# 2016 Oral Presentations

## Day 1, Thursday September 8

**Oral Session 1: Tuberous Sclerosis Symposium**
*Sponsored by the Tuberous Sclerosis Center at Washington University School of Medicine*

Washington University
Tuberous Sclerosis Center

Discussant: Brad Schlaggar

**Anna Jeong,** Washington University in St Louis
*O.1.1.***Tuberous Sclerosis Complex - A Clinical Overview**
Tuberous Sclerosis Complex (TSC) is model disorder for the study of cognitive dysfunction, epilepsy, and autism. This talk will serve as an overview of TSC, specifically addressing the clinical manifestations, pathological features, and inheritance pattern of the disease. The underlying pathophysiology of TSC will also be discussed, with a focus on the mechanistic/mammalian (mTOR) pathway.

**Shafali Jeste,** UCLA
*O.1.2.* **Timing and mechanisms of atypical development in Tuberous Sclerosis Complex**
Tuberous Sclerosis Complex confers a high risk for neurodevelopmental disorders, including Autism Spectrum Disorder (ASD) and Intellectual Disability (ID). The high rate of ASD and ID, combined with the fact infants are diagnosed with the genetic syndrome prior to the onset of social communication or cognitive delays, has led to TSC being considered a model disorder for studying the emergence of atypical development. We recently completed the first prospective, longitudinal study of early development in infants with TSC (Jeste, 2014, 2016), with the goal of defining the timing and understanding the emergence of developmental delays in infancy. We integrated electrophysiological and behavioral assays to investigate specific mechanisms underlying atypical development, with particular focus on visual processing, face perception, attention and nonverbal communication. Results from this study have informed a new early intervention study targeting social communication skills in these high risk infants.

**Michael Wong,** Washington University in St Louis
*O.1.3.* **Cellular and Molecular Mechanisms of Cognitive Deficits in Tuberous Sclerosis Complex: Insights from Mouse Models**
Cognitive deficits, autism, and epilepsy are common neurological manifestations of tuberous sclerosis complex (TSC), but biological mechanisms causing the neurological phenotype of TSC are poorly understood. The prototypic structural brain abnormalities of cortical tubers in TSC led to the “tuber hypothesis”, in which these gross pathological lesions account for cognitive and other neurological dysfunction. However, recent advances in molecular genetics have identified cellular and molecular abnormalities, such as in the mTOR pathway, which contribute to neurological symptoms of TSC independent of tubers. Mouse models have been particularly useful in identifying underlying mechanisms and therapeutic strategies for neurological deficits in TSC.

**Jurriaan Peters,** Harvard Medical School

*O.1.4.* **MRI biomarkers and early medical interventions in TSC**

The neurological phenotype in Tuberous Sclerosis Complex (TSC) is highly variable and unpredictable. It is determined by multiple interrelated factors including genotype, clinical variables, and lesion burden. Improved long-term cognition with early treatment of epilepsy has been reported in small retrospective series. Recently, routine clinical EEG abnormalities were shown to precede seizure onset, allowing for risk-stratification in a treatment trial with preventative anti-seizure medication. Early structural magnetic resonance imaging (MRI) studies revealed a group effect of lesion burden, but had no individual predictive ability. More recently, diffusion tensor imaging (DTI) metrics of the normal appearing white matter (NAWM) were associated with outcome measures. Moreover, a longitudinal DTI study showed improvement of white matter maturation in patients treated with mTOR inhibitors. Although currently still non-specific, DTI could be a biologically relevant, non-invasive and widely available biomarker for neurological outcome in TSC.

