Evidence for an altered resting-state network in adults with Asperger's Disorder

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INTRODUCTION

Low frequency (< 0.08 Hz) synchronized oscillations in resting state timecourses have been detected in recent fMRI studies [1-3]. These fluctuations are important as a potential measure of connectivity between functionally related areas of the brain. It has also been shown that these functional connectivity patterns are altered in some neurological diseases, such as Alzheimer's [4], and in response to psychopharmacological agents, (i.e., cocaine [5]). Thus, detection of functional connectivity patterns may serve as an indicator of typical brain activity and its pathophysiology.

In this work, we examined resting state functional connectivity using fMRI in adults with Asperger's Disorder (AD), a diagnosis that describes individuals with atypical social development [6]. Functional connectivity associated with the posterior cingulate was analyzed and compared with results from control subjects. Previous studies have identified a resting state network comprised of the posterior cingulate, medial prefrontal cortex, and lateral parietal cortex [7-8]. This study examined this network in adults with AD as compared to healthy controls.

METHODS

Acquisition

Resting state MR scans were acquired on a 3 T Siemens Trio scanner (Tuebingen, Germany), using an EPI pulse sequence. Pulse sequence parameters were TR/TE/FA/FOV of 750 ms/35 ms/50°/22 cm. Ten contiguous 5-mm thick axial slices were acquired in each TR, with an in-plane resolution of 3.44 mm x 3.44 mm, covering the posterior cingulate, as well as medial prefrontal cortex. Resting date data were acquired while subjects were lying still (eyes open, looking at a visual fixation cross). A total of 280 volumes were collected during a 3.5 minute scan. Five AD patients and eight healthy controls, comparable in age and IQ level, were studied. A neuropsychological assessment was performed by a Ph.D.-level clinical psychologist to document IQ and confirm the AD diagnosis in the target population. In addition, a brief neuropsychological screening was conducted to assess IQ level and rule out the presence of psychiatric disorders or history of chronic illness in the control population. Written informed consent was obtained for all subjects prior to enrollment in the study.

Analysis

All individual data were transformed to Talaraich space using SPM2 (Wellcome Department of Imaging Neuroscience, London, UK). The dorsal posterior cingulate cortex was identified (Talaraich: -2,-48,27), and the corresponding seed ROI (four voxel block) was selected in the original acquisition space. The timecourse of this ROI in the resting state data was averaged across all four voxels, and low-pass filtered < 0.08 Hz. This low frequency reference timecourse was then correlated with the low-pass filtered resting state data across the entire brain volume to form functional connectivity maps (i.e., low frequency timecourse correlation maps), a common method for examining resting state functional connectivity [1-3]. The generated functional connectivity correlation maps were then transformed to Talaraich space to define the anatomic location of the correlated voxels, and to assess group differences. Five slices (ranging from approx. z=+5 mm to z=+30 mm) common to all subjects were used in the analysis. Qualitative changes in functional connectivity between groups were assessed through visual inspection of the resultant functional connectivity maps. Quantitative changes were defined by the degree of overlap between the functional connectivity maps and a standard anatomical template for the medial structures that comprise the resting state network of interest [including PCC, anterior cingulate cortex (ACC), medial prefrontal cortex]. This mask was formed using WFU_PickAtlas [9] in SPM2. The coefficient of areal correspondence was defined as the overlap between two maps divided by their union. This method yielded an areal correspondence coefficient measure for every subject.

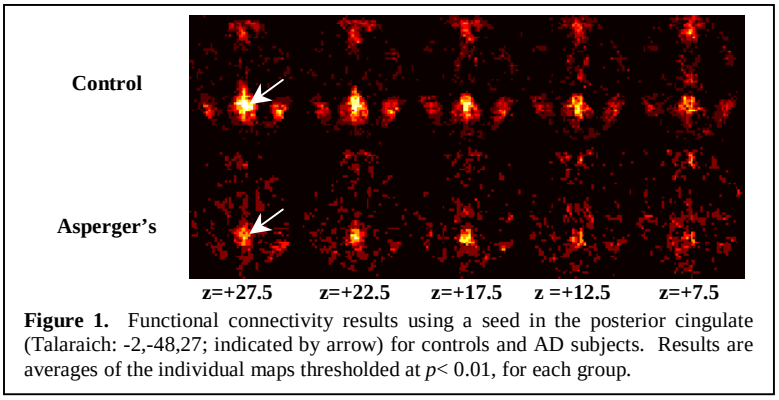

Figure 1. Functional connectivity results using a seed in the posterior cingulate (Talaraich: -2,-48,27; indicated by arrow) for controls and AD subjects. Results are averages of the individual maps thresholded at $p < 0.01$, for each group.

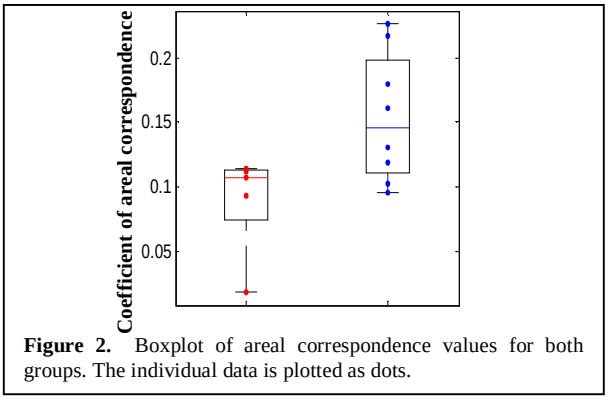

Figure 2. Boxplot of areal correspondence values for both groups. The individual data is plotted as dots.

RESULTS

Results for the average functional connectivity maps for each group are shown in Figure 1. The connectivity maps for the control subjects exhibited significant temporally correlated activity in the PCC, anterior cingulate cortex (ACC), medial frontal cortex (MFC), and bilateral BA 39. This pattern is comparable to that found in previous 'default mode' connectivity studies [7-8]. The connectivity maps for the AD subjects exhibit reduced connectivity within the PCC, ACC, MFC, and BA 39. Figure 2 plots the areal correspondence coefficients for both groups using the anatomical template defined for this study. Examination using t-test of group values revealed a significant difference between the two groups (Mean(SD)= Controls 0.15(±0.05), AD: 0.08(±0.04); $p < 0.03$).

CONCLUSION

Functional connectivity patterns associated with the dorsal posterior cingulate cortex differentiated between control subjects and adults with Asperger's Disorder. Functional connectivity may thus serve as a diagnostic or prognostic marker of Asperger's Disorder. Future studies will determine the stability of these findings in a larger population, and will examine their clinical significance.

REFERENCES

[1] Biswal B,et al. 1995. MRM 34:537.
[2] Lowe MJ, et al. 1998. Neuroimage 7:119.
[3] Peltier SJ, Noll DC. 2002. Neuroimage 16:985.
[4] Grecius MD, et al. 2004. PNAS 101: 4637.
[5] Li SJ, et al. 2000. MRM 43:45.
[6] APA, 1994. DSM-IV, Washington DC.
[7] Raichle, ME, et al. 2001. PNAS 98:676.
[8] Grecius MD, et al. 2003. PNAS 100: 253.
[9] Maldjian, et al. 2003. Neuroimage 19:1233.

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