Neural Correlates of Aggression in Medication Naïve Children with Adhd: Multivariate Analysis of Morphometry and Tractography.


Neuropsychopharmacology. 2015 Feb 3. doi: 10.1038/npp.2015.18. [Epub ahead of print]

Abstract
Aggression is widely observed in children with attention deficit/hyperactivity disorder (ADHD) and has been frequently linked to frustration, or the unsatisfied anticipation of reward. Although animal studies and human functional neuroimaging implicate altered reward processing in aggressive behaviors, no prior studies have documented the relationship between fronto-accumbal circuitry-a critical cortical pathway to subcortical limbic regions- and aggression in medication naive children with ADHD. To examine this, we collected behavioral measures and parental reports of aggression and impulsivity as well structural and diffusion MRI from 30 children with ADHD and 31 healthy controls (HC) (mean age, 10±2.1 SD). Using morphometry and probabilistic tractography combined with multivariate statistical modeling (partial least squares regression and support vector regression), we identified anomalies within the fronto-accumbal circuit in childhood ADHD, which were associated with increased aggression. Specifically, children with ADHD showed reduced right accumbal volumes and frontal-accumbal white matter connectivity compared with HC. The magnitude of the accumbal volume reductions within the ADHD group was significantly correlated with increased aggression, an effect mediated by the relationship between the accumbal volume and impulsivity. Furthermore, aggression, but not impulsivity, was significantly explained by multivariate measures of fronto-accumbal white matter connectivity and cortical thickness within the orbitofrontal cortex. Our multi-modal imaging, combined with multivariate statistical modeling, suggests that the fronto-accumbal circuit is an important substrate of aggression in children with ADHD. These findings suggest that strategies aimed at probing the fronto-accumbal circuit may be beneficial for the treatment of aggressive behaviors in childhood ADHD.