**Science of Learning Symposium: Part 1**

*Winners of the Early Career Award, supported by the Jacobs Foundation*

JACOBS FOUNDATION
Our Promise to Youth

Discussant: Tim Brown, University of California, San Diego

**Samantha DePasque**, UCLA

*S. 1.1.* **Motivation and feedback-based learning in adolescent corticostriatal networks**

During adolescence, youth must learn about the consequences of their choices as they hone their decision making skills. Performance-related feedback is one tool educators use to guide learning; however, its learning efficacy depends upon motivation. Corticostriatal systems play a critical role in motivation and learning, so it is important to understand how ontogenetic changes in these systems might scaffold feedback-based learning. This study uses fMRI to compare adolescents' (age 11-15) and adults' (age 23-30) neural responses to feedback under varying motivational contexts. Participants complete a learning task in three phases: 1) study, 2) feedback, 3) post-test. During the feedback phase, 4 blocks of trials were framed as a test (threat) and 4 as practice (nonthreat). Regardless of motivational condition, both age groups improve after feedback, and adults outperform adolescents. However, at post-test, adolescents achieve the same percent correct as adults for items previously answered incorrectly, having corrected significantly higher numbers of errors under threat. Feedback engages the same brain network in both age groups, including striatum, mPFC, and PCC. Under threat, adolescents exhibit higher activation to feedback in amygdala, hippocampus, insula, and mPFC. ROI analyses identified age x threat interactions in nucleus accumbens, caudate, amygdala, and hippocampus, suggesting age-related differences in the effects of the motivation manipulation. Further analyses will examine relationships between these results and individual differences in achievement motivation.

**Alyssa Kersey,** University of Rochester

*S.1.2.* **Neural patterns of reading and mathematics development from controlled versus naturalistic stimuli**

Patterns of neural activity evoked by stimuli in well-controlled tasks are important for isolating the neural substrates of cognitive functions. However, that approach may not be ideal for measuring individual variability in neural functioning over development. Our study compares children's neural responses to reading and mathematics stimuli in controlled tasks versus naturalistic educational videos using functional magnetic resonance imaging (fMRI). First, we measure neural activation from 4- to 8-year-old children during controlled mathematics and reading tasks and compare those patterns to activations that relate to individual variability

in mathematics and reading. Next, we compare activation patterns elicited by controlled tasks with those related to natural viewing of educational videos. The data show dissociations between the functional networks underlying reading versus mathematics. Within those networks some regions show uniform patterns of activation over development whereas others show robust individual variability related to cognitive development in each domain. This suggests that the naturalistic and controlled stimulus approaches provide distinct but complimentary information about neural development. These results are important for understanding children's cognitive and neural development in the real world.

**Wouter van den Bos,** Max Planck Institute for Human Development

*S.1.3.* **Navigating Uncertainty: Neural Correlates of Decisions form Experience in Adolescence**

Despite the increased prevalence of adolescent risk-taking behavior in the real world, laboratory evidence of adolescent specific risk taking propensity remains scarce. In contrast with the lab, in the real world adolescents often have only incomplete information about risks, but may have the opportunity to gather more information before they decide. There is currently very little known about how adolescents make decisions under these uncertain conditions. To address this issue we studied how adolescents make decisions based on experience. In a large behavioral study (N=105,ages 8-22) we found adolescents searched for less information before making a decision, were less averse of uncertainty, and made more risky decisions. In a follow up fMRI study, comparing adults (N=25, ages 18-25) and adolescents (N=30, ages 11-15), we focused on the processes involved in learning probabilities through experience and subsequent decision-making. Again, we found that adolescents were less skilled in learning probabilities and were more risk-seeking. Furthermore, we found that the VMPFC is encoding the uncertainty during learning and decision-making. However, this was not the case for the adolescents. This suggests that adolescents may not take the uncertainty associated with their choices into account. This hypothesis was further supported by our finding that adolescents self-reported confidence was not well calibrated. This research provides important new insights in the role of learning processes that contribute to increased risk-taking in adolescence.

**Science of Learning Symposium: Part 2**

**Jason Yeatman**, University of Washington

*S.2.1.* **The neural circuitry of skilled reading**

Quantitative neuroimaging measurements have generated new insights into the neurobiology of learning and provided a means to understand the mechanisms underlying individual differences in academic performance. For example, learning to read depends on communication between visual, auditory and language processing circuits. The white matter tracts that carry signals between these regions are critical for skilled reading. We find that the dynamics of an individual’s white matter development predicts their acquisition of reading skills and that this biological process can be influenced through targeted behavioral interventions. These findings pave the way for conversations between education and neuroscience on how to optimize reading instruction with respect to brain development.

