



2017 Oral Presentations

Day 1, Saturday September 16

Translational Neuroscience Symposium – Part 1

Chair: Bitá Moghaddam, Oregon Health & Science University

Discussant: Bonnie Nagel, Oregon Health & Science University

Bitá Moghaddam, Oregon Health & Science University

Adolescent dopamine disobeying adult rules: recent electrophysiological and behavioral findings

Our knowledge of the dopamine system and most influential theories related to the function of the dopamine neuron in the context of reward processing and cognition are primarily from data collected in adult models. The organization of dopamine circuitry, however, is a protracted process, which peaks in adolescence and ends only in early adulthood. Accordingly, reward processing and higher order cognition including behavioral inhibition undergoes changes in adolescence. Because of their extended developmental course, the shaping of midbrain dopamine neurons is particularly susceptible to life experiences, especially those occurring during adolescence. Yet, we know very little about the neurobiological events underlying the adolescent maturation of the dopamine system. I will focus on recent behavioral and electrophysiological studies in rodents that describe critical differences in reward processing between adolescence and adulthood and their influence on cognition. These studies show that reduced, and not exaggerated, activity of adolescent dopamine neurons during the encoding of reward anticipation may underlie the uniqueness of reward processing at this age.

Brian O'Roak, Oregon Health & Science University

The rapidly accelerating pace of autism genetics as a model for genetic studies in mental health

Moving from candidate gene discovery to definitive validation of risk genes has been tremendously difficult in complex brain disorders, such as autism. A large part of this difficulty is the result of genetic heterogeneity, which refers to many different genes playing a role. However, over the past few years new approaches and strategies have begun to unlock autism genetics. I will review these recent developments, which have led to tractable strategies for robustly implicating many individual genes that when mutated are likely to result in a child developing autism. I will discuss how these new high-confidence risk genes are informing our understanding of autism at the molecular level and beyond. Finally, I will discuss several new

frontiers in autism genetics and how these efforts may be applied generally to improve mental health.

Cris Niell, University of Oregon

Development and plasticity of local and long-range cortical circuits in the mouse

Brain function depends on coordinated activity in neural circuits that are established during development and modified by learning. We have implemented imaging methods in mouse cortex that allow measurement of neuronal activity from the level of individual neurons within a cortical area, up to large-scale dynamics across cortical areas. Using these methods, we have studied how learning a sensory discrimination task changes patterns of neural activity across these different length scales. We are now extending this approach in order to investigate the maturation of cortical connectivity during adolescence, by linking structural and functional imaging methods.

Translational Neuroscience Symposium – Part 2

Discussant: Fred Sabb, University of California, Los Angeles

Dan Marks, Gates Foundation

Healthy brain development programs in global health

There is increasing global recognition of the importance of supporting early child neurodevelopment from birth as a critical component of fostering healthy and thriving children and also to promote gains in future human capital. Approximately 250M under-5 children are not reaching their developmental potential in resource-limited settings that are exposed to stunting or extreme poverty. Our vision is to ensure all children reach their developmental potential in order to foster gains in child thriving and global human capital. We aim to do so by better characterizing the burden of children who are not reaching their full potential, characterize targetable risk factors contributing to this deficit and develop preventative public health interventions in our prioritized countries. Central to these objectives are assessment tools capable of identifying infants and children not on track to reach their potential that are sensitive enough to evaluate the impact of interventions.

Trygve Bakken, Allen Institute

Adult human cortical cell type diversity defined by single nucleus RNA-sequencing

The human cortex is composed of approximately 16 billion neurons that are densely interconnected and have diverse morphology, molecular signatures, and firing properties. Neurons can be grouped into types based on shared features, and these cell types simplify the description of cortical circuits. Recent technological advances, including high-throughput transcriptomic profiling of single cells, have led to a refined census of cell types in mouse cortex and a much coarser census in human cortex. In this study, we identify a comprehensive set of human cortical cell types by clustering single nucleus RNA-sequencing data from over 10,000 nuclei isolated from middle temporal gyrus of adult human cortex. Neuronal types have dramatically different expression patterns, including ion channels, G-protein-coupled receptors, and synaptic genes. Putative homologous cell types between mouse and human were identified based on shared marker gene expression, although there were substantial expression

differences between species. These reference cortical cell types can be compared to disease states and will guide development of genetic tools to target cell types in human tissue.

Science of Learning Symposium

Co-chair: Silvia Bunge, University of California at Berkeley

Co-chair: Bruce McCandliss, Stanford University

This symposium showcases the work of four researchers who study how experience-dependent brain plasticity supports learning. First, Grégoire Borst will discuss how brain anatomy – specifically, individual variability in sulcal morphology – influences an individual’s capacity to learn. Then, Jason Yeatman will tell us how experience can influence white matter microstructure on a fast timescale. Next, Olga Ozernov-Palchik will examine how changes in white matter over the first few years of schooling support learning, and how they are moderated by early life experience. All three of these talks use structural brain imaging methods to explore how children learn to read. Last but not least, Carolyn Johnson will provide mechanistic insights into the effects of early life stress on learning, using a rodent model to examine, at a cellular level, how prior experience influences the ability to learn from feedback.

Gregoire Borst, Paris Descartes University

S.1.1 Early cerebral constraints on academic learning in children, adolescents and adults

Fundamental school learning such as reading and intense training produce fundamental functional and structural changes in the brain. We will present studies investigating the converse issue namely whether fundamental school learning and the receptivity to executive training are constraint by the anatomy of the brain. In particular, we will first present converging evidence that the sulcal morphology (i.e., a qualitative feature of the brain determined in utero and not affected by brain maturation, learning and training) of the left lateral occipito-temporal sulcus (OTS) hosting the visual word form area (VWFA) predicts reading skills in children and adults. In addition, we will present data from three studies showing that inhibitory control efficiency is constrained by the sulcal morphology of two key regions of the inhibitory control network namely of the anterior cingulate cortex and of the inferior frontal sulcus in children and adolescents. Finally, we will present preliminary data suggesting that the sulcal morphology of these two regions (ACC and IFS) predicts in part the receptivity to inhibitory control training in children (9-year-old) and adolescents (16-year-old).

Jason Yeatman, University of Washington

S.1.2 White matter plasticity and reading: Network level changes track the learning process

White matter tissue properties correlate with children's performance across domains ranging from reading, to math, to executive function. These correlations are generally interpreted as reflecting stable anatomical differences that affect the way children learn particular skills. However, this interpretation rests on an untested assumption that anatomical properties are stable, at least over a relatively short time-scale. Here, we use an intervention design to examine experience-dependent growth in reading skills and white matter in a group of children with dyslexia. Diffusion MRI data were collected longitudinally at regular 2-week intervals during an intensive, 8-week reading intervention. These measurements reveal large-scale

changes throughout an extensive network of white matter tracts, over a rapid timescale. Changes within this network track individual improvements in reading skill. Additionally, we identify a network whose properties predict reading skill but remain fixed throughout the intervention, suggesting that some anatomical properties stably predict the ease with which a child learns to read, while others dynamically reflect the effect of immediate experience. In the latter case, correlations between white matter and behavior depend on recent educational experience. Thus, altering a child's educational environment through a targeted training program can alter both white matter and behavior on the timescale of weeks. Large-scale change within this network may be a hallmark of rapid, short-term plasticity associated with intensive training of reading skills.

Ola Ozernov-Palchik, Tufts University/MIT

5.1.3 The relationships among SES, white matter, and reading development: a longitudinal investigation from kindergarten to 2nd grade.

