networks. The strength of these connections increased/decreased between control children and adults, but to a smaller extent in TS and were indicative of immaturity in adulthood TS. These two distinct patterns of atypical development may be supported by different mechanisms. Divergently stronger functional connectivity in adulthood TS may be associated with frequent, coordinated engagement of attention, top-down control, and sensorimotor processes that accompanies a history of tics. The incomplete maturation of the integration and segregation of the subcortex and cortical sensory and attention networks may be a factor in persistent tics in adulthood.

Benjamin Conrad Vanderbilt University, USA

Neural mechanisms of digit processing in kindergartners: An fMRI study

Number symbol processing is a critical foundation for math achievement. Evidence in adults suggests preferential engagement of a "Number Form Area" (NFA) in the ventral occipito-temporal cortex (vOTC), during the processing of Arabic numerals compared to other symbols, and that the function of this region relates to individual differences in calculation ability. It is currently unknown, however, 1) when preferential processing of the NFA develops, 2) what mechanisms drive category specificity in the NFA, and 3) how NFA function relates to behavior in children. We address these questions using fMRI in typically-developing kindergartners who performed a symbol classification task. Participants ($n=46$, Mean age 6.1 ± 0.4 yo) saw digits, letters, or scrambled symbols, deciding whether they "knew the name" of the stimulus. We found no evidence for preferential processing of digits in the NFA in relative activation level, nor in representational distinction via MVPA. Similarly, we found no evidence of differences across symbol categories in NFA-to-parietal connectivity, as would be predicted from a biased-connectivity account of vOTC functional development. In a brain-behavior correlation, a significant negative association was observed between digit-related activity in the NFA and digit naming speed ($r = -0.52$, $p < 0.001$), with higher performance related to lower activation to digits relative to other symbols. The relationship remained significant ($p < 0.02$) after controlling for letter naming speed. This finding suggests NFA function is relevant for digit recognition in kindergarten, albeit in the opposite direction than expected. Overall, our results are not easily reconcilable with prior findings in adults, suggesting a complexity to NFA development which requires further investigation, including longitudinal assessment of NFA functional maturation.

Ana Cubillo University of Zurich, Switzerland

Response time variability is associated with more current and future negative life outcomes in children

Aims: Intra-individual variability in response times (RT-variability) has been associated with symptom severity in ADHD, ASD, schizophrenia, and dementia. This study investigates its potential as a marker of risk for negative outcomes in terms of both psychopathology and more general well-being. **Methods:** We recruited 28 typically developing 7-8 year-old children from an on-going longitudinal study on working memory training. They performed an fMRI-adapted N-Back as well as several other cognitive tasks. We used a step-wise regression analysis including accuracy and RT-variability measures from the N-Back task as independent variables and scores from Strength and Difficulties Questionnaire (total and externalising scores) and Math performance at 6 or 12 months after training as outcome measures. We

also tested for similar relationships in a sample of 3,223 children from the ABCD study. For the ABCD sample, we used the total and externalising T-scores from the Child Behaviour Check List (CBCL) and body-mass-index (BMI) as outcome measures. Results: In the longitudinal sub-sample, RT-variability during the N-Back was significantly associated with future SDQ total scores (Standardized Beta=0.44, $p=0.013$), externalizing scores (Standardized Beta=0.44, $p=0.01$), and Math performance (Standardized Beta= -0.612, $p=0.002$). We found a similar association in the ABCD study. There, RT-variability in the N-Back was significantly related to CBCL total (Standardized Beta=0.023, $p=0.014$) and externalizing (Standardized Beta=0.029, $p=0.003$) measures, as well as BMI (Standardized Beta=0.027, $p=0.003$). Conclusions: RT-variability during the N-Back task is correlated with adverse outcomes on measures of academic performance, general behavior, and health. This increased RT-variability might be thus an early signal reflecting inefficient processes underlying the dynamic control of sustained or selective attention, or interference inhibition processes, response selection and/or execution.

Day 2 Saturday, August 31

Oral Session 2 - Prenatal influences on brain development and subsequent behaviour

Chair: **Alice Graham** Oregon Health & Science University, USA

Claudia Buss Charité – Universitätsmedizin Berlin, Germany

Fetal programming of brain development – Role of maternal-placental-fetal stress biology

The origins of alterations in brain anatomy and connectivity, that may underlie cognitive impairment and mental illness, can often be traced back to the fetal period of life when the developing embryo/fetus responds to suboptimal conditions during critical periods of brain development (“Fetal Programming”). Maternal stress during pregnancy may affect fetal developmental trajectories by altering stress-sensitive endocrine and immune biological mediators, such as cortisol and interleukin-6 (IL-6). Evidence in humans will be presented in support of elevated maternal cortisol and IL-6 concentrations during pregnancy being associated with offspring brain anatomy and connectivity with implications for cognitive function and mental health.