**Daniel Ansari**, University of Western Ontario

*S.2.2.* **Number Symbols and the Developing Brain**

Numerical symbols are a recent cultural invention. I will review what has been learned from developmental cognitive neuroscience research about the way in which numerical symbols are represented in the brain and mind. I will examine what is known about developmental changes in the brain representation of number symbols and how individual differences in symbolic number processing skills (such as mental arithmetic) relate to variability in brain activation during symbolic number processing and the educational implications thereof. Finally, I will discuss several future directions for research on the brain’s representation of number symbols.

**John Gabrieli**, MIT
*S.2.3.* **Education Neuroscience**
Education neuroscience aims to understand the brain basis of learning that supports academic achievement. I will summarize a number of studies in which we have examined brain differences associated with difficulty in learning to read (dyslexia) and with the relation of socioeconomic status (family income, parental education) to performance on statewide standardized tests that are widely used to assess academic achievement.

## Huttenlocher Lecture

**Michael Posner**, University of Oregon
**Brain Changes with Development and Training**
During development connectivity improves particularly between remote brain areas. Adults respond much faster than children probably related in part to this improved connectivity. Children and adults also improve in reaction time with practice on the task. For adults, we have shown that a month of mental training with meditation results first in improved axial diffusivity and later radial diffusivity. In this lecture we examine similarities and differences between development and training in the brain mechanisms related to the speed of responding.

# Day 2, Friday September 9

**Oral Session 2: NeuroLaw Symposium**

Discussant: Kim Taylor Thompson, NYU Law

**Jason Chein,** Temple University
*O.2.1.* **Development of the social brain and the peer influence on adolescent crime**
Unlike their adult counterparts, adolescents are more likely to commit both violent and non-violent crimes when in the presence of their peers. While this phenomenon has traditionally been explained in terms of affiliation patterns and explicit peer pressure, our work has explored how structural and functional brain development might account for the increase in social influence observed during adolescence. In this talk, I will discuss findings regarding the links between structural development and sensitivity to social information, and how development impacts activation and functional connectivity as adolescents render decisions about the potential risks and rewards of their actions.

**Ali Cohen**, Sackler Institute
*O.2.2.* **When is adolescent an adult?**
The age of adulthood varies for different legal and social policies. We assessed cognitive control in neutral and emotionally arousing situations, which may be relevant to these policies. Eighteen- to 21-year-olds showed diminished performance, relative to adults over 21, under brief and prolonged negative emotional arousal. Differences in performance were paralleled by decreased activity in fronto-parietal circuitry, implicated in cognitive control, and increased sustained activity in the ventromedial prefrontal cortex, involved in emotional processes. These findings suggest a developmental shift in cognitive capacity under negative emotion that coincides with dynamic changes in prefrontal circuitry and may inform age-related policies.

**Adrianna Galvan**, University of California, Los Angeles

*O.2.3.* **Risk Triangle: The combined effects of peer presence, social cues and rewards on cognitive control capacity in adolescents**

The developmental science literature has examined the independent contextual effects of peer presence, social cues and rewards on adolescent decision-making and cognitive control. Yet, these contextual factors often co-occur in real world social situations for teens. The current study examined the combined effects of all three factors on cognitive control capacity and underlying neural circuitry using a task with experimental manipulations that may better capture real world interactions. A community sample of 176 participants (71 adolescents, 48 young adults, and 57 adults) from Los Angeles and New York City were scanned while performing an emotional go/no-go task alone or in the presence of a virtual peer, matched in age and gender.. The task included brief social cues and sustained periods of arousal (e.g., anticipation of winning money). Compared to older age groups, adolescents showed diminished cognitive control capacity to positive social cues when anticipating reward in the presence of peers than when alone. This behavioral pattern was paralleled by enhanced orbitofrontal activation in the adolescent group relative to the older age groups. Together, the results suggest a common neural and behavioral effect of social and reward influences on cognitive control capacity in adolescents and that prior studies may be underestimating the impact of peers on this capacity in real world situations for teens.