Reading is a learned skill crucial for educational attainment. Children from lower compared to higher socioeconomic status (SES) families tend to have poorer reading outcomes and this gap widens across years of schooling. Reading relies on the integration of multiple neural systems and the formation of specific white matter pathways. An emerging literature documents correlations between SES and structural/functional brain measures. Here we examine the relations among SES, white matter, and reading development in 119 children longitudinally from early kindergarten to 2nd grade. Three bilateral white matter tracts important for reading were selected: arcuate fasciculus (AF), superior longitudinal fasciculus (SLF), and inferior longitudinal fasciculus (ILF). There was a significant positive association between SES and (pre-) reading skills in kindergarten and 2nd grade. SES was positively associated with fractional anisotropy (FA) in the left ILF in kindergarten and explained a significant proportion of its variance above language and home literacy variables. In the higher SES group, better 2nd grade reading performance was associated with decreased FA in the right SLF in kindergarten, likely reflecting an initial left-lateralization of early reading skills. In contrast, in the lower-SES group reading was positively associated with right ILF FA. These results suggest that SES may influence the development of reading networks in pre-reading children but the underlying neurobiological mechanisms and environmental variables facilitating this effect need to be further examined.

Carolyn Johnson, Harvard University

5.1.4. Altered processing of reward and punishment following early life stress

The maturing brain is exquisitely sensitive to experience and environmental influences. We propose that early life stress (ELS) may alter the developmental trajectory of response to reward and punishment, resulting in abnormal learning. We utilize a mouse model to probe neural circuit changes following ELS. Dams are given limited access to nest material from postnatal days 2-9 in the ELS group. Control and ELS mice then participate in behavioral testing in the early adolescent period. A naturalistic foraging task assesses learning of cue-reward associations and flexible updating of associations during reversal. Separate groups are implanted with cranial windows and trained on a head-fixed task to facilitate two-photon imaging of neural responses to reward and punishment. Auditory cues predict the delivery of sucrose solution or aversive air puff. We find sex-specific effects of ELS, with females exhibiting slow learning and inflexible reversal learning in the foraging task. Reinforcement learning

modeling of choice patterns revealed a deficit in learning from reward experience in ELS females. Histology uncovered precocious condensation of peri-neuronal nets around PV inhibitory neurons in the prefrontal cortex (PFC), a region previously implicated in task performance. We therefore focused our in vivo imaging experiments on inhibitory neurons in the PFC. We find that separate inhibitory networks are tuned for reward and punishment and that tuning sharpens with age. We will discuss the potentially altered developmental trajectory of inhibitory networks in ELS mice.

Young Investigator Award

Damien Fair, Oregon Health & Science University

Huttenlocher Lecture

Linda Spear, Binghamton University

Adolescence: Experience-seeking, experience-sculpting and phenotypic stabilization

Though the brain dynamically responds to experiences throughout the lifespan, its intrinsic potential for plasticity is actively dampened gradually during ontogeny. As a result, neural systems developmentally sculpted by experience are stabilized and their efficiency is increased. Heightened plasticity followed by subsequent stabilization continues in forebrain regions through adolescence, resulting in the emergence of relatively durable phenotypes that may be molded to some extent by the physical, social, cognitive or emotional circumstances experienced by the adolescent. Thus, maturational changes occurring in the adolescent brain not only support adolescent-typical “experience-seeking” behaviors, but may themselves be customized commensurate with those experiences. As an example, basic science studies will be briefly highlighted showing adolescent-specific alcohol sensitivities that: a) may promote relatively high, binge levels of alcohol use among vulnerable adolescents; and b) often persist into adulthood after such exposure, producing an enduring “adolescentized” phenotype. Much remains to be learned about the nature of adolescent experiences that lead to lasting phenotypic change, their age-specificity, and the mechanisms underlying different types of experience-associated plasticity and stabilization.

Day 2, Sunday September 17

Oral Session 1: Development of Psychopathology

Chair: Nick Allen, University of Oregon

Discussant: Erika Forbes, University of Pittsburgh

Roger Clem, Mount Sinai School of Medicine

0.1.1 Early postnatal development of prefrontal-amygdala synaptic transmission

A brain network comprising the medial prefrontal cortex (mPFC) and amygdala plays important roles in developmentally regulated cognitive and emotional processes. However, very little is known about the maturation of mPFC-amygdala circuitry. We conducted anatomical tracing of mPFC projections and optogenetic interrogation of their synaptic connections with neurons in the basolateral amygdala (BLA) at neonatal to adult developmental stages in mice. Results indicate that mPFC-BLA projections exhibit delayed emergence relative to other mPFC pathways and establish synaptic transmission with BLA excitatory and inhibitory neurons in late infancy, events that coincide with a massive increase in overall synaptic drive. During subsequent adolescence, mPFC-BLA circuits are further modified by excitatory synaptic strengthening as well as a transient surge in feedforward inhibition. The latter was correlated with increased spontaneous inhibitory currents in excitatory neurons, suggesting that mPFC-BLA circuit maturation culminates in a period of exuberant GABAergic transmission. These findings establish a time course for the onset and refinement of mPFC-BLA transmission and point to potential sensitive periods in the development of this critical network.

Amy Roy, Fordham University

0.1.2 Temper Tantrums as Indicators of Emotion Dysregulation in Children

In recent years, there has been an increase in empirical attention paid to the phenomenology of irritability in children and adolescents. Most studies have focused on populations of children suffering from chronic irritability, such as those with disruptive mood dysregulation disorder (DMDD). However, in our work, we have found that the presence of severe temper outbursts (STO) in middle childhood, even in the absence of chronic mood concerns, is associated with significant functional impairment and is not adequately addressed with current interventions. Further, we have identified alterations in intrinsic functional brain networks that appear to be specifically associated with STO, even when controlling for other psychopathology such as ADHD. Thus, we propose that when STO persist beyond the preschool years, they represent a clinically-relevant, transdiagnostic indicator of underlying deficits in emotion reactivity and regulation. Our work on the phenomenology and neurobiology of STO will be discussed along with implications for future research and treatment development.

Koraly Perez-Edgar, Penn State University

0.1.3 Affect-biased Attention as a Core mechanism of Emotion Reactivity and Regulation

Affect-biased attention, particularly if stable and entrenched, may act as a developmental tether that helps sustain early socioemotional and behavioral profiles over time, placing some individuals on maladaptive developmental trajectories. Much of the evidence focuses on anxiety, although it is likely a domain-general mechanism. The current presentation will outline the neural circuitry that may underlie the links between temperament, behavioral markers of affect-biased attention, and emerging risk for anxiety.

Oral Session 2: Development of Attention

Chair: Sarah Durston, University of Utrecht

Sarah Durston, University of Utrecht

O.2.1 Brain development in Attention Deficit Hyperactivity Disorder

Studies of brain development in Attention Deficit Hyperactivity Disorder have shown relatively stable decreases in cortical thickness that relate to outcome: individuals with remitting symptoms also show some normalisation of cortical thickness, suggesting that individual differences in may be indicative of resilience (Shaw et al., 2006). However, different measures of the cortex may reflect differing aspects of early cortical development (Rakic, 2000). In this presentation, I will discuss a study of the development of cortical thickness, surface area and gyrification in ADHD.

Gaia Scerif, University of Oxford

O.2.1 Beyond the attentional homunculus: The developmental dynamics of attention, learning and memory

Attentional control plays a crucial role in biasing incoming information in favour of what is relevant to further processing, action selection and long-term goals. Developmental cognitive neuroscience illustrates how attentional processes are best understood not simply as a control homunculus, but rather as bidirectionally influencing and influenced by prior experience. Our recent data highlight change and stability in the interplay between attentional control, memory and learning. Children and young adults differ in the extent to which they deploy visuo-spatial attentional control to optimize maintenance in short-term memory. At the same time, attentional effects on memory are not unidirectional: previously learnt information and resistance to distraction during learning guide later attentional deployment, in adulthood and in childhood. In conclusion, assessing attentional development and its dynamics point to the bidirectional influences between attention, learning and memory.