Elinor Sullivan Oregon Health and Science University, USA

Maternal metabolic and dietary environmental influences on offspring behavior

Perinatal environmental factors such as poor maternal diet influence the risk of pediatric neurodevelopmental disorders. In a nonhuman primate model, exposure to maternal obesity and a Western-style diet (high in saturated fat and sugar) altered brain development resulting in long-lasting changes in behavior including increased anxiety and impaired social behavior. These findings indicate that poor maternal nutrition initiates a fetal environment that may result in neural reprogramming and predisposes offspring to pediatric neurodevelopmental and metabolic disorders.

Cynthia Rogers Washington University, USA

Aberrant structural and functional connectivity underlies neurodevelopmental impairment and psychopathology in preterm children

Despite advances in neonatal care, preterm birth remains a leading risk factor for neurodevelopmental disabilities and is linked with high rates of co-occurring attention deficit hyperactivity, anxiety and autism spectrum disorders. Affected children also demonstrate elevated rates of aberrant cerebral structural and functional connectivity, with persistent changes across MRI modalities evident as early as

the neonatal period. This talk highlights alterations in connectivity within key functional networks and white matter tracts underlying the neurodevelopmental impairments and psychiatric diagnoses common in this population, including detailing the effects of early life adversity and related clinical and psychosocial risk factors modifying these relationships.

Chris Smyser Washington University, USA

Aberrant structural and functional connectivity underlies neurodevelopmental impairment and psychopathology in preterm children

Despite advances in neonatal care, preterm birth remains a leading risk factor for neurodevelopmental disabilities and is linked with high rates of co-occurring attention deficit hyperactivity, anxiety and autism spectrum disorders. Affected children also demonstrate elevated rates of aberrant cerebral structural and functional connectivity, with persistent changes across MRI modalities evident as early as the neonatal period. This talk highlights alterations in connectivity within key functional networks and white matter tracts underlying the neurodevelopmental impairments and psychiatric diagnoses common in this population, including detailing the effects of early life adversity and related clinical and psychosocial risk factors modifying these relationships.

Oral Session 3: Big data and open science: Relevance for developmental cognitive neuroscience

Chair: **Damien Fair** Oregon Health & Science University, USA

Mike Milham Child Mind Institute, USA

Large-scale, open neuroimaging datasets are increasing more than just sample size

An increasing number of multimodal imaging datasets are becoming available, each creating novel opportunities for discovery – both individually and collectively. Using selected examples, this presentation will provide a survey of opportunities that exist for generating and addressing novel questions capable of advancing developmental neuroscience. Additionally, the impact of the open datasets on how we are conducting research, not just what is being asked, will be discussed. Relevant examples from the existing literature will be highlighted. Potential pitfalls to avoid will be discussed as well.

Jenn Pfeiffer University of Oregon, USA

Improving practices and inferences in developmental cognitive neuroscience: Open science tools for research design, analysis, and publication

The open science movement has produced introspection and concern regarding research practices and publication biases. To move forward, we must make changes to our analytical strategies and publication standards that are simultaneously transformative and accessible. This talk focuses specifically on implementing such changes in developmental cognitive neuroscience (DCN), from my dual perspective as a lab director and journal editor. I describe some common and useful open science tools for DCN, as well as distinguish between confirmatory and exploratory approaches. Doing so reveals tools particularly suited to each approach, such as pre-registration, registered reports, and specification curve analysis.

Kathrine Skak Madsen Danish Research Centre for Magnetic Resonance, Denmark

Opportunities and challenges of sharing and pooling data from existing longitudinal neuroimaging cohorts

Longitudinal (developmental) neuroimaging studies have acquired rich data on e.g. cognition, mental health, lifestyle, genetics and biological measures. Given their expensive and time-consuming nature, the number of assessed participants, however, is often limited. Pooling data from different developmental cohorts may improve statistical power and representativeness, both critical for elucidating more complex relationships between e.g. brain and behavioral development and the impact of intrinsic and extrinsic factors. However, as data sharing and pooling rarely have been thought into existing studies by design, researchers need to overcome several challenges before effective and productive data sharing and pooling can be realized.

YIA Lecture

Chair: **Brad Schlaggar** Kennedy Krieger Institute, USA

Eva Telzer University of North Carolina at Chapel Hill, USA

Info to come

Flash Talks

Chair: **Jess Church** University of Texas at Austin, USA

Kathy Do University of North Carolina, Chapel Hill, USA

Peers exert a stronger prosocial than antisocial influence on adolescent attitudes: Evidence from brain and behavior