**Oral Session 3: Infant Development Symposium**

Discussant: Joel Nigg Oregon, Health & Science University

**Alice Graham**, Oregon Health & Science University

*O.3.1.* **Towards an Increased Understanding of Prenatal Influences on Neurodevelopment**

Identifying prenatal influences on brain development is of critical importance for understanding risk for psychiatric disorders and potential for preventive intervention. We have examined the influence of prenatal stress and nutrition on the newborn brain, and cognitive and emotional development through 24-months-of-age. The results suggest the importance of considering specific stress-sensitive aspects of maternal-placental-fetal (MPF) biology, such as the pro-inflammatory cytokine interleukin-6, which we have found to be associated with newborn amygdala volume and connectivity. The results also highlight the utility of modeling approaches which allow for inclusion of a broad range of prenatal influences to predict neurodevelopment through 24-months-of-age.

**John Gilmore,** University of North Carolina

*O.3.2.* **Brain structure and cognitive development in early childhood**

Early childhood is a period of rapid development of brain structure and cognitive function, though very little is known about structure-function relationships during this time. The UNC Early Brain Development Study is a longitudinal imaging study of brain development from birth to age 6 years in typically developing children, children at high risk for psychiatric disorders, and twins. Major patterns of gray and white matter development in the first years of life will be reviewed, and new information about the relationships between cortical gray and white matter growth and cognitive development at ages 1 and 2 years will be presented.

**Sean Deoni,** Brown University

*O.3.3.* **The Developing Brain : MRI Assessments of structural and Functional Development**

How does the healthy brain grow? Across the first 1000 days of a child's life (from conception to age 2) and throughout early childhood, the brain undergoes remarkable change in response to diverse genetic and environmental pressures. This age span encompasses the most rapid period of brain growth, and coincides with the emergence of nearly all fundamental cognitive and behavioral skills. Activity-dependent processes such as synaptogenesis, synaptic pruning, and myelination help shape the neural systems that underlie these

functions; with deviations associated with a spectrum of cognitive and behavioral abnormalities. Magnetic resonance imaging allows the characterization of complementary aspects of tissue maturation, including cortical morphology, white matter microstructure, tissue fibre architecture, as well as brain function and connectivity. Adopting these techniques for use in pediatric populations, salient new insight into brain maturation, including timelines of development, relationships between evolving brain structure and cognitive function, and potential alterations in specific disorders, can be elucidated. In this talk, we will highlight results from on-going longitudinal studies of fetal, infant, and early child neurodevelopment, specifically looking at patterns of development and their relationship to evolving cognitive functioning. Further, we will broadly examine potential environmental influences that affect early development.

**Oral Session 4: Translational Animal Models Symposium**

Discussant: Nim Tottenham, Columbia University

**Regina Sulivan**, NYU School of Medicine
*O.4.1.* **Caregiver Influence Over the Infant Brain and Behavior**
In many mammalian species, including humans and rodents, the caregiver regulates the infant brain to alter brain and behavior. Here we use rodent mother-infant interactions to illustrate maternal influence over pup brain activity using ecologically relevant examples of how the attachment figure defines brain activity and social signals. This work illustrates how learned cues from the mother influence neurobehavioral processing of fear and safety in infancy, but also how poor quality infant attachment to the mother compromises this maternal influence.

**Mar Sanchez**, Emory University
*O.4.2.* **Early Maternal Care Regulates the Development of Emotional Behavior and Neurocircuitry: a Nonhuman Primate Model**
Early life stress, including adverse experiences such as child maltreatment, lead to increased risk for psychopathology. Evidence from a translational macaque model of infant maltreatment shows negative developmental impacts on social behavior, emotional and stress regulation, and the developmental trajectory of underlying cortico-limbic circuits. Using a crossfostering, randomized, design to disentangle experience from heritability effects and longitudinal neuroimaging approaches we have detected reduced prefrontal-amygdala connectivity, resulting in impaired fear regulation in maltreated animals during adolescence. Nonhuman primates are unique animal models to examine neurodevelopmental underpinnings and sensitive periods of early adverse experiences of translational value for humans.

