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Relationship between brain stem volume and aggression in children diagnosed with autism spectrum disorder[☆]

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ABSTRACT

Background: Aggressive behaviors are common in individuals diagnosed with autism spectrum disorder (ASD) and may be phenotypic indicators of different subtypes within ASD. In current research literature for non-ASD samples, aggression has been linked to several brain structures associated with emotion and behavioral control. However, few if any studies exist investigating brain volume differences in individuals with ASD who have comorbid aggression as indicated by standardized diagnostic and behavioral measures.

Method: We examined neuroimaging data from individuals rigorously diagnosed with ASD versus typically developing (TD) controls. We began with data from brain volume regions of interest (ROI) taken from previous literature on aggression including the brainstem, amygdala, orbitofrontal cortex, anterior cingulate cortex, and dorsolateral prefrontal cortex. We defined aggression status using the Irritability subscale of the Aberrant Behavior Checklist and used lasso logistic regression to select among these predictor variables. Brainstem volume was the only variable shown to be a predictor of aggression status.

Results: We found that smaller brainstem volumes are associated with higher odds of being in the high aggression group.

Conclusions: Understanding brain differences in individuals with ASD who engage in aggressive behavior from those with ASD who do not can inform treatment approaches. Future research should investigate brainstem structure and function in ASD to identify possible mechanisms related to arousal and aggression.

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[☆] Brain volumes associated with high levels of aggression in male children diagnosed with autism spectrum disorder.

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1. Introduction

Aggressive behavior is a common symptom of autism spectrum disorders (ASD) that can be particularly difficult for families to manage (Dominick, Davis, Lainhart, Tager-Flusberg, & Folstein, 2007; Farmer et al., 2014; Horner, Carr, Strain, Todd, & Reed, 2002; Kanne & Mazurek, 2011; Mazurek, Kanne, & Wodka, 2013). In particular, parents frequently report that aggression in their child is more distressing than poor adaptive skills (Lecavalier, Leone, & Wiltz, 2006).

In typically developing (TD) children, there is mounting evidence that increased aggression is associated with brain functioning in regions of emotional or behavioral control (Lamm, Granic, Zelazo, & Lewis, 2011; Lozier, Cardinale, VanMeter, & Marsh, 2014; Paus, 2005; Sterzer & Stadler, 2009). Particular regions identified include the amygdala, brainstem, orbitofrontal cortex (OFC), dorsolateral prefrontal cortex (DLPFC), and anterior cingulate cortex (ACC) (Coccaro, McCloskey, Fitzgerald, & Phan, 2007; Ducharme et al., 2011; Kolla et al., 2015; Rylands et al., 2012; Saxbe, Del Piero, Immordino-Yang, Kaplan, & Margolin, 2016; Siegel & Victoroff, 2009; Visser et al., 2014). These regions might also be associated with increased aggression in children with ASD. Because brain function is linked in some degree to brain structure (Meier et al., 2016; Ponten, Daffertshofer, Hillebrand, & Stam, 2010; Stam et al., 2015), we reasoned that these findings from functional scans would provide a useful starting place for examining structural integrity.

To date, few if any studies exist investigating brain volume differences in individuals with ASD who have comorbid aggression. Because aggression is likely related to brain function in regions of emotional control and occurs in some children with autism but not others, it may be useful to use aggression as an indicator of different subcategories of ASD. This approach may increase the likelihood that researchers will find reliable associations between symptoms and brain regions (Chaste et al., 2015). Improved understanding of brain correlates with behavioral outcomes could go a long way towards identifying effective interventions (South, Wolf, & Herlihy, 2012). Understanding brain differences in individuals with ASD who engage in aggressive behavior from those with ASD who do not have frequent aggressive behaviors can inform treatment

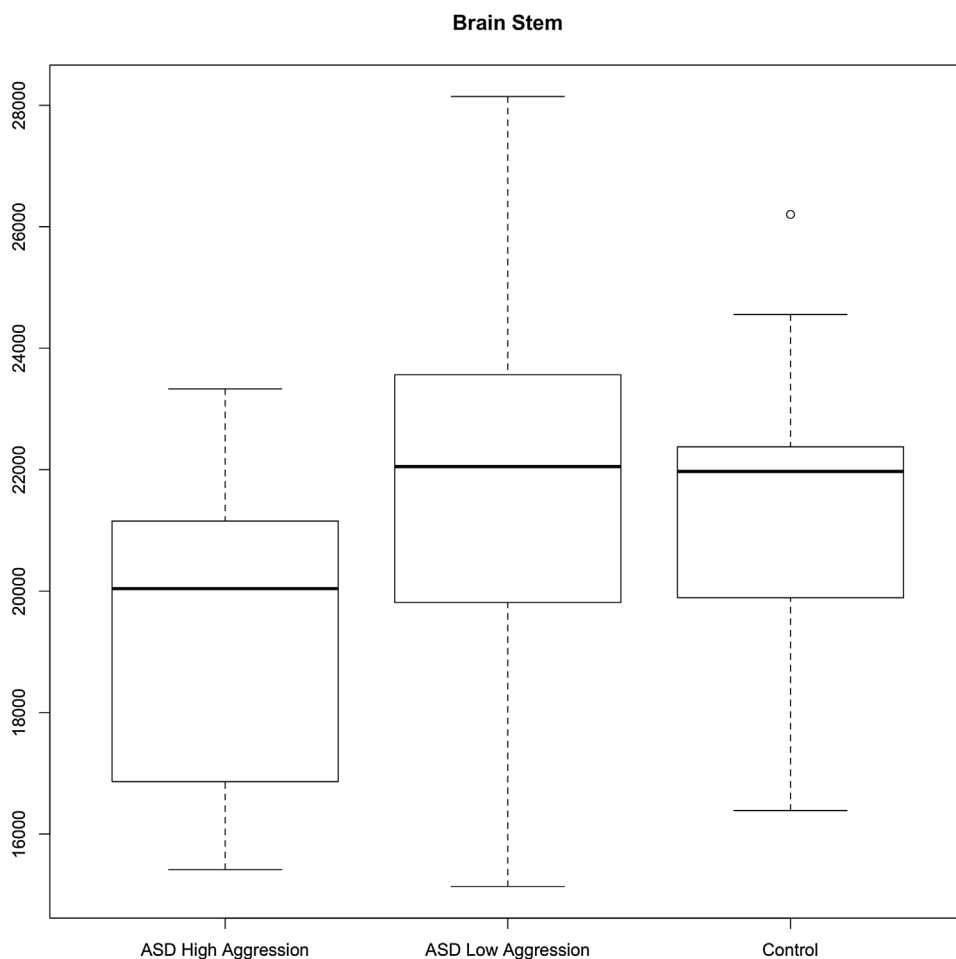


Fig. 1. Brainstem volume (in mm^3) by group. The boxes represent the median and the first and third quartiles for each group. The whiskers represent the minimum and maximum of all data in each group. The low aggression ASD group is more similar to the control group on brainstem volume.

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