Parents and peers differentially influence decision making during adolescence, yet little is known about social conformity in contexts where parents and peers exert competing influences. The present fMRI study examined adolescent conformity to different types of behaviors in the face of conflicting influences from parents versus peers. Adolescents (n=39; 12-14 years) and their parents rated their attitudes toward everyday positively and negatively valenced behaviors that adolescents might engage. During a brain scan one week later, adolescents were shown their parent's and an unknown peer's ratings of these same behaviors, which were manipulated to conflict with adolescents' initial ratings, and indicated who they agreed with. Generalized linear mixed effects models indicated adolescents were equally likely to conform to their parent and peer when their parent's ratings conflicted with their peer's ratings, with no differences in the brain. When their parent's or peer's ratings conflicted with their initial ratings, adolescents tended to stick with their initial ratings 70% of the time. When they did conform, adolescents were more likely to conform to their peer on positive than negative behaviors, which was paralleled by decreased vmPFC activation to positive behaviors but increased vmPFC activation to negative behaviors. Furthermore, an interaction between the valence of the behavior and magnitude of peer influence suggests that adolescents were more likely to conform on negative behaviors when their peer endorsed prosocial ratings (i.e., peer rated negative behavior as "less good") than antisocial ratings (i.e., peer rated negative behavior as "more good"). These results suggest that adolescents are relatively autonomous in the face of conflicting social influence but selectively conform to positive peer influences, thereby challenging prevailing conceptions of adolescence as a period of increased and unmitigated susceptibility to negative social influences.

Bridget Callaghan Columbia University, USA

Hippocampal multivoxel encoding signatures predict long-term memory across middle childhood and adolescence in humans.

The episodic memory system changes dramatically across the first few years of life. However, subtle alterations in episodic memory continue throughout middle childhood/adolescence. The neural mechanisms underlying such nuanced memory development are elusive, and studies using traditional Region of Interest (ROI) based approaches provide conflicting evidence for the role of hippocampal functional maturation during those ages. In this study we employ an advanced statistical technique, multivoxel correlation structure (MVCS), to functional magnetic resonance imaging (fMRI) data, while children and adolescents were engaged in an item-context associative learning task, which was sandwiched between two resting state scans. This statistical approach enables us to examine coordinated activity within the hippocampus at rest, during learning, and immediately after learning in a purported consolidation period. We report that such multivoxel activity changes across middle childhood-adolescence, with representations at learning and rest becoming more granular (i.e., less coordinated) with age. We also report that age changes in hippocampal multivoxel activity are regionally specific, with the posterior areas of the hippocampus changing the most across development. Importantly, we find that the level of representational granularity in the hippocampus during learning, and in the post-learning consolidation period, is associated with better immediate recognition memory, and delay associative memory (1 week after the scan), respectively. These data support the use of multivariate analysis approaches for uncovering subtle changes in hippocampal maturation across middle childhood and adolescence.

Lourdes Delgado Reyes University of East Anglia, UK

The role of toddler myelination in preschool executive function development

Infancy and early childhood are times of rapid change in the organization of cognition and behaviour, as well as brain development. An important process during this period is the maturation of myelinated white matter (WM), which facilitates rapid communication across the neural systems thought to underlie the emergence of complex cognitive abilities. Previous studies have linked WM development with cognitive development, but few studies have examined these relationships in early development. Here, we aim to explore the relationship between myelination and executive function (EF) in early development. Executive function refers to an interrelated set of neurocognitive systems that underlie behavioral control and cognitive flexibility. EF has pervasive influences on cognition and later development. A key challenge is to understand how EF develops early in development where early interventions might have the most impact. Diffusion tensor imaging studies have identified several WM tracts that are important for performance on EF tasks: cingulum bundle (CB), the superior longitudinal fasciculus (SLF), the anterior thalamic radiations (ATR), and inferior longitudinal fasciculus (ILF). We measured WM myelination using a multicomponent relaxation approach (mcDESPOt) to calculate the myelin water fraction in 30-mo toddlers. Participants also completed the Minnesota Executive Function Scale (MEFS) at 30- and 42-mo. We will examine the relationship between myelination in the previously identified WM structures, as well as, whole brain WM when participants are 30mo and executive function performance at 42-mo. We hypothesize that EF at 42-mo will be related to myelination in these WM structures, in particular in the ATR and SLF such that participants with more myelin will have better EF scores, even after controlling for age, SES and EF at 30-mo. These results will provide new insights into the neuroanatomical correlates of executive function in early development.

Giorgia Picci The Pennsylvania State University, USA

The moderating role of socioeconomic status on relations between level of responsibility and cortical thinning during adolescence

