

Heterogeneous Structural Connectivity of Default Mode Network in Patients with Autism Spectrum Disorder

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Target audience: People interested in the default mode network, structural MRI, and autism spectrum disorder.

Purpose: Several functional studies have shown abnormalities in the default mode network (DMN) in patients with autism spectrum disorder (ASD) [1]. However, there are few studies to probe the underlying structural differences of DMN in ASD, and fiber tracking of DMN is limited by the inability of diffusion tensor imaging to differentiate crossing fibers. Diffusion spectrum imaging (DSI) can resolve the problem of crossing fibers, and so in this study it was used to track the white matter fiber tracts interconnecting the brain regions of the DMN, namely the medial prefrontal cortex (MPFC), posterior cingulate cortex (PCC), inferior parietal lobe (IPL), and hippocampal formation (HF). White matter integrity was evaluated in terms of generalized fractional anisotropy (GFA) and compared between ASD patients and typically developing controls (TD).

Methods: 14 ASD patients (gender (M/F): 13/1; mean age: 22.43±4.11 years) and 14 TD controls (gender (M/F): 13/1; mean age: 21.07±4.53 years) were included in the study. Images were acquired on a 3T MRI system with a 32-channel head coil (Siemens, Erlangen, Germany). DSI was performed using a twice-refocused balanced echo diffusion EPI sequence, TR/TE = 9600/130 ms, matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm², and slice thickness = 2.5 mm. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity $b_{max} = 4000s/mm^2$ were sampled on the grid points of a half sphere in the 3D q-space with $|q| \leq 3.6$ units [2]. A subject specific template (SST) was created from all recruited subjects using the Large Deformation Diffeomorphic Metric Mapping (LDDMM) method [3]. Fiber tracking was done on the SST using regions of interest (ROIs) defined in the Automatic Anatomical Labeling system. Each tract was subdivided into multiple steps with even spacing [4] and the step coordinates along tract bundles were saved as sampling coordinates. The sampling coordinates were transformed to the native space of each subject to sample the GFA of each tract. Mean GFA values were checked for normal distribution and compared between ASD and TD using either independent t-tests or Kruskal-Wallis tests.

Results: Fiber tracts were found between every two ROIs except those between MPFC-IPL, MPFC-HF, and IPL-HF (Fig 1). The tract connecting MPFC-PCC was the dorsal cingulum bundle (CB_{dorsal}), and the tract connecting PCC-HF was the ventral cingulum bundle ($CB_{ventral}