Alison Gopnik, University of California at Berkley

O.2.2 When children are more open-minded learners than adults are: computation, evolution and phenomenology

Our recent studies show a surprising developmental pattern across several different kinds of problems and age ranges. Younger learners are better than older ones at learning unusual abstract causal principles from evidence. I explore the possibility that this is because younger minds and brains, with less frontal control, are intrinsically more flexible and exploratory, although less efficient as a result. From a computational perspective, this developmental shift may provide the benefits of "simulated annealing" in machine learning. An initial broad "high-temperature" search through a hypothesis space, followed by a narrower and more focused search, allows optimal learning in complex and variable environments. From an evolutionary perspective, our distinctively long human childhood and slow frontal maturation may reflect this computational strategy. Such early high-temperature searches may have a distinctive, unfocused and uncontrolled but vivid phenomenology, analogous to certain kinds of adult experiences in which similarly flexible and open-ended learning takes place.

Yuko Munakata, University of Colorado Boulder

O.2.3 Developing Inhibitory Control: The Role of Temporal Dynamics in Children's Attention

Children show remarkable limitations and developments in their ability to inhibit inappropriate thoughts, actions, and emotions. I will show how these changes in inhibitory control are likely driven by developments in how children engage attention. Children's inhibitory control can also be improved using novel approaches motivated by this attentional framework.

Janice Juraska, University of Illinois

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

The cerebral cortex decreases in volume during adolescence in humans while the underlying white matter increases. These changes also occur in the adolescent/peripubertal rat. In the rat prefrontal cortex, synapses, dendrites and neurons are pruned peripubertally. These decreases are larger in females and more definitively tied to puberty. The increase in the white matter is due to myelination, not differences in the number or size of axons. The basolateral amygdala will also be presented where the relationship between the size and cellular composition of a structure is not as clear as in the cortex.

Oral Session 3: Cellular & Molecular Mechanisms in Development

Chair: Nim Tottenham, Columbia University

Frances Champagne, Columbia University

0.3.2 Epigenetic Variation in Developmental Trajectories: Role of Prenatal and Postnatal Experiences

Development is shaped by environmental influences occurring at various life stages and there is increasing evidence for the role of epigenetic mechanisms in this process. The experience of parents can likewise shape the development of offspring leading to environmental impacts that persist across generations. In this talk, I will highlight research investigating the epigenetic impact of prenatal maternal exposure to stress/toxins, variation in the quality of postnatal mother-infant interactions shaped by maternal exposure to adversity and the impact on development of paternal exposure to stress. These studies individually explore the epigenetic influence of parental environmental exposures and collectively illustrate the dynamic and interactive routes through which the environment can lead to behavioral and neurobiological effects across generations.

Siobhan Pattwell, Fred Hutchinson Cancer Research Center

0.3.3 Leveraging Dynamic Changes in Neural Circuitry During Adolescence to Persistently Attenuate Fear Memories

Fear can be highly adaptive in promoting survival, yet it can also be detrimental when it persists long after a threat has passed. Malleability of the fear response may be most advantageous during adolescence when there is an increased prevalence to explore novel, potentially threatening environments. Using microprisms to image prefrontal-cortical spine maturation longitudinally and retrograde tracing of neurons across development, we delineate dynamic circuit reorganization associated with shifts in adolescent fear behaviors. Exploiting this sensitive-period of neural development, we modified existing behavioral interventions in an age-specific manner to attenuate adolescent fear memories persistently into adulthood by highlighting contextual contributions.

Bridget Nugent, University of Pennsylvania

0.3.4 Placental mechanisms underlying sex differences in neurodevelopmental vulnerability

Gestational stress is a risk factor for male-biased neurodevelopmental disorders, including schizophrenia and autism. Our mouse model of early prenatal stress (EPS) imparts HPA stress axis and metabolic deficits to male offspring, endophenotypes similar to male-biased disorders. The placenta provides necessary factors for early brain development, thus sex differences in placental function may influence sex biases in neurodevelopmental vulnerability. We identified placental OGT (a nutrient sensing enzyme) as a mediator of the effects of EPS on brain development. OGT modifies the H3K27me_{2/3} methyltransferase, EZH2, enhancing its activity. Using trophoblast-specific OGT reduction, we found that OGT determines higher levels of placental H3K27me₃ in females and genome-wide sex differences in placental H3K27me₃ patterns. We hypothesized that this female-biased epigenetic repression is protective against prenatal insults. To test this hypothesis, we reduced H3K27me₃ using trophoblast-specific manipulations of EZH2 in conjunction with EPS. Decreasing placental EZH2/H3K27me₃ created female vulnerability to EPS, sensitizing HPA axis reactivity and causing long-term increases in body weight. To evaluate the role of X and Y-linked H3K27 demethylases in establishing sex differences in H3K27me₃, we generated trophoblast-specific mouse lines with reducible UTX and inducible UTY. We predict that reducing placental UTX (hence enhancing H3K27me₃) will protect males from the developmental deficits produced by EPS. In addition, we predict that reducing UTX while inducing UTY expression in female trophoblasts will masculinize genome-wide placental H3K27me₃ patterns and neurodevelopmental responses to environmental perturbations. These studies bring us closer elucidating the etiology of sex-biased neurodevelopmental disorders by investigating the complex interactions of genetic/epigenetic programs with prenatal environment.

Oral Session 4: ABCD Symposium

The Adolescent Brain and Cognitive Development (ABCD) Study: Early Mental Health, Substance Use, and Neurocognitive Outcomes

The NIH-funded Adolescent Brain and Cognitive Development (ABCD) Consortium aims to be the largest longitudinal multi-site study of brain and behavioral development to date. The goal is to enroll over 11,000 9-to-10 year-old singleton and twin participants who represent the United States population and follow them through adolescence and into young adulthood. Participants and their families complete comprehensive behavioral assessments of mental health, substance use, cognitive function, social function, and personality as well as a two-hour brain imaging protocol that includes structural, diffusion tensor, resting-state, and task-based scans. This symposium will feature initial findings from the first year of assessment, including a description of the study sample, mental health and substance use outcomes, early findings from the neurocognitive assessment and imaging findings. A particular focus will be on individual variations in these outcomes due to high risk status and substance use. The presenters will engage in discussion with the audience regarding the utility of this epidemiological approach, challenges in multi-site integration, and implications for the prospective study of substance use liability.

Chair: Monica Luciana, University of Minnesota

Hugh Garavan, University of Vermont

0.4.1 How to describe neurodevelopment at the population level: Recruitment and sampling characteristics of the ABCD study.

The ABCD study, being a landmark study of adolescent neurodevelopment, has prioritized an epidemiologically rigorous approach to recruitment. This is motivated by an appreciation that larger, more diverse samples are required to capture the sociodemographic variability that is needed to generalize to the larger US population. The ABCD study is recruiting 11,000+ children aged 9/10 from 20 sites across the USA. I will describe the school-based, stratified random sampling approach ABCD employs to recruit children matched to national demographics for sex, race and ethnicity, socioeconomic status and urbanicity.

Susan Tapert, University of California San Diego

0.4.2 Assessing mental health and substance use in 9 and 10-year-olds: The ABCD Assessment Protocol and early outcomes

Adolescence is a time of dramatic physical, emotional, and intellectual growth, and also a critical neurodevelopmental period associated with dramatic increases in rates of substance use and psychiatric disorders. Alcohol and marijuana use are common in adolescence; rates of binge drinking remain high, and the potency of many marijuana products now used is higher than in past decades. Identifying pathways to substance use, mental illness, and their effects on development is critically important. The Adolescent Brain Cognitive Development (ABCD) study is enrolling over 11,000 children and following them from age 9 - 10 years of age through adolescence and into early adulthood. Participants undergo a comprehensive baseline assessment, including developmentally appropriate assessment of substance use and mental health that show stable sensitivity and construct validity across childhood and adolescence, minimize participant burden, and capture emergence of substance use and subtle changes in mental health. These data will elucidate: 1) effects of substance use on the adolescent brain; 2) effects of substance use on behavioral and health outcomes; 3) bidirectional relationships between psychopathology and substance use; 4) effects of genetic, behavioral, neurobiological, and environmental differences on risk profiles and substance use outcomes; and 5) "gateway interactions" between substances.