The development of autonomy and goal-directed behaviors are key milestones of adolescence. Expectations from parents to engage in responsible behaviors (e.g., household chores, outside work) may support this emergent process by recruiting brain regions that subserve executive functions (EFs) which, when in deficit, underlie poor outcomes such as substance use (SU). Adolescent responsibility, however, may exert either beneficial or detrimental effects, depending upon the context; e.g., parental pressure to be responsible may induce stress. Outcomes related to responsibility may be moderated by family resources (SES), indicative of whether parental demands for responsibility are due either to need or personal choice. The relationship between level of responsibility and neurocognitive development has yet to be examined. Further, such a study requires delineation of contexts likely to play a role in helpful vs. harmful effects of responsibility. We explored relationships between responsibility, SES (low vs. high), SU, and brain structure in drug-naïve adolescents (N=114; 11-14 years; 60 females), some of whom initiated SU at 18- or 36-month follow-up (N=37). Contrary to expectation, greater levels of responsibility predicted earlier SU onset (Cohen's $d=0.7$). The low SES group reported higher levels of responsibility than the high group ($d=.5$). In low SES (and not high SES), higher levels of responsibility corresponded with cortical thinning in regions implicated in EF (i.e. left precuneus and right middle frontal) ($d=.8$), which may indicate a developmental deficit. In high SES, responsibility positively correlated with performance in a problem-solving task (Stockings of Cambridge) ($d=.7$). These results suggest a moderating role of SES in the positive vs. negative effects of responsibility on adolescent neurobiology and behavior, with greater responsibility predicting impaired development of regions subserving EF in low SES and improved EF behavior for those in higher SES.

Adam Grabell University of Massachusetts, USA

Using fNIRS and Galvanic Skin Response as a novel approach to infer Limbic-Prefrontal processes in early childhood

Objective. Functional Near-Infrared Spectroscopy (fNIRS) is a popular approach to measure neural activation in early childhood populations that cannot tolerate fMRI, and provides good spatial resolution of prefrontal cortex (PFC) areas important for emotion regulation. However, fNIRS cannot reach sub-cortical limbic structures or measure limbic-prefrontal connectivity crucial to emotion regulation. Galvanic skin response (GSR) is a sensitive index of autonomic arousal heavily influenced by myriad limbic structures, suggesting GSR could be combined with fNIRS to infer limbic-prefrontal processes. We recorded simultaneous PFC activation via fNIRS and GSR in 3 to 5 year old children during a rewarding and frustrating task. We tested associations between PFC activation and GSR reactivity and recovery and whether associations were moderated by children's level of irritability. **Methods.** Thus far 40 3-5 year old children (M = 54 months; SD = 7.6; 55% male) completed a developmentally sensitive task (Incredible Cake Kids) comprising win and frustration blocks while fNIRS and GSR were recorded. **Results.** Regression models showed children with greater LPFC activation during reward had greater GSR reactivity ($b= 11.5$, $p < .05$) and weaker GSR recovery post-reward ($b= 9.1$, $p < .05$) than peers. Children with greater LPFC activation during frustration had lower GSR reactivity ($b= -160.7$, $p < .05$) and greater GSR recovery post-frustration ($b= -108.3$, $p < .05$). There was a significant irritability*GSR reactivity interaction ($b= 17.3$, $p < .05$) such that the inverse association was strongest for children with moderate irritability and absent those with high irritability. **Conclusions.** Combining fNIRS and GSR may be a promising novel approach for inferring limbic-PFC processes underpinning early emotion regulation and psychopathology. Results suggest an inverse association between PFC activation and GSR reactivity that is disrupted in children with high irritability.

Jin Wang Vanderbilt University, USA

Higher quality neural representations of phonemes scaffold longitudinal reading gains in 5- to 7-year-old children

The objective of this study was to investigate, using a brain measure of phonological awareness, whether phonological awareness is crucial for the development of reading skill (i.e. scaffolding hypothesis) and/or whether learning to read words refines phonological awareness (i.e. refinement hypothesis). We specifically looked at how different grain sizes of phonology and how two different phonological processes (i.e. phonological representation in the posterior superior temporal gyrus, STG, and phonological access in the dorsal inferior frontal gyrus, IFG) played a role in this bidirectional relation. 36 children completed a reading test outside the scanner and an auditory phonological awareness task inside the scanner which included both small (i.e. onset) and large (i.e. rhyme) grain size conditions. Children were tested when they were 5.5-6.5 years old (Time 1) and once again approximately 1.5 years later (Time 2). To study the scaffolding hypothesis, a regression analysis was carried out by entering brain activation for either small (onset>rhyme) or large (rhyme>onset) grain size in either STG or IFG at T1 as the predictor and reading skill at T2 as the dependent measure. Non-verbal IQ, phonological working memory and reading skill (all at T1) were entered as covariates of no interest. In order to study the refinement hypothesis, the regression analysis included reading skill at T1 as the predictor and brain activation for either small or large grain size in either STG or IFG at T2 as the dependent measure. Non-verbal IQ, phonological working memory and brain activation (all at T1) were entered as covariates of no interest. Our results provided the first neural evidence supporting the scaffolding hypothesis, by showing that the better the representational quality for small grain size phonology in the brain at T1, the larger growth of reading skill over time. This has important implications for early reading identification and interventions.

