Cortical Volumes Predict Intervention Outcomes to Propranolol in Autism Spectrum Disorder

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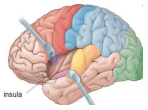
Introduction

- Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social communication deficits and repetitive behaviors
- Recent studies on the efficacy of using propranolol, a ß-adrenergic antagonist, as an intervention for ASD have shown strong improvements in social communication symptoms (Beversdorf et al, 2008).
- Past neuroimaging studies have examined structure differences in the volumetrics of individuals with ASD.
- It has been seen that there is a reduced functional connectivity across language regions, particularly Wernicke's area (Wan et al, 2010).
- Altered functional connectivity has been found in the insular cortex, (Uddin & Menon, 2009), which could contribute to poorly developed emotional awareness, or inability to recognize others mental state in ASD.

Objective

The present study sought to provide evidence that cortical brain volume predicts a change in social behavior in response to propranolol in those with ASD.



Methods

Participants

A sample of 5 individuduals diagnosed with ASD participated in this study *(M=17.2) (SD=2.8)*. These individuals were recruited from the Thompson Center for Autism and Neurodevelopmental Disorders during their clinical visit.

Image Acquisitioning and Processing

Individuals with ASD participated in a magnetic resonance imaging (MRI) session utilizing a Siemens 3T Trio scanner (Siemens, Malvern, PA) and standard 8-channel head coil at the Brain Imaging Center. Structural T1-weighted 3D MR images were acquired for each participant (MPRAGE, TR=1920 ms, TE=2.92 ms, Flip Angle=9 degrees, FOV=256x256, matrix size=256x256, 1 mm^3 resolution with sagittal acquisition). T1-weighted images were processed to obtain gray matter volume using FreeSurfer version 6.0 image analysis suite (surfer.nmr.mgh.harvard.edu/).

General Social Outcome Measure (GSOM)

GSOM2-A was developed in 2012 to measure an individual's social behavior. It is separated into four parts: conversational reciprocity, facial expressions, social problem solving, and affect demonstration. The conversation was discontinued after lack of response to any prompting and the individual was rated using a Likert Scale throughout entire measure. These scores were then accumulated to form an overall GSOM score that represented a measure of their social ability..

Drug Administration

Individuals with ASD are allowed to participate in an open-label trial of propranolol for 15 weeks following completion of a 12-week, double-blinded trial of propranolol. 40 mg of propranolol is administered nightly for one week (as with previous dose titration), then increased to 40mg twice a day for one week, then maintained at 100mg a day in divided doses (40/20/40). The dose is immediately decreased back to the previous level if the heart rate dropped below 55 or systolic blood pressure drops below 90 after the increase, which is assessed in a visit within the first 48 hours after each change in dose. A follow up call is also used to confirm no further problems before each increase. After 12 weeks, subjects are weaned off by decreasing the dose to one 40mg each day and then a 20mg pill each day for the last week.

Results

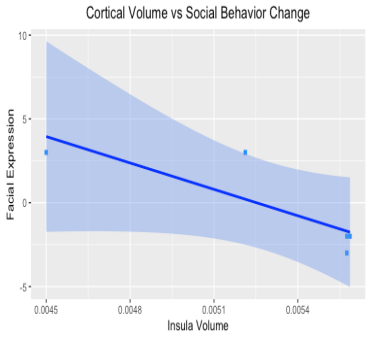


Figure 1: Linear regression model of Insuala Volume and change in Facial Expression GSOM after propranolol. ***p = 0.021***

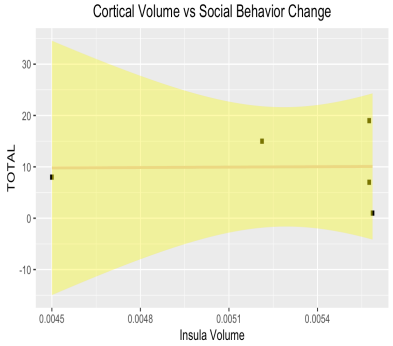


Figure 2: Linear regression model of Insula Volume and change in Total GSOM after propranolol is nonsignificant.

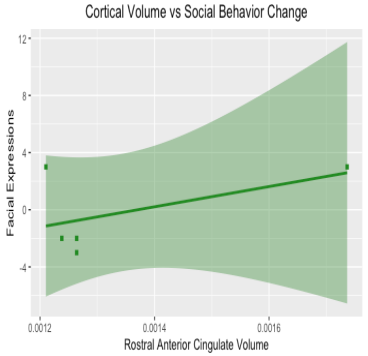


Figure 3: Linear regression model of Rostral Anterior Cingulate Volume and change in Facial Expression GSOM after propranolol. ***p = 0.015***

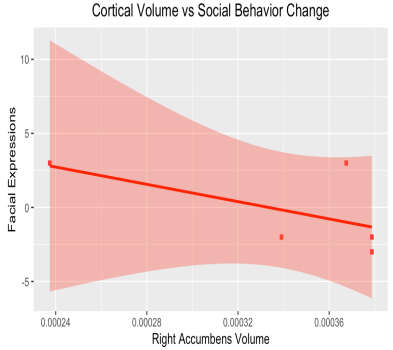
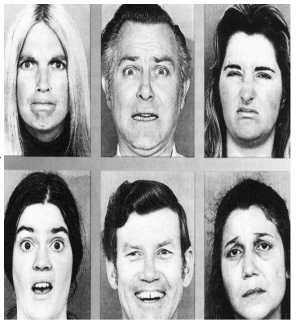


Figure 4: Linear regression model of Right Accumbens Volume and change in Facial Expression GSOM after propranolol. ***p = 0.023***

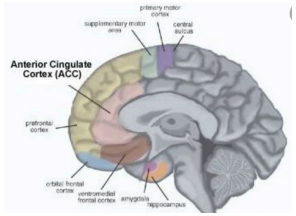
Results Summary

- Significant relationships between gray matter volume and GSOM scores were found only within the Facial Expressions (FE) category.
- Multiple regions across frontal, temporal, and occipital lobes had significant relationships to GSOM FE change, including the left hemisphere insula and right hemisphere rostral anterior cingulate cortex (rACC).
- Subcortical volumes were also analyzed and areas of the right caudate and both the right and left accumbens were found to have significant relationships.
- There were no significant relationships between left or right superior temporal gyrus and GSOM.



Conclusion

- These results validate that there are regions of the brain that can be used as biomarkers for the efficacy of propranolol improving social behavior.
- These findings indicate how the insula and ACC play a role in the decrease of functional connectivity within these regions in individuals with ASD.
- Results regarding subcortical areas, like the accumbens and caudate are also important to initiate research of the reward network and propranolol.



Limitations and Future Work

The power of the results in this study is decreased due to limited sample size (N=5). A larger sample size is necessary to assess the validity of these brain regions.

Pursuing research in identifying the biomarkers correlated with an increase in social behavior will help further studies evaluating how propranalol directly effects certain brain regions.

References

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