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Understanding the Heterogeneity in Children with ADHD Through Neurophysiologically Defined Subtypes

by Stacey Aggarwal

We are all unique, but the heterogeneity observed in children diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) makes it extremely difficult for clinicians and caregivers to properly plan comprehensive services. Many of these individual differences are clinically meaningful such as behavioral symptoms, developmental trajectories, and responses to treatment. Nevertheless, our current understanding of ADHD doesn't allow us to sort through these individual differences to make meaningful decisions about intervention strategies or predictions of future developmental patterns. Personalized, targeted treatment of ADHD starting at an early age could dramatically improve management and outcomes of this complicated disorder.

Anne Arnett's research focuses on identifying subtypes of children with attention deficit hyperactivity disorder (ADHD) with the ultimate goal of achieving more personalized intervention approaches.

Anne Arnett, PhD, acting assistant professor of psychiatry and behavioral sciences and CHDD research affiliate, hopes to address this issue in a recently funded new investigator project. In this project, Arnett uses electroencephalography to record electrical patterns in the brains of children with ADHD. Electroencephalograms (EEGs) are recorded while the child sits comfortably in a chair wearing a cap fitted with electrodes. EEG data previously generated by other research labs supports the idea of different neurobiological profiles across children with ADHD. Arnett hopes to extend this work with her own EEG data to better understand these profiles and ultimately determine if they are predictive of etiology, trajectory, or treatment response. Furthermore, Arnett will add to this powerful data using a related measure known as Event Related Potentials (ERPs). This technique uses EEGs to measure discrete electrophysiological responses to sensory (audio or visual) stimuli. This ERP data will provide additional information about how children react to stimuli to help Arnett better understand the neurophysiological heterogeneity observed in children with ADHD. She works closely on this project with research affiliates Raphael Bernier, PhD, professor of psychiatry and behavioral sciences and Mark Stein, PhD, professor of psychiatry and behavioral sciences, and director of the PEARL clinic.

Sorting through the differences in ADHD

While past work has established some behavioral classifications of ADHD (i.e., primarily inattentive or hyperactive/impulsive subtypes), they fall short of predicting clinical outcomes or informing about possible etiology. These classifications, Arnett says, "can be helpful in the short term to figure out the child's biggest challenges when interacting with his/her world, but they're not very stable constructs … Most kids, up to 80%, will meet criteria for a different subtype within 1-8 years of the initial diagnosis."

Arnett plans to explore three central questions aimed at achieving a deeper understanding of the heterogeneity seen within ADHD: (1) How do electrophysiology frequencies differ in children with ADHD? (2) How are their neurophysiological responses to stimuli different? and (3) Can we use these data to identify clinically meaningful subtypes of ADHD? Ultimately, Arnett says, the goal of her study is "to identify neurobiological markers using electrophysiological measures that may be useful in predicting outcomes

down the road." Such biomarkers could result in earlier diagnoses and more personalized treatment plans.

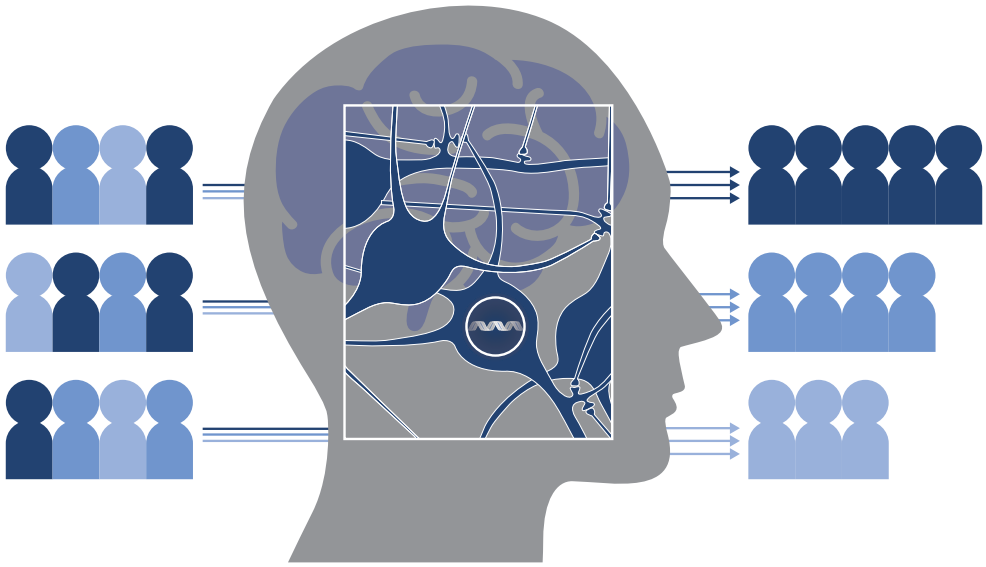
Examining brain waves throughout development

Arnett will use quantitative EEG and ERP, combined with bioinformatics clustering of her data, to observe and classify the differences in children with ADHD. EEG will help her assess spectral power and frequency differences in school-age children. ERP will help her to better understand how these children process stimuli. For the ERP experiments, children will be given two tasks: one simple and one more complicated. Arnett can determine attention capacity by assessing changes in ERP between these two tasks. Children will also face 'distractor stimuli' that will gauge how well they're allocating their attention to the task at hand. Once all of this information is collected, Arnett will use bioinformatic cluster analysis to identify neurobiological profiles. By identifying these profiles, she aims to define ADHD subtypes by electrophysiological data, rather than the more unstable parameters of behavior.

The project has three phases. In the first phase, Arnett is collecting data from 100 school-aged children (ages 7-11 years) with ADHD and 30 children without ADHD. This age group is often thought of as the earliest point for a stable ADHD diagnosis. She will collect and cluster the data as described above, with the end goal of identifying neurobiological profiles in ADHD. The next phase of the project will involve the collection of electrophysiological data from 100 younger children (ages 2.5-4 years) with familial risk for ADHD to identify profile similarities during early development. The final phase is a comprehensive longitudinal study following the development of at-risk infants to monitor electrophysiological changes and how they relate to her findings from the previous two phases.

Down the road: Clinical impact of ADHD profiles

With this ambitious project, Arnett hopes to be able to sort through the heterogeneity of ADHD. The data generated by this undertaking is designed to help children receive earlier and more accurate diagnoses. Additionally, a better understanding of a child's developmental trajectory "can itself be a good intervention to help children and their families know what they need to be prepared for," Arnett points out. Ultimately, this in-depth profiling aims to spark the development of personalized treatment options based on the neurobiological features of an individual child with ADHD.



Arnett and her team hope to use information from patterns of brain electrical activity to sort the heterogeneous population of children with ADHD (represented on the left) into clinically relevant, homogenous subgroups (right).

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