Arianna Gard University of Michigan, USA

Unique effects of age and pubertal development on amygdala-PFC connectivity during face processing

Processing facial expressions of threat (anger) and distress (fear) is linked to psychopathology and is thought to be mediated, in part, by connectivity between the amygdala and regions of the prefrontal cortex (PFC). Though resting-state approaches have found that amygdala-mPFC connectivity strengthens with age (Gabard-Durnam et al., 2014), and several task-based studies suggest that amygdala-mPFC connectivity shifts from positive to negative connectivity with increasing age (Gee et al., 2013), there have been no studies to parse the effects of age from correlated pubertal development. The current study examined the overlapping and distinct effects of age and puberty on amygdala-PFC connectivity during emotion processing. Participants were from the Michigan Twin and Neurogenetics Study (N=265; Age=8-18 years), a population-based sample of twins (Burt & Klump, 2013). We used a large prefrontal mask of Brodmann's Areas 9,10,11,24,25,32, and 47 to characterized amygdala connectivity patterns with multiple prefrontal regions during an implicit emotional faces matching task. We examined changes in connectivity during angry and fearful face versus shapes conditions using Generalized Psycho-Physiological Interactions (McLaren et al., 2012). Perceived pubertal development was measured with the Pubertal Development Scale (Peterson et al., 1998). Covariates included gender and child race. Although both advancing pubertal development and chronological age were associated with greater right amygdala - right orbitofrontal (BA 11) and right amygdala - right medial prefrontal (BA 9) connectivity during fearful face processing, only pubertal development exerted unique effects (i.e., after accounting for age). Pubertal development was also associated with condition-specific changes in amygdala connectivity during angry face processing, where chronological age was not. Measures of pubertal development should be integrated into developmental studies of corticolimbic maturation.

Ashley Parr University of Pittsburgh, USA

Striatal dopamine contributions to the development of frontostriatal connectivity in a reward learning context

Developmental changes within the mesolimbic dopamine system are thought to contribute to heightened motivation and risk taking in adolescents. Initial studies indicate developmental decreases through adolescence in connectivity between reward striatal and executive prefrontal systems, possibly reflecting animal models of pubertal changes in dopamine (DA). However, the role of DA in developmental changes in frontostriatal reward processing is not understood in vivo in humans. Using direct and indirect measures of DA processing within the context of reward learning, we tested the hypothesis that there is heightened nucleus accumbens (NAcc)/ventromedial prefrontal cortex (vmPFC) connectivity associated with increased DA in the adolescent period versus adults. A Siemens 3T mMR was used to obtain MR (12-30 yo) and PET (18-30 yo) measures in 115 participants. Background connectivity, a measure of context-dependent changes in functional connectivity, was assessed by regressing out task-related components during a reward learning task. R2' was used to measure tissue iron changes as a non-invasive indirect measure of striatal DA processing. PET [11C]dihydrotetrabenazine (DTBZ) in adults provided a measure of presynaptic vesicular DA storage. Linear mixed-effects models revealed that during a state of reward-guided decision-making, functional coupling between the NAcc and ventral anterior cingulate ($t=2.79$, $p=0.006$), subgenual cingulate ($t=2.29$, $p=0.02$), and posterior medial orbitofrontal ($t=2.24$, $p=0.03$) cortices decreased from adolescence to adulthood. These age-related decreases in NAcc-vmPFC connectivity were mediated by R2' indices of NAcc dopamine levels that were confirmed to be associated with PET DTBZ. These results provide new in vivo evidence of DAergic changes in adolescence underlying reward processing frontostriatal connectivity.

Kristina Rapuano Yale University,

Predicting vulnerability to risk behaviors in a large cohort of children

The prevalence of risky behaviors and substance abuse increases during adolescence. Using a data-driven approach, we sought to develop behavioral and neural models of vulnerability to risky behaviors in childhood. To identify a behavioral indicator of risk for use, responses to substance use-related questions were assessed in 11,875 nine- and ten-year-olds participating in the Adolescent Brain and Cognitive Development (ABCD) study (Casey et al., 2018; Lisdahl et al., 2018). A principal components analysis of responses revealed two orthogonal components that loaded highly on child knowledge of and intention to use substances (i.e., PC1) and familial factors related to substance use (i.e., PC2). Component loadings were validated across twenty-one sites to determine the reliability of dimensions associated with risk. Behavioral components were used to generate connectome-based predictive models (CPM; Shen et al., 2017) of risk based on resting-state neural connectivity. Individual differences in PC1 scores were significantly predicted in left-out subjects using CPM; however, neural models were not predictive of PC2 scores. These findings suggest that substance use-related risk factors can be quantified and predicted prior to initiation. Moreover, they may distinguish risk associated with child intent from familial risk that may emerge later in development. These findings set the groundwork for future prediction of early substance use initiation and chronicity.