Monica Luciana, University of Minnesota

0.4.3 Neurocognition in early adolescence and risk for later substance use: findings from ABCD's first year of study

Adolescence is characterized by strivings toward independence, numerous social, physical changes, and increased risk-taking. Dual systems models attribute adolescent risk-taking to tensions between developing capacities for cognitive control and heightened reward sensitivity. A comprehensive understanding of adolescents' neurocognitive development is necessary so that consequences of behaviors such as substance use can be clarified in relation to these dynamics. The prospective assessment of cognitive development is fundamental to the aims of the newly launched Adolescent Brain and Cognitive Development (ABCD) Consortium. This presentation will provide an overview of ABCD's neurocognitive battery, which include the NIH Toolbox Cognition Battery, a one-item Cash Choice task, a novel variant of the Rey Auditory Verbal Learning Test (RAVLT), the Matrix Reasoning task, and a measure of visuospatial ability, the Little Man Task. Initial findings from ABCD's first year of data collection, including assessments of nearly 5000 children, will be presented. To date, we observe that children from high risk backgrounds demonstrate lower levels of working memory as well as diminished

performance on learning and memory trials of the RAVLT. These outcomes will be considered in relation to individual differences in specific mental health and substance use risk factors. Implications for neural development will be discussed.

Deanna Barch, Washington University

0.4.4 Mapping neural development supporting cognitive and emotion process in the ABCD

This presentation will outline the constructs and approaches being collected for the functional neuroimaging component of the ABCD project, which includes both resting state and task related functional activity, along with the details of the paradigms being used to assess the cognitive and affective constructs of working memory, inhibitory control, reward anticipation and receipt, emotional face processing, and episodic memory. We will present initial results on both validation of these approaches in this sample and relationship to key variables of interest to neurodevelopment in the 9 and 10-year-old children being assessed as part of this large-scale project.

Day 3, Monday September 18

Oral Session 5: Methods for Developmental Imaging

Chair: Monica Rosenberg, Yale University

Michael Hallquist, University of Pennsylvania

0.5.1 Developmental changes in the effect of emotional cues on value-based decision-making and information maintenance in borderline personality disorder

Borderline personality disorder (BPD) often emerges in adolescence and is characterized by emotion dysregulation and interpersonal hypersensitivity. Although decision-making in emotional contexts is impaired in BPD, little is known about its neurodevelopmental basis. In this study, 92 participants (47 with BPD symptoms, 45 matched controls) between the ages of 13 and 30 ($M = 20.61$) completed 8 runs of a reinforcement-based timing task during an fMRI scan. Runs consisted of fifty trials in which a dot revolved 360° in 4 seconds around a central stimulus (fearful, happy, or scrambled face). Participants pressed a button to obtain a probabilistic reward from a time-varying contingency. Behavioral data were fit using a novel computational model of expected value, complexity of the value distribution (entropy), prediction error (PE), and decay of unchosen actions. HRF-convolved decision signals were entered in model-based fMRI analyses using FLAME1+2 software (FSL 5.0.9). Behaviorally, whereas controls selected high-value actions after a negative PE in the fearful face condition, those with BPD symptoms did not ($p < .001$), suggesting disrupted learning from PEs by negative emotion in BPD. In model-based fMRI analyses, the BPD group had weaker representation of value entropy in the frontal eye fields and intraparietal sulcus. Moreover, modulation of social cognitive regions (e.g., dmPFC, MTG, TPJ, and temporal pole) to fearful PEs diminished in with age in BPD, but was relatively stable in controls. Implications of these findings for the development of BPD will be discussed.

Tamara Vanderwal, Yale University

0.5.2 Movies in the Magnet: The use of naturalistic stimuli in developmental neuroimaging

The use of naturalistic viewing conditions, including movies, in fMRI continues to expand rapidly. This talk will provide an overview of the advantages of using movies as fMRI stimuli and cover current efforts underway in developmental neuroimaging. One focus will be on the paradigm Inscapes, a 7-minute publicly available movie we created to serve as an alternative to resting state for young children (Vanderwal et al., 2015, NeuroImage). The talk will also highlight publicly available data sets that use movies as acquisition states across the lifespan (e.g., O'Connor D., et al. 2017, GigaScience,, Alexander L.M., et al., bioRxiv 2017) and the use of movies to study individual differences in functional connectivity (Vanderwal et al., 2017 NeuroImage).

Oral Session 6: Adolescent Motivation

Chair: Leah Somerville, Harvard University

Niko Steinbeis, Leiden University

0.6.1 The role of control and motivation in the development of prosocial behavior

A central question in the study of prosocial behavior is whether this occurs automatically and as a function of people's inherent kindness or instead results from effortful control and regulation. I argue that prosocial behavior carries a cost and this cost needs to be regulated for prosocial behavior to occur. In a series of developmental studies I show that impacting behavioral control influences how children share valuable resources. I also draw on recent lines of research on motivational aspects of behavioral control and how this can affect prosocial behavior. These insights can be leveraged to devise behavioral control interventions that increase sharing during childhood.

Mirella Dapretto, University of California Los Angeles

0.6.2 Variation in the oxytocin receptor gene modulates reward circuit connectivity in youth with and without autism

Oxytocin is a key mediator of social behavior across species and common variants in the oxytocin receptor gene (OXTR) have been linked to alterations in brain structure and function in neurotypical adults, as well as increased risk for autism spectrum disorders (ASD). In this talk, I will present data from a recent study where we examined how cumulative genetic variation across several OXTR single-nucleotide polymorphisms affect functional connectivity of the reward network in youth with and without ASD. By showing differential genetic effects on neuro-endophenotypes in these populations, our findings highlight how integrating genetic risk across multiple loci with neuroimaging data can further elucidate neural mechanisms of vulnerability vs. resilience in carriers of disease-associated risk alleles.

Flash Talks – Part 1

Co-chair: Nim Tottenham, Columbia University

Co-chair: Bea Luna, University of Pittsburgh

Rosa Li, Duke University

F.1.1. Striatal reward anticipation decreases from adolescence to young adulthood - but only when watched by a peer

Many everyday decisions occur in the presence of peers and feature outcomes that are shared with those peers. Both peer presence and reward for others have been found to independently activate reward- and social-processing neural regions, but it is still unknown how peer presence and reward for peers interact to influence neural activity. We collected fMRI data from 40 late adolescents and young adults (18-28 y.o.) while they completed a monetary incentive delay task to earn reward for self and for a friend. Half of the participants completed the task alone, and half completed the task while watched by the friend. Across all participants, reward for self and friend were similarly processed in striatal and insular reward-related regions, while peer presence increased activity in medial PFC. Additionally, peer presence significantly interacted with age to predict activity in bilateral striatum: There was a significant age-related decrease in striatal reward anticipation for self and for friend in participants who were watched by their friend, but no significant correlation between age and striatal reward anticipation in those who completed the task alone. We show that reward for self and for friend are similarly neurally processed, and that the effect of peer presence on reward-related neural responses does not end at legal adulthood, but instead linearly diminishes from late adolescence to young adulthood. Thus, interventions to reduce maladaptive reward-seeking behaviors in peer groups should not end at age 18 and should instead extend into the early 20s.

Ashley Nielsen, Washington University in St. Louis

F.1.2. Patterns of functional connectivity predict maturity and diagnostic status of individuals with Tourette syndrome.