**Shannon Gurley**, Emory University
*O.4.3.* **Developmental factors in toggling between actions and habits: Effects of adolescent adversity and relation to depression-like behavior**
The prefrontal cortex undergoes structural reorganization and refinement during adolescence. This plasticity may open a window of vulnerability to insults and the development of neuropsychiatric illnesses such as depression. I will discuss evidence collected from both male and female mice that deep-layer excitatory prefrontal cortical neurons remodel considerably in response to social isolation or stress hormone exposure in adolescence. Further, some neural subsets fail to recover by adulthood. Aberrant neural structures are associated with anhedonic-like behavior and a propensity to engage reward-seeking habits in adulthood. Identification of associated factors such as Rho-kinase signaling may elucidate novel mechanisms of, and therapeutic approaches to, neuropsychiatric disease.

# Day 3, Friday September 10

**Oral Session 5: ABCD Symposium**

Discussant: Ted Satterthwaite, University of Pennsylvania

**Nico Dosenbach**, Washington University in St Louis
*O.5.1.* **Real-time motion analytics during brain MRI improve data quality and reduce costs**
Even sub-millimeter movements of the head between measurements systematically distort MRI data, especially functional connectivity metrics. Motion-driven distortions can be removed by excluding data frames with > 0.2 mm framewise displacement (FD) relative to the previous data frame. While effective, post-hoc frame censoring can lead to data loss rates of up to 50%, forcing MRI researchers to collect large amounts of buffer data, to decrease the risk of having to exclude entire subjects because of insufficient low-movement data. Even when using this very expensive 'overscanning' approach, researchers will still have to exclude some subjects from their final cohorts because of excessive head motion. Therefore, we developed an easy-to-setup, easy-to-use fMRI Integrated Real-time Motion Monitoring (FIRMM) software suite that provides scanner operators with head motion analytics in real-time, allowing them to scan each subject until the required amount of low-movement data has been collected. Our analyses show that using FIRMM to identify the scanning sweet spot that provides the required amount of low-movement data at the lowest cost can reduce scan times and associated costs by 50%.

**Terry Jernigan,** University of California, San Diego
*O.5.2.* **Overview of the ABCD Study**
This presentation will provide an overview of the Adolescent Brain Cognitive Development (ABCD) Study focusing on its administrative and operational structure, the recruiting strategy and target cohort characteristics, and on the methods for assessing development, health, and behavioral characteristics of the participants. Plans for resource sharing with the wider research community will be described and opportunities for leveraging ABCD in future research will be highlighted.

**Anders Dale**, University of California, San Diego
*O.5.3.* **Harmonized Human Connectome Protocols for the ABCD Study**
The imaging protocols to be applied in the ABCD Study build on the Human Connectome Lifespan protocol and have been enhanced and harmonized across GE, Siemens, and Philips scanners. Specific enhancements include real-time motion estimation and correction, protocol compliance checking, and advanced diffusion MRI acquisitions and analysis methods. All raw- and derived data, along with associated computational analysis pipelines, will be freely shared with the research community.

**Oral Session 6: Parcellating the Human Brain Symposium**

Discussant: Steve Petersen, Washington University in St Louis

**Evan Gordon**, VISN 17 Center of Excellence (VISN CoE)
*O.6.1.* **Boundary-based parcellation of human cerebral cortex using functional connectivity MRI**
The human cerebral cortex is organized into a large number of interacting cortical areas with discrete patterns of architectonics, connectivity, and function. Abrupt transitions in fMRI resting state functional connectivity patterns can noninvasively identify locations of putative borders between cortical areas. Here, we used this "boundary mapping" technique to generate and evaluate discrete cortical parcels in a group of healthy adults.