Oral Session 4: Individual differences in brain development: Moving beyond the average developmental trajectory

Chair: **Angie Laird** Florida International University, USA

Andrik Becht Leiden University, The Netherlands

Moving beyond the mean level: A longitudinal study examining individual differences in social brain developmental trajectories

Aim: Adolescence is considered a key period for the development of advanced social cognitive and high quality social relationships. Parallel to these psychosocial changes, massive structural brain changes occur in a network of brain regions that are considered crucially involved in social cognition and social relationships. These brain regions consist of the medial prefrontal cortex (Brodmann area 10, mBA10), temporoparietal junction (TPJ), posterior superior temporal sulcus (pSTS), and precuneus (Mills et al, 2014). To date, existing research has largely focussed on average development across ages, which may have obscured meaningful individual differences in the speed of development in social brain regions (Foulkes & Blakemore, 2018). Therefore, the aim of this study was to empirically examine individual differences in social brain development. Moreover, we examined whether and how individual differences in social brain development predicted individual differences in the quality of peer relationships. **Method:** To this end, 270 adolescents (Mage 14.14 years at T1) were followed across three biannual waves (T1-T3). Peer relationship quality was assessed at T3. **Results:** Consistent with previous studies, latent growth curve models revealed decreases in grey matter area and thickness in social brain regions across adolescence. However, our findings revealed significant individual differences in both the level (i.e., intercepts) and change (slopes) in social brain regions across adolescence. These individual differences in the speed of development were meaningfully related to individual differences in peer relationship quality; Those adolescents who showed a slower decrease in thickness in precuneus, TPJ, and pSTS, relative to other adolescents, reported less positive peer relationships over time. **Conclusion:** Our findings emphasize the importance to move beyond the study of average trajectories for structural social brain regions in adolescence. In doing so, our findings highlight possible developmental neurobiological markers of adolescents' social functioning in the peer context.

Rogier Kievit University of Cambridge, UK

Modelling the dynamics of brain structure and cognitive development

In this talk, I will discuss findings from the Danish HUBU cohort, which scanned N=93 typically developing children (age 7.5-19) up to 11 times with Diffusion weighted imaging alongside a broad battery of cognitive tests. In this talk, I will focus on the interplay of white matter microstructure (5 waves) and processing speed (3 waves). I will illustrate how cognitive ability and white matter microstructure develop in concert across developmental time, and how to use tailored SEM's to better understand lead-lag relationships between brain and behaviour.

Kate Mills University of Oregon, USA

The strategic adolescent brain: functional brain organization during adolescence relates to behavioral strategies

The malleability of the developing brain helps us learn to navigate our social environment. This presentation will examine how brain networks involved in mentalizing, cognitive control, and reward valuation develop in adolescence and how interactions between these networks relate to behavioral strategies. The first study investigates how the preference for delayed rewards, which is typically considered a marker of developmental maturity, can be better understood when considering an individual's functional brain organization in relation to chronological age. The second study examines how individual differences in functional connectivity between mentalizing and reward valuation networks facilitates the development of intimacy between friends.

Day 3 Sunday, September 1

Oral Session 5: New progress in understanding memory development from infancy to childhood

Chair: **Sarah Durston** University Medical Center Utrecht, The Netherlands

Nicholas Turk-Browne Yale University, USA

Functional brain imaging of learning and memory in human infants

Tremendous progress has been made in understanding the brain systems that support human learning and memory. However, this progress is based predominantly on adult data and mostly neglects the astonishing learning that occurs early in life. A major stumbling block is that key brain systems like the hippocampus are accessible only with fMRI, a difficult technique in infants, especially when they need to be awake during tasks. We have devised approaches that make it possible to obtain considerable high-quality data of this type. This is allowing us to characterize the nature and early development of statistical learning and episodic memory.

Simona Ghetti University of California, Davis, USA

The what, where, and when of memory in toddlers: Behavioral and neural evidence

Relational processes are responsible for forming memory representations that include various elements of an experience such as spatial and temporal details. These processes provide the foundation for episodic memory. Episodic memory emerges during late infancy and improves during early childhood. However, many open questions remain including whether different features of young children's memories (e.g., spatial versus temporal details) improve at similar rates, and whether memory performance in toddlers is related to hippocampal structure and function. In my presentation, I will discuss the results of recent studies that have attempted to address these questions.

Sang Ah Lee Korea Advanced Institute of Science and Technology, Korea

The binding of space and time in episodic memory

In the present study, we explored whether the ability to bind spatiotemporal information plays an important role in the development of episodic memory. We tested children's binding of what and where and when components of memory in an active object-placement task. Results suggest that children first develop the ability to reliably bind together space and time around 4 years and then bind objects onto this representation at ~6 years. These results are not due to improvements in object or spatial processing alone and suggest that spatiotemporal binding occurs early in development and provides a scaffold for episodic memories.

Zoë Ngo Temple University, USA

Development of holistic episodic recollection

Episodic memory binds together the diverse elements of an event into a coherent representation, allowing for the reconstruction of multidimensional experiences when triggered by a cue related to a past event—a process of pattern completion. Such holistic recollection is evident in young adults, as shown by contingency the retrieval success different within-event associations. However, the ontogeny of pattern completion is uncharted. Here, we found that, akin to adults, 4 and 6-year-olds retrieve complex events in a holistic manner. Nevertheless, the degree of holistic retrieval increased from age 4 to adulthood, suggesting a protracted refinement in pattern completion in development.