While a common developmental course for tic symptoms has been described for Tourette Syndrome (TS), many patients do not follow this typical trajectory. Previously, we demonstrated that multivariate support vector machine (SVM) learning can classify children with TS based on correlations in spontaneous fMRI activity between regions across the brain (resting-state functional connectivity: RSFC). Here, we extended this work to test if patterns of RSFC can indicate maturity and diagnostic status of individuals with and without TS across development. Resting state fMRI data was collected from a group of tic-free children (C-TF; N = 39), tic-free adults (A-TF; N = 39), children with TS (C-TS; N = 39), and adults with TS (A-TS; N = 39). RSFC data among 264 regions underwent strict preprocessing to minimize motion-related artifact. While SVM is most commonly used to predict binary class labels, it can be extended to predict multiple classes (mc-SVM). We used mc-SVM to create a multivariate model separating C-TF, C-TS, A-TF, and A-TS individuals with RSFC and tested this model with leave-one-out cross validation. The mc-SVM model was able to classify individuals according to maturity and diagnostic status with 64% accuracy (chance=25%). Individuals were more likely to be misclassified according to diagnostic group than age group. The way in which an individual is misclassified with mc-SVM provides a richer characterization of the individual than binary SVM, which may be useful for predicting the clinical outcomes and developmental course of symptoms for TS individuals.

LM Wierenga, University Leiden

F.1.3. Unraveling age, sex, puberty and testosterone effects on subcortical brain development across adolescence

The onset of adolescence in humans is marked by hormonal changes that give rise to secondary sexual characteristics, noted as puberty. It has, however, proven challenging to unravel to what extent pubertal changes may have organising effects on the brain beyond chronological age, as reported in animal studies. The present longitudinal study aimed to characterise the unique effects of age and puberty on subcortical brain volumes and included three waves of data collection at two-year intervals and 680 MRI scans of 271 participants aged between 8 and 29 years old. Gamm model procedures were used to assess the effects of age, self-report pubertal status and testosterone level on basal ganglia, thalamus, hippocampus, amygdala and cerebellum gray matter volumes. We observed age-related increases in putamen and pallidum volumes, and decreases in accumbens and thalamus volumes, all also showing main effects of sex. Only the cerebellum showed an interaction effect of age by sex. Furthermore, we showed that changes in puberty status and testosterone described developmental change in several structures better than chronological age. These effects differed per structure and between sexes. Changes in testosterone level were related to development of striatum, hippocampus and amygdala volumes in males and caudate and hippocampal volumes in females. The approach of the present study allowed us to characterise the complex interactions between chronological age and pubertal maturational changes, and the findings indicate puberty unique changes in brain structure that are sex specific.

Barbara Braams, Harvard University

F.1.4. Developmental trajectories of social influence on ambiguous decision-making

Adolescence is a life period associated with increased risk-taking, especially in the context of peers. Two factors that are important for the propensity for risk-taking are attitudes towards ambiguity and risk. Risk refers to variability in outcome, whereas ambiguity refers to unknown chances for outcomes. Studies have investigated social influence on risky decisions, but it remains unclear how social influence shapes adolescent risk-taking in ambiguous situations. Participants (N=99, age range 12-22) completed an economic choice task. Choice options were systematically varied on levels of risk and ambiguity. On each trial a safe choice (low outcome variability) and a risky choice (high outcome variability) were presented. Participants made choices in three conditions: a solo condition, a social condition in which they saw choices of peers and a computer condition in which they saw choices of a computer. Data were analyzed with non-linear mixed effects models with factors risk, ambiguity and condition. For the solo condition, results showed no developmental changes for risk and ambiguity tolerance. For the social condition, results showed that participants' choices conform to the preferences indicated by the peers, but not the computer. Furthermore, when ambiguity was high and peers preferred the risky choice, especially young adults (19-21 years) were more likely to make a risky choice. These results show that tolerance towards ambiguity, but not risk, might depend on choice preference of peers. Furthermore, we show that this effect is specific to early adulthood.

Anthony Dick, Florida International University

F.1.5. Development of the lateral lemniscus and its relation to receptive vocabulary

The lateral lemniscus (LL) is a bilateral fiber pathway comprised of axonal projections from the superior olivary complex to the inferior colliculus (Naidich et al., 2009). It is thus the major

conduit for the transmission of auditory perceptual information in the brainstem. Although the pathway is an important component of this early auditory system, its development has not been investigated using modern diffusion-weighted imaging (DWI) techniques. Our study aims to be the first, to our knowledge, to track the LL in vivo and to explore potential behavioral associations in a sample of typically developing individuals. In this study, we examined the LL in 129 participants (70 females, age = 0-18 years, M= 8.67 years) using DWI. Bilateral ROIs were manually drawn in the midbrain using the superior cerebral peduncle as a landmark. Tracking was successful in 94 participants. Fractional anisotropy (FA) increased linearly in the LL from infancy to late adolescence, which is consistent with extended development of the auditory system more broadly (Litovsky, 2015; $t(90) = 7.21$, $p < .001$; controlling for age, whole brain FA, and gender). We also assessed the LL's relation to vocabulary development and found that axial diffusivity (AD) of the LL is associated with improved PPVT scores ($t(77) = 2.21$, $p < .05$, controlling for age, gender, and wholebrain AD). This study provides preliminary evidence of the development and behavioral associations of the LL. Successful tracking of this pathway is potentially important for clinical treatment of auditory disorders in children.

Tara Madhyastha, University of Washington

F.1.6. Modeling fMRI Data in R using Neuropointillist

fMRI analysis has become an important tool for scientists across disciplines with different modeling needs. In particular, developmental cognitive neuroscience researchers are concerned with longitudinal growth and correlated change of brain and behavior. At the same time, constraints imposed by major fMRI analysis packages limit the range of models that can be applied, and the tight connection between image preprocessing and statistical analysis make it difficult for scientists from different disciplines to bring new modeling expertise to fMRI analysis. We describe a new R package, Neuropointillist (<http://ibic.github.io/neuropointillist/>), designed by our group to address this issue by facilitating implementation of more complex longitudinal models. The presentation will include a tutorial that translates fMRI analysis implemented in the FMRIB Software Library (FSL) into an R longitudinal mixed effects framework. Because conducting fMRI analyses in R can be memory and CPU-intensive, Neuropointillist was also designed to parallelize execution and take advantage of cloud-based computing. We show how this software and approach can be used to compare longitudinal growth models on simulated fMRI data. More generally, using parameters estimated from first level analyses, it can be used to facilitate any voxel-wise analysis that can be defined in R, including structural equation frameworks for growth. The presentation will cover the wide array of new modeling capabilities that will now be available for examining developmental change in fMRI data.

Scott Marek, University of Pittsburgh

F.1.7. Anterior cingulate theta band oscillations support development of cognitive flexibility through adolescence into adulthood

Adolescence is a unique developmental period characterized by improvements in cognitive control abilities, including cognitive flexibility. Theta band (4-8 Hz) activity within the anterior cingulate cortex (ACC) increases several hundred milliseconds after onset of a cue signaling the need to switch rule sets in adults. However, the developmental of ACC theta band oscillations and their contribution to the development of cognitive flexibility have not been examined. MEG data was collected from 47 subjects aged 14-31 years. Subjects completed a modified version of

the multi-source interference task where subjects had to switch between congruent and incongruent trial types. After preprocessing and a novel approach for deconvolution of MEG data, we contrasted switch vs. repeat trials and projected these results into source space for each subject. We next executed a time/frequency decomposition and tested for age effects. Lastly, we related brain activity during task switching to behavioral performance, once again testing for developmental effects. Across ages, there was significantly greater theta band ACC activity in switch vs. repeat trials within 200ms of a cue signaling the need to switch tasks. In addition, increased theta band power was related to increased switch cost. Developmentally, ACC theta band power decreased with age with increased theta band power resulting in a greater switch cost for adolescents compared to adults. These findings present electrophysiological evidence that mechanisms supporting cognitive control instantiation are immature during adolescence.