Connectivity patterns of the resulting parcels were highly homogenous when compared to a permutation-based null model, and specific parcels conformed to known cytoarchtectonically-defined cortical areas. This boundary-based parcellation may thus represent a highly useful set of a priori ROIs.

**David Van Essen**, Washington University in St Louis
*O.6.2.* **A multimodal parcellation of human cerebral cortex**
Using multi-modal magnetic resonance images from the Human Connectome Project (HCP) and an objective semi-automated neuroanatomical approach, we delineated 180 areas per hemisphere bounded by sharp changes in cortical architecture, function, connectivity, and/or topography in a precisely aligned group average of 210 healthy young adults. The parcellation includes 97 new areas and 83 areas previously reported using specialized study-specific approaches. A machine-learning classifier trained to recognize the multi-modal 'fingerprint' of each cortical area enabled automated and reliable identification of these areas in new HCP subjects and could correctly locate areas in individuals with atypical parcellations. The parcellation and associated datasets are shared freely via the BALSA database.

**Oral Session 7: Large Scale Networks Symposium**

Discussant: Olaf Sporns, University of Indiana

**Martijn Van Den Heuval,** University Medical Center Utrecht, The Netherlands
*O.7.1.* **Richness of the human brain network**
Using network science as a general framework to study the network of connectivity our brain -the human connectome, more and more studies have highlighted the human brain to display features of an efficient communication network, showing cost-effective wiring, pronounced community structure, short communication relays, and the existence of richly connected 'hub regions'. In my talk, I will highlight and discuss recent findings of a 'rich club organization' of the human connectome, discussing the important role of a densely connected 'rich club' core in brain systems, suggesting the existence of a selective group of high-degree hub regions to form a densely connected backbone of neural connectivity in the brain; a system argued to be crucial for bringing integration among segregated brain systems. I will discuss a potential 'richness' of this club at different scales of brain organization and discuss the early emergence of the rich club in the neonatal brain. Furthermore, I will discuss findings of changes in connectome wiring and structure across brain development and the lifespan, as well as discuss how deviating growth of connectome and rich club organization may form an important factor in the aetiology of neurodevelopmental disorders, in particular brain disorders that are characterised by a disruption of integrative brain processes, such as schizophrenia.

**Alex Fornito,** Monash University, Australia
*O.7.2.* **Genetic and developmental influences on large-scale brain networks**
Some brain regions posses a large number of connections and act as network hubs. These hubs support the integration of distributed neural systems, but can also represent potential points of vulnerability in disease. This talk will present evidence to indicate that hubs are topologically central elements of brain networks that carry a high metabolic and physical cost. This cost defines the transcriptional signature of hub connections, and is a heritable property of hub connectivity. Although hub connectivity is established early in development, it continues to be remodeled throughout late adolescence, coinciding with a period of peak risk for many psychiatric disorders.

**Danielle Bassett,** University of Pennsylvania

*O.7.3.* **Evolution of brain network dynamics in neurodevelopment**

Cognitive function evolves significantly over development, enabling flexible control of human behavior. Yet, how these functions are instantiated in spatially distributed and dynamically interacting networks or graphs that change in structure from childhood to adolescence is far from understood. Here, we apply a novel machine learning method to track continuously overlapping and time-varying subgraphs in the brain at rest within a sample of 200 healthy youth (aged 8-11 and 19-22) drawn from the Philadelphia Neurodevelopmental Cohort. We uncover a set of subgraphs that capture surprisingly integrated and dynamically changing interactions among known cognitive systems. We observe that subgraphs that are highly expressed are especially transient, flexibly switching between high and low expression over time. This transience is particularly salient in a subgraph predominantly linking fronto-parietal regions of the executive system, which increases in both expression and flexibility from childhood to young adulthood. Collectively, these results suggest that healthy development is accompanied by a greater precedence of executive networks and a greater switching of the regions and interactions subserving these networks.