Oral Session 6: Early social markers of social competency: Translational studies in primates

Chair: **Jocelyne Bachevalier** Emory University, USA

Amanda Dettmer Yale University, USA

Early mother-infant interactions and social development in rhesus monkeys

Owing to their social, behavioral, anatomical, physiological, and genetic similarities to humans, nonhuman primates are especially strong translational models to determine how early life experiences shape later social development. This presentation will focus on individual variability in mother-infant interactions in the neonatal period in rhesus monkeys. I will describe some of the factors that contribute to this variability, as well as the developmental sequelae of infant monkeys experiencing different levels of early caregiver interactions. A particular focus will be an early face-to-face intervention tested in nursery-reared infant monkeys, and the social development of these infants compared to typically nursery rearing.

Pier Francesco Ferrari Univeristà di Parma, Italy

Early social experience, genetic influences and epigenetic regulation in the developing social brain

Infants' capacity to engage in social interactions is fundamental to their psychological development, and in primates it includes the spontaneous tendency to attend to a limited set of socially-salient stimuli and to respond selectively to them. During mother-infant face-to-face interactions infants are also capable to modulate both intensity and timing of facial expressions in response to mother's facial gesture. These early forms of matching/synchronous behaviors are important in tuning mother-infant emotional exchanges and in predicting later infant social development and brain maturation. Perturbations or absence of such early social exchanges have important short and long term consequences on social development and emotional regulation with significant implications on the emergence of psychological disturbances.

Neurochemical regulation of these infants' behaviors through oxytonergic administration suggest that oxytocin have a major role in modulating early social interactions. Moreover, the differential expression of its receptor at the brain level, due to early social adversities, is responsible for diminished social responses and increased stress reactivity.

From a neurophysiological standpoint, there is evidence that specific brain networks specifically process social information related to others' emotions and behaviors, and are therefore potential markers of brain development under normal and perturbed social conditions. One of these brain networks, the mirror neuron network comprises the parietal-premotor circuit and the connected regions involved in affective/emotional regulation, such as the amygdala-prefrontal circuit, the anterior cingular cortex, the hippocampus and the anterior insula. We are collecting evidence that these areas are sensitive to the effects of early social adversity. Preliminary data, in fact, suggest that the effects of early social deprivation has not only an impact on such functional brain networks in the early postnatal period but also at a later stage of development, in the pre-pubertal/peri-adolescence period, when the main psychiatric disturbances emerge.

Mar Sanchez Emory University, USA

Development of macaque face visual processing using combined eye-tracking and MRI: in search of nonhuman primate models of social deficits of relevance to Autism

Reading faces in social interactions is crucial to understanding intentions and emotions in others, and is impaired in individuals with neurodevelopmental disorders such as Autism Spectrum Disorder (ASD). Characterizing the emergence and development of these skills and underlying brain circuits may help understand impaired socioemotional development in children with ASD. A theory in the etiology of ASD is that early neonatal visual attention is “reflex-like”, becoming voluntary –reward-based- at later ages, so that disruptions in this transition result in ASD pathology. Using longitudinal eye-tracking and structural and MRI methods, our group has shown that infant rhesus monkeys also exhibit inflections in developmental trajectories of fixation in the eye region of faces that parallel those reported in humans. This critical period for social skills refinement takes place around 4-8 weeks of age, in parallel to switches in brain networks that seem to underlie the inflections in developing social skills. Our results show similarities to developmental trajectories of social visual engagement in human infants (Jones & Klin, 2013), and further validate rhesus monkeys as a translational model of early socioemotional development to examine the underlying neurodevelopmental mechanisms.

Oral Session 7: Computational/predictive coding and development

Chair: **Gregoire Borst** Université Paris-Sorbonne, France

Richard Aslin Yale University, USA

The promise and challenges of using fNIRS to study predictive mechanisms in human infants

Predictive Coding entails a comparison of bottom-up data-driven signals with top-down hypothesis-driven signals. Despite the sluggish time-course of hemodynamic measures, there is substantial evidence of top-down signals in adults using fMRI and in infants using fNIRS. While this neural architecture is efficient, it is not necessary as a mechanism for making predictions, which can be accomplished based solely on sophisticated (i.e., contextually based) bottom-up signals. Indeed, infants at risk of cognitive delay/deficit due to extreme prematurity exhibit little evidence of top-down signals, yet display normative behavioral evidence of prediction. The promise of using MVPA techniques to separate bottom-up from top-down signals as an estimate of prediction error will be reviewed, along with the challenges of obtaining such data from human infants using fNIRS.