Hillary Raab, New York University

F.1.8. Pavlovian and instrumental contributions to motivated behaviors across development

Across development individuals must acquire a repertoire of behaviors to function adaptively in diverse environments. Pavlovian "stimulus-outcome" learning elicits reflexive reactions, whereas instrumental "action-outcome" learning affords flexible adaptive behaviors that yield beneficial outcomes. Through Pavlovian-instrumental transfer (PIT), hard-wired Pavlovian responses either facilitate or undermine instrumental learning. When Pavlovian and instrumental outcomes are aligned, Pavlovian responses invigorate reward-driven instrumental actions and inhibit action in the face of punishment. When in opposition, Pavlovian responses interfere with adaptive, instrumental behaviors. PIT has yet to be well characterized developmentally. Here, we examined PIT in children, adolescents, and adults (aged 8-25), who performed a Go/No-go task in which valence and action were orthogonalized. Across trial types, Pavlovian and instrumental responses were either aligned (Go to win, No-go to avoid losing) or in opposition (Go to avoid losing, No-go to win). We found a valence-by-action-by-trial effect that was differentially impacted by age. Overall, learning was enhanced when Pavlovian and instrumental responses were aligned versus in opposition. Moreover, a Go bias further facilitated 'Go to win' learning. The degree of PIT was greatest in children, with instrumental action growing increasingly resistant to Pavlovian interference with age. This shift in the balance between learning systems may foster more flexible adaptive behaviors during the transition from adolescence into adulthood.

Christy Rogers, University of North Carolina at Chapel Hill

F.1.9. "No, don't do it!" Neural correlates of sibling closeness during risky decision-making

Accumulating evidence suggests that sibling relationships are a prominent influence on the development of risk-taking behavior across adolescence. Siblings predict adolescents' engagement in risk taking above and beyond the effects of parent and peers. Yet, no prior study has tested how siblings influence the neurobiology of risk taking. We investigated the neural correlates of sibling relationships on adolescent risk-taking behavior. The sample included 73 adolescents (Mage = 13.37 years; 38 females) who played a risk-taking task during an fMRI scan. Participants reported on closeness (e.g., trust, communication, support) with their siblings, parents, and peers, and indicated the frequency with which they engaged in risky behaviors such as substance use. Higher sibling closeness was associated with suppressed activation in the dorsolateral PFC and insula during risky decision-making. Moreover, higher

sibling closeness indirectly predicted less adolescent real-life risk-taking via suppression of the insula during risky decision-making. Birth order effects were also found, indicating that sibling closeness differentially predicts activation in the caudate depending on whether adolescents are the oldest child in the family or not. Importantly, these findings persisted above and beyond parental and peer closeness, highlighting the significant influence of sibling relationships on adolescent risk taking through the brain.

David Montez, University of Pittsburgh

F.1.10. Developmental stabilization of neural gain signals improves mean behavioral performance and behavioral variability

Cognitive development during adolescence is characterized by improvements in mean performance and by decreases in behavioral variability, which is an important barometer of cognitive functioning. Mechanistically accounting for the stabilization of behavior is critical to our understanding of adolescent neural development. Here, we report results from a longitudinal working memory study performed over 10 years in a cohort of 126 subjects between the ages of 8 and 33 years. We develop a computational model of memory-guided saccade (MGS) performance and provide evidence that improvement in mean behavioral performance and behavioral variability can be accounted for by the stabilizing neural variability. We find that behavioral performance in the memory-guided saccade task improves and stabilizes during adolescence. By incorporating multiple sources of independent neural gain variability in a high-dimensional drift diffusion race model we accounted for the improvements in mean performance and variability that are observed during adolescent development. Analysis of the trial-to-trial relationship between memory-guided saccade reaction times and accuracies reveals a U-shaped speed-accuracy relationship, which was accounted for by a balance of independent variability affecting working memory and response threshold gain signals. Our results indicate that independent trial-to-trial variability in gain signals that affect working memory maintenance and response thresholds can account for the speed-accuracy relationships observed in our data.

Kaja LeWinn, University of California, San Francisco

F.1.11. The representative developing brain: Does sampling strategy matter for neuroscience?

Despite calls to incorporate population science into neuroimaging research, most studies recruit small, non-representative samples. We examined whether sample composition influences conclusions about age-related variation in global measurements of grey matter volume, thickness and surface area in a large, community-based sample of children aged 3-18 (N=1,162) from the Pediatric Imaging, Neurocognition and Genetics Study (PING). Structural MRI data were analyzed using Freesurfer to generate cortical area and thickness measures for each lobe of the brain (frontal, parietal, occipital, temporal), as well as for total cortical thickness, area, and volume. To approximate associations of age with brain structure in a representative sample of U.S. children, we applied a commonly-used epidemiologic method called raking to weight the sample according to the distributions of socioeconomic status, race/ethnicity, and sex in the U.S. Census. We compared associations between age and brain structure in this weighted sample to estimates derived from the unweighted original sample. Compared to unweighted models, we observed a more complex functional form (cubic versus quadratic) for cortical surface area and subcortical volume, earlier maturation of sub-cortical structures, and regional patterns of cortical maturation that better reflected known

developmental trajectories in weighted models. Our empirical examination of non-representative sampling in neuroimaging studies suggests that sample composition is likely to have a meaningful impact on cognitive neuroscience findings.

Oral Session 7: Hippocampal Development

Chair: Noa Ofen, Wayne State University

Noa Ofen, Wayne State University

0.7.1 Progress and limitations in assessing hippocampal functional maturation

There is growing interest in measuring the structural properties of the human hippocampus and assessing its functional maturation, yet the little data available, combined with differences in methodological applications limit what we currently know. In this talk I will summarize recent advances in our understanding of hippocampal development, while highlighting several of the limitations in our current knowledge, as well as some of the productive efforts to achieve progress in our understanding of how the development of the human hippocampus and the functional specialization of hippocampal sub-components supports memory functioning across the lifespan. Better characterization of the typical trajectories of hippocampal development is highly desirable not only for understanding how this structure supports memory but for generating clinically important insights in populations where hippocampal development is altered.

Simona Ghetti, University of California Davis

0.7.2 Hippocampal Contributions to the Development of Episodic Memory

Behavioral research has consistently shown that episodic memory, or the ability to remember events in their spatio-temporal context, improves during childhood and adolescence. The hippocampus plays a critical role in forming and reinstating representations that integrate information about events and their spatio-temporal context. However, little is known about how developmental changes in the hippocampus support these behavioral improvements. Furthermore, despite a purported role of the hippocampus in the emergence of episodic memory in the first few years of life, little direct evidence links hippocampal function to early manifestations of episodic memory in humans. I will present new findings that begin to address both of these gaps in knowledge. First, results from a large longitudinal study show that volumetric structural and functional changes in the hippocampus predict developmental changes in episodic memory from 7- to 14 years of age; I will discuss the role of puberty. Second, results from a functional neuroimaging study show that hippocampal activation associated with a past experience in 2-year-olds is associated with overt memory for that experience. Overall, these findings suggest that it is possible to trace early memory capacity to hippocampal function, but this function continues to change from early childhood into adolescence.

Patricia Bauer, Emory University

0.7.3 Self-derivation of new knowledge through memory integration: The importance of binding and detection of deviatio

Building a semantic knowledge base requires integration of memory traces established at different times and in different contexts. Rapid accumulation of knowledge further depends on productive processes that allow self-derivation of new knowledge based on integrated memory traces. Through work with children and college students, we have identified component processes involved in self-derivation through integration. fMRI indicates that the processes are hippocampally dependent. Behavioral assays, eye tracking, and ERPs suggest that limitations on memory integration or binding present challenges to successful self-derivation in childhood, whereas failures to detect deviation between newly and previously learned information limits performance among college students.

