Novel imaging technique reveals brain abnormalities that may play key role in ADHD

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A study published today in the online advance edition of The *American Journal of Psychiatry* for the first time reveals shape differences in the brains of children with ADHD, which could help pinpoint the specific neural circuits involved in the disorder. Researchers from the Kennedy Krieger Institute in Baltimore, Md. and the Johns Hopkins Center for Imaging Science used a new analysis tool, large deformation diffeomorphic mapping (LDDMM), which allowed them to examine the precise shape of the basal ganglia. The study found boys with ADHD had significant shape differences and decreases in overall volume of the basal ganglia compared to their typically developing peers. Girls with ADHD did not have volume or shape differences, suggesting sex strongly influences the disorder's expression.

Previous studies examining the basal ganglia in children with ADHD were limited to volume analysis and had conflicting results, with some reporting a smaller volume and some reporting no difference in volume. LDDMM provides detailed analysis of the shape of specific brain regions, allowing for precise examination of brain structures well beyond what has been examined in previous MRI studies of ADHD. In this study, LDDMM was used to map the brains of typically developing children in order to generate a basal ganglia template. This is the first reported template of the basal ganglia. After creating LDDMM mappings of the basal ganglia of each child with ADHD, statistical analysis was conducted to compare them to the template.

In this study, the initial volume analysis revealed boys with ADHD had significantly smaller basal ganglia volumes compared with typically-developing boys. Moving beyond the standard volume analysis, the LDDMM revealed shape abnormalities in several regions of the basal ganglia. Comparison of the standard volume and LDDMM analysis of girls with ADHD and their typically developing peers failed to reveal any significant volume or shape differences.

The multiple shape differences found in boys with ADHD suggests that the disorder may not be associated with abnormalities in one specific neural circuit. Rather, it appears the disorder involves abnormalities in parallel circuits, including circuits important for the control of complex behavior and more basic motor responses, such as hitting the brake pedal when a traffic light turns yellow. Findings revealing abnormalities in circuits important for basic motor response control may be crucial to understanding why children with ADHD have difficulty suppressing impulsive actions.

"This study represents a major advancement in our ability to examine the neuroanatomic features of ADHD and other developmental disorders," said Dr. Stewart H. Mostofsky, senior study author and a pediatric neurologist in the Department of Developmental Cognitive Neurology at the Kennedy Krieger Institute. "Using LDDMM, we can more accurately measure the impact of ADHD on brain development, which will not only bring us closer to unlocking the biological basis of the disorder, but help us better diagnose and treat patients."

Researchers used MRI scans to examine children ages 8-13 years, including: 47 children with ADHD and a control group of 66 typically developing children. Researchers compared the LDDMM mappings of children with ADHD to their typically developing peers, and then went a step further by repeating the analysis separately for boys and girls. Children with ADHD who had a history of other neuropsychiatric

diagnoses including conduct disorder, mood disorder, generalized anxiety disorder, separation anxiety disorder and/or obsessive-compulsive disorder were excluded from the study. Additionally, none of the children with ADHD had a learning disability or a history of speech/language disorders.

Potential next steps include research that carefully examines whether the brain abnormalities found in this study can predict certain behavioral features of ADHD. Future studies will also examine structural features associated with the ability to compensate and respond to therapy. The researchers also plan to use LDDMM analysis on children in a wider age range to see if changes in the basal ganglia occur over time.

Source: Kennedy Krieger Institute