Elizabeth Bonawitz Rutgers University - Newark, USA

Predictive "EN"-coding: How prior beliefs influence preschooler's memory

Models of children's inductive inference provide a framework for how children's prior beliefs and new evidence are integrated to support learning. In this talk, we follow on previous research demonstrating cases when prior beliefs help and hinder recall. In one set of studies, we show that children, like adults, rely on category information in their recall of color. In another set of studies, we find that given strong model expectations, event violations have both benefits and costs to future event encoding. Taken together, these studies present a glimpse of how prior beliefs can influence children's encoding of information.

Randy O'Reilly Colorado University, USA

Deep predictive learning in the neocortex and pulvinar

Early developmental learning in babies appears largely passive, and yet forms the deep foundation of all that follows. We propose that, hidden under that passive exterior, a very active form error-driven predictive learning is taking place, based on the temporal difference over the Pulvinar between predictions generated by deep neocortical layers and a ground truth signal from strong, one-to-one projections via layer 5B bursting cells, at the alpha frequency (every 100 msec). This model is consistent

with a wide range of biological data, and it can self-organize invariant, categorial object representations in its simulated inferotemporal cortex.

Oral Session 8: The effects of pubertal and sex hormones on brain maturation: Current research across different phases of development, and across species

Chair: **Jiska Peper** Leiden University, The Netherlands

Megan Herting University of Southern California, USA

Androgens and structurally distinct amygdala subregion development in children and adolescents

The amygdala is comprised of a heterogeneous set of nuclei that are vital to emotional processing, motivation, and social behaviors that continue to develop across childhood and adolescence. This talk will discuss a novel method to segment and measure the developmental patterns seen in amygdala subregions across adolescence. Specifically, findings will be presented as to how amygdala subregion development varies by sex, physical and hormonal characteristics of sexual maturation, and androgen receptor genotype in typical developing adolescents. Lastly, we also discuss how disruptions to early life androgens may impact amygdala development as seen in children with Congenital Adrenal Hyperplasia.

Sarah Whittle University of Melbourne, Australia

Pubertal hormones predict sex-specific trajectories of pituitary gland volume during the transition from childhood to adolescence

Pituitary gland volume (PGV) increases during childhood and adolescence, yet no work has investigated the contribution of hypothalamic-pituitary-adrenal axis hormones that play a role in the earliest pubertal phase of adrenarche. To address this question, longitudinal data from 249 children (409 datasets, age range 8 to 13 years) were used to explore associations between PGV and dehydroepiandrosterone (DHEA), its sulfate (DHEA-S) and testosterone. We found that all three hormones explained variance in PGV development over and above age. In all cases, associations were stronger in females. Our findings suggest a key role for the hormones of adrenarche in PGV development.

Tuong-Vi Nguyen McGill University, Canada

Prenatal masculinization of the auditory system in infants: the MIREC-ID study

Sex differences in inner-ear function are detectable in infants, notably through the measurement of otoacoustic emissions (OAEs). Prevailing theories posit that prenatal exposure to high levels of androgens in boys may weaken OAEs, and that this phenomenon may predominantly affect the right ear/left hemisphere (Geschwind-Galaburda (GG) hypothesis). Yet, actual tests of these models have been difficult to implement in humans. Here we examined the relationship between markers of fetal androgen exposure collected at birth (anogenital distances (AGD); penile length/width, areolar/scrotal/vulvar pigmentation) and at 6 months of age (2nd to 4th digit ratio (2D:4D)) with two types of OAEs, click-evoked OAEs (CEOAEs) and distortion-product OAEs (DPOAEs) (n=49; 25 boys; 24 girls). We found that, in boys, scrotal pigmentation was inversely associated with the amplitude and reproducibility of CEOAEs in the right ear at 4 kHz, with trends also present in the same ear for mean CEOAE amplitude and CEOAE amplitude at 2 kHz. Penile length was inversely associated with the mean amplitude of DPOAEs in both the right and left ears, as well as with DPOAE amplitude in the right ear at 2 kHz and the reproducibility of CEOAEs in the left ear at 2.8 kHz. Finally, AGD-scrotum in boys was positively associated in boys with the amplitude of DPOAEs in the left ear at 2.8 kHz. Unexpectedly, there were no sex differences in the amplitude or reproducibility of OAEs, nor, in girls, any associations

between androgenic markers and auditory function. Nonetheless, these findings, reported for the first time in a sample of human infants, support both the prenatal-androgen-exposure and GG models as explanations for the masculinization of auditory function in male infants.

Janice Juraska University of Illinois, USA

Cortical reorganization during adolescence: what the rat can tell us about the cellular basis

The human cerebral cortex decreases in volume during adolescence while the underlying white matter increases. These changes also occur in the adolescent/peripubertal rat prefrontal cortex, where synapses, dendrites and neurons are pruned peripubertally. These decreases are larger in females and more definitively tied to puberty. In addition, perineuronal nets that alter the efficacy of inhibitory interneurons increase in both sexes but female puberty changes the time course. In contrast, the increase in white matter is due to myelination, not differences in the number or size of axons. Thus size changes are an amalgam of cellular alterations.