Paul Frankland, Hospital for Sick Children

0.7.4 Hippocampal neurogenesis, forgetting and infantile amnesia

Neurogenesis persists throughout life in the hippocampus, and there is a lot of interest in how the continuous addition of new neurons impacts hippocampal memory function across development. Our studies in rodents have shown that high rates of neurogenesis during the post-natal period contribute to accelerated forgetting (i.e., infantile amnesia) (e.g., Akers et al [2014] Science). Our more recent studies address whether amnesia is associated with storage vs. retrieval failure. Using optogenetic approaches we find that otherwise 'lost' infant memories may be recovered via direct stimulation of ensembles of neurons that were active during initial encoding.

Flash Talks – Part 2

Co-chair: Nim Tottenham, Columbia University

Co-chair: Bea Luna, University of Pittsburgh

Louise Baruël Johansen, Centre for Functional and Diagnostic Imaging and Research, Copenhagen University Hospital Hvidovre

F.2.1. Reduced orbitofrontal functional network centrality characterizes high neuroticism across childhood and adolescence

Neuroticism is a risk factor for anxiety and mood disorders. Recently, we showed that children and adolescents scoring higher on neuroticism had a less efficient information exchange in resting-state functional brain networks and a less influential orbitofrontal (OFC) network. In the present longitudinal study, we investigate if associations between functional network topology and neuroticism change over the course of adolescence. Resting-state functional magnetic resonance imaging was acquired for up to six times from 74 typically-developing children and adolescents aged 10-18 years. Using graph theory we quantified global efficiency and modularity, and local network features including betweenness centrality and participation coefficient of five networks of interest. Linear mixed-effects models confirmed that the OFC played a less central role (i.e. lower betweenness centrality) in adolescents with high neuroticism. The lack of a significant neuroticism by age interaction suggests that this association may be stable across childhood and adolescence. Although we observed a fair reliability (intraclass correlation (ICC)=0.4-0.5) for the OFC betweenness centrality measure, the reliability with which graph theoretical measures could be measured longitudinally was generally low (ICC<0.4). Fluctuations in cognitive and mental states during and between the

scanning sessions may well underlie the observed within-subject variability. Our results stress the importance of replicating findings of cross-sectional studies, as these are inherently "blind" to intra-individual variability.

Katherine Reding, National Institutes of Health

F.2.2 Influence of sex and pubertal development on functional connectivity

Sex differences in the prevalence of psychopathology emerge during adolescence and may reflect the pubertal surge in gonadal steroid production. Despite this, little is known about the direct effects of puberty on brain function. To examine neurodevelopment across puberty, we studied functional connectivity (FC) in children categorized by clinician-rated pubertal stage (PS). Participants (N=72) were grouped as prepubertal (PS1, N=41, 8.7 ± 0.3 yrs, 18 girls) or pubertal (PS2-5, N=31, 13 ± 0.7 yrs, 14 girls). Resting state fMRI scans were collected at 3T, processed with AFNI and ANTs, and analyzed using a connectome-wide association study (CWAS) to identify 1) prepubertal sex differences and 2) sex-by-pubertal group main and interaction effects in whole-brain FC. Identified clusters were used as seed regions in voxel-wise analyses to clarify underlying regional patterns of FC. Prepubertal sex differences were identified in the medial prefrontal cortex, a key region of the default mode network (DMN, $p < .001$). Seed-based analysis ($p < .05$ FDR-corrected) showed that girls had more robust FC than boys within the DMN and the executive control network (ECN). In the sex-by-pubertal group model (p 's $< .05$ FWE-corrected) main effects of sex were reproduced in DMN/ECN, while main and interaction effects of pubertal group converged on basal ganglia FC. Seed-based analysis ($p < .001$) showed that caudate FC with the salience network increased across puberty in girls, but decreased in boys. These data suggest that development of network connectivity may be influenced by both sex and pubertal status.

Sylvia Rusnak, Georgetown University

F.2.3. The Developing Frontoparietal Network: Spatial Imitation Performance Predicts Activation in Young Children

The neural signature of visuo-spatial working memory (VSWM), the short-term ability to retain and manipulate information, is well characterized in older children and adults by frontoparietal activation that strengthens with development and memory load (Moriguchi & Hiraki, 2013). Due to the technical difficulties associated with studying young children using fMRI, knowledge of the neural basis of VSWM in preschoolers is limited. Functional near infrared spectroscopy (fNIRS) may be a suitable alternative. Due to a lack of standardization of VSWM measurement in fNIRS studies, prior findings have been mixed (Moriguchi & Hiraki, 2013). In the present study, we collected fNIRS data from 5- to 8-year-olds during two multi-step spatial imitation tasks: one well-established (Subiaul et al., 2015) and one novel. An experimenter demonstrated a sequence of actions and then the child was tested. We hypothesized frontoparietal activation during the test phase due to the demands of holding multiple steps in mind. Memory load was manipulated by sequence length (2 to 5 steps), with all children performing at ceiling across loads. All children exhibited frontoparietal activation during the test phase of each task. However, for high relative to low load, younger children showed only parietal activation, while older children exhibited the canonical frontoparietal activation. Data collection with 3- to 8-year-olds is ongoing. Understanding the neural mechanisms underlying the development of imitation and load-dependent VSWM has important implications for the science of learning.

Stephen Boyd, Oregon Health & Science University

F.2.4. Sex Differences in the Effect of Nucleus Accumbens Volume on Adolescent Drinking: The Mediating Role of Sensation Seeking and Positive Alcohol Expectancies

The nucleus accumbens (NAcc) is implicated in reward sensitivity and development of alcohol use disorder (AUD). Larger NAcc volume has been found among adolescents at high-risk for AUD; though, it is unclear whether NAcc volume predicts drinking. This study examined direct and indirect effects of NAcc volume on adolescent drinking after two years. Mediation through sensation seeking (SS) and positive alcohol expectancies (PAE), both known risk factors of AUD, was explored, as well as sex differences in a sample of 808 adolescents (mean age = 16.2±6.4; 51% female). Baseline bilateral NAcc volume was determined by segmenting subcortical brain structures on T1-weighted, magnetic resonance images. SS and PAE were assessed one year post-baseline, and alcohol use measured after two years. Controlling for intracranial volume and age, NAcc volume predicted later drinking in males ($\beta=.09$, $p=.04$) and females ($\beta=.11$, $p=.02$). After accounting for SS and PAE, the effect of NAcc volume remained significant for females ($\beta=.09$, $p=.04$), but not males ($\beta=.05$, $p=.29$). In males, the indirect effect through SS and PAE accounted for more than half of the effect of NAcc volume ($\beta=.05$, $p=.01$). These findings suggest that delayed structural maturation of the NAcc may be a risk factor for alcohol use. In males, a larger NAcc was associated with greater SS and PAE, which in turn predicted more alcohol use. Mediation was not evident in females. Although NAcc volume influenced later drinking for both sexes, these results suggest that the mechanism by which this region infers risk differs by sex.

