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**A model for Attention-Deficit/Hyperactivity Disorder: Linking brain asymmetry patterns and temporal integration deficits**

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**A**DHD is a highly heritable (60-75%), 1 child-onset neurodevelopmental disorder that effects ~ 5% of school aged children. It is characterized by problems with sustained attention and task prioritization, which often diminish an individual's productivity and social relationships. Both structural and functional neuroimaging studies have demonstrated that individuals with ADHD have alterations in fronto-striatal circuitry<sup>2</sup>, and a recent mega-analyses by the ENIGMA working group demonstrated consistent diminutions in subcortical volumes (e.g., amygdala) across the lifespan. Nonetheless, results from quantitative structural and functional MRI studies have varied with respect to the laterality of findings<sup>3</sup>. Recently, our group has shown that alterations in inter-hemispheric asymmetries across volumetric and morphometric measurements may be a more sensitive measure for detecting baseline differences in the ADHD brain<sup>4</sup> as well as response to therapeutic intervention via pharmaceuticals that alter dopamine signaling. In particular, these patterns of asymmetry differences were most prominent in white matter tracts, as evidenced by metrics derived from diffusion imaging. Here, we suggest that these asymmetries may either result from or be a compensatory mechanism related to temporal integration deficits in the ADHD brain. For example, changes in fiber

myelination, and axonal diameter that are reflected in DTI measurements, are correlated with conduction velocities in the brain. Increased asymmetries may therefore lead to unbalanced conduction speeds, and improper integration of sensorial information at higher levels of processing. This temporal integration model may also help explain some of the hallmark behavioral traits of ADHD including increased reaction time (RT) variability. Additionally, studies documenting the genetic basis for ADHD suggest either hyper-active reuptake of dopamine or diminished postsynaptic receptor sensitivity due to alterations in the dopamine transporter allele<sup>5</sup>. Our model is therefore also consistent with recent findings indicating the importance of precise dopamine regulation in the perception of time.<sup>6</sup>

**Speaker Biography**

PK Douglas completed a PhD in neuroengineering at UCLA, postdoctoral work at the University College London, and is currently an assistant professor in the Modeling and Simulation Department at UCF, and in the department of Psychiatry and Biobehavioral Medicine at UCLA. Dr. Douglas has a long history of publishing work in utilizing decoding approaches to study functional representations in fMRI and EEG. Recent work in Dr. Douglas's lab includes applying both supervised and unsupervised learning approaches to study structural-functional integration in youths with Attention-Deficit/Hyperactivity disorder, with a focus on modeling excessive novelty seeking behavior observed in certain phenotypic presentations within this childhood neurodevelopmental disorder.

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