THE HARTWELL FOUNDATION

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Beyond the Cerebrum: Multimodal Imaging of the Brainstem in Autism Spectrum Disorder

Autism spectrum disorder (ASD) is a neurodevelopmental disability characterized variously by difficulties in social interaction, verbal and nonverbal communication, and repetitive behaviors. ASD affects 1 in 68 children in the US. The symptoms are debilitating, but there are few biology-based treatments available, possibly due in part to the high degree of individual differences in autistic symptom profiles. The inability to accurately sub-categorize the spectrum of autism disorders has substantial negative implications for appropriate diagnosis and treatment. Longitudinal shifts in severity due to age-related effects or therapeutic mediation only add to this lack of clarity. Unfortunately, most treatment trials for ASD select subjects based on subjective social behavior, which may omit children who barely miss the diagnostic cutoff because social behaviors are diffuse and often difficult to characterize. The focus on categorizing ASD by behaviors is driven in part by prevailing opinion that continues to dictate long-held views that autism is a disorder associated with the upper part of the brain (cerebrum) responsible for controlling higher-order functions, such as thought and action. However, abnormalities in basic motor functions responsible for basic motor functions like breathing, locomotion, ingestion, and aggression, as well as more advanced functions like sleep and attention may be symptomatic of ASD. For example, Brittany has demonstrated in preliminary research that postural stability during standing is a fundamental motor skill that is impaired in individuals with ASD. She found that objective measures of the postural sway at which balance is lost and corrective action is required are directly correlated with ASD symptom severity and that the extent of white matter in specific circuits of the brainstem can be used to predict the observed differences in symptoms. To address the unmet need for rigorous biology-based features that can be used to characterize ASD, she now proposes to extend her observations using multimodal MRI for mapping the functional, structural, and metabolic organization in the brainstem of 100 children with ASD and related disorders. If Brittany is successful, new, biology-based sub-classifications of ASD that link brainstem pathology to specific autism symptoms will make it possible to develop apply effective and targeted interventions to specific subgroups of affected children. The use of brainstem MRI-based metrics as biomarkers will also enable the measurement of longitudinal shifts in ASD severity due to age-related developmental effects or as the result of therapeutic mediation in personalized treatment plans.