Arianna Gard, University of Michigan

F.2.5. Neighborhood effects on the brain: Impoverishment in early childhood predicts amygdala reactivity to ambiguous faces in young adulthood

Although children from disadvantaged neighborhoods are at risk for poor cognitive and social outcomes, the biological mechanisms linking neighborhood impoverishment to youth outcomes is unclear. We previously found (Gard et al., under review) that a Census-derived measure of neighborhood impoverishment at age 2 predicted greater amygdala reactivity (AR) to ambiguous neutral faces at age 20. The current study extends and deepens this work by examining (1) neighborhood danger as a potential mediator of this pathway; and (2) unique effects of each Census-based indicator of neighborhood impoverishment in early childhood on amygdala reactivity to ambiguity at age 20. The Pitt Mother & Child Project (Shaw et al., 2003) is a longitudinal study of low income boys followed from 18 months to 23 years. Neighborhood impoverishment during early childhood (2, 5 years) was measured using seven block-level Census tract variables used across many studies of neighborhood effects: median family income, % families below poverty line, % households on public assistance, % unemployed, % single-mother households, % African American, and % with > Bachelor's degree. Neighborhood danger was parent-reported. AR to neutral faces (versus shapes) was measured using fMRI at age 20. Results indicated that neighborhood danger did not mediate neighborhood impoverishment associations with greater AR to neutral faces in adulthood. Within the neighborhood impoverishment variable, median family income was most strongly related to AR to neutral faces, over and above other neighborhood attributes and family income.

Moriah Thomason, Wayne State University / Perinatology Research Branch, NICHD/NIH

F.2.6. Hatching a Pokémon Egg By Closing Your Eyes: A new Paradigm for Measuring Resting-State in Preschoolers

Resting-state paradigms are becoming increasingly popular in neuroscience. In adults, resting-state is often measured in eyes-closed condition. This procedure is not easily applicable in preschool populations, since they often refuse to close their eyes for extended periods. A standardized task to increase the feasibility of measuring eyes-closed resting-state in this population is needed. Here, we present a novel eyes-closed paradigm for measuring resting-state in preschoolers. Continuous EEG data were collected in 50 preschoolers (ages 4.5-5.1) while they participated in a novel Pokémon resting-state experiment. Children were signaled to place their chin on a custom-built "incubator" and close their eyes in order to hatch a Pokémon egg. An egg appeared on the screen to cue the start of a trial. After 25sec, they would be signaled by a cracking sound to open their eyes. The egg would then virtually hatch and they would be given a matching sticker for the hatched character. This procedure was repeated up to 8 times. The average number of trials completed across all subjects was 7.7 trials. EEG data processed for 12 participants revealed rapid emergent alpha frequency at the onset of rest epochs in all cases. This task meets criteria of being both well tolerated by preschoolers, and producing desired neurophysiological results, suggesting it is a sound approach for investigating spontaneous neural activity across the brain. A complexity warranting discussion is the low-level processing component of this procedure.

Kristen Tummeltshammer, Brown University

F.2.7. Visual learning is modulated by reward value in infancy

Using eye-tracking, we investigated whether 7-month-old infants would demonstrate a key feature of prediction learning: the transfer of reward value from rewarding stimuli onto reward predictive cues. Fifty infants (M=7 months, 8.3 days) were presented with high and low value faces and cartoons (i.e., infant's own mother and an unfamiliar female; colorful dynamic and gray-scale static) as well as four cue stimuli (i.e., unique shapes). Infants viewed the cues and rewards in isolation, and then in 24 randomized cueing trials, in which a cue was closely followed by a paired reward in the same quadrant of the screen. Results show that infants' distribution of looking times to the reward stimuli transferred to the cues during the cueing task: infants looked longer at cues paired with high value than with low value cartoons, while looking times for cues paired with faces did not differ. Infants' pattern of pupil dilations also transferred to the cues, as pupil dilations were larger at post-test for cues paired with high value than with low value rewards, and particularly for the cue predicting the infant's own mother compared to an unfamiliar female face. In addition, infants' increased pupil size for the cue paired with their own mother's face was associated with the amount of time mothers reported spending with their infants. Lastly, infants showed decreased saccadic latencies, reflecting greater spatio-temporal learning, to cues that preceded high value rewards. These results demonstrate that visual prediction learning is indeed modulated by stimulus reward value in infancy.

David Piekarski, UC Berkeley

F.2.8. Ovarian hormones organize the maturation of inhibitory neurotransmission in the frontal cortex at puberty onset in female mice.

The frontal cortex matures late in development, showing dramatic changes after puberty onset, yet few experiments have directly tested the role of pubertal hormones in cortical maturation.

One mechanism thought to play a primary role in regulating the maturation of the neocortex is an increase in inhibitory neurotransmission, which alters the balance of excitation and inhibition. We hypothesized that pubertal hormones could regulate maturation of frontal cortex by this mechanism. Here, we report that manipulations of gonadal hormones do significantly alter the maturation of inhibitory neurotransmission in the cingulate region of the mouse medial frontal cortex, an associative region that matures during the pubertal transition and is implicated in decision making, learning, and psychopathology. We find that inhibitory neurotransmission increases onto cingulate pyramidal neurons during puberty and that this increase can be blocked by prepubertal but not post-pubertal gonadectomy. Further, prepubertal hormone treatment can induce this effect in frontal cortex, but not somatosensory cortex, suggesting that earlier puberty can advance cortical maturation in a regionally specific manner. Prepubertal hormone treatment also affects a frontal cortex-dependent reversal learning task. These data provide rare evidence of enduring, organizational effects of ovarian hormones at puberty and provide a potential mechanism by which gonadal hormones could regulate the maturation of associative neocortex.

Brenden Tervo-Clemmens, University of Pittsburgh

F.2.9. Neural Correlates of Latent Internalizing and Externalizing Psychopathology During Adolescence

Across the lifespan, latent variable modeling reveals dimensional, internalizing and externalizing factors that account for patterns of comorbidity amongst common mental health disorders. However, little is known about the association between these transdiagnostic factors and brain function during adolescence. To identify functional brain correlates of internalizing and externalizing psychopathology, we utilized resting-state functional magnetic resonance imaging (rsfMRI) data and psychopathology symptom endorsement from 598 subjects from the Philadelphia Neurodevelopmental Cohort. Latent internalizing and externalizing factors were estimated using confirmatory factor analysis (CFA) informed by Krueger et al., (1998). rsfMRI data (6 min) were preprocessed using standard measures and adjacency matrices were computed using the parcellation from Power et al. (2011). The CFA model of psychopathology symptom endorsement demonstrated good fit (robust CFI: = .964, RMSEA = .06). Preliminary rsfMRI results revealed subjects with high latent internalizing scores had increased connectivity within canonical default mode network (DMN) nodes (t 's > 2.75, $p < .05$, corrected). In contrast, subjects with higher latent externalizing scores had increased connectivity between frontoparietal (DLPFC) and DMN nodes (MTL) ($t = 3.99$, $p < .05$, corrected). Our results suggest distinct connectivity profiles of internalizing and externalizing psychopathology. However, we highlight a potential common role of the DMN in transdiagnostic psychopathology risk during adolescence.

Sung Jun Joo, University of Washington

F.2.10. Automaticity in the reading circuitry: A hallmark of skilled reading

Skilled reading requires years of practice with learning to associate visual symbols (letters) with speech sounds (phonemes), and over the course of the learning process, this association becomes almost effortless. Indeed, skilled readers show activation to visually presented words in both ventral temporal cortex (VTC), which is involved in orthographic processing, and the superior temporal sulcus (STS), which is involved in phonological processing. Here we hypothesize that automatic activation of this circuit in response to a visually presented word is

a hallmark of successfully learning to read. To test this hypothesis, we used magnetoencephalography (MEG) to measure cortical responses to printed words while children engaged in an attention-demanding task (color discrimination on a fixation dot) for which the words were irrelevant. We found that the stimulus-evoked visual response to words in VTC peaked at 180 ms and all children, regardless of reading skill, showed similar VTC responses. Importantly, even though children were not actively reading the words, we found significant activation in the STS which peaked at 240 ms. This automatic response to the visual stimulus in a canonical language region was indicative of good reading skills: the stimulus-driven STS response was only present in good readers but not in children with dyslexia. Our results suggest that automatic recruitment of phonological processing circuits is a hallmark of skilled reading; with practice, reading becomes effortless as the brain learns to automatically translate letters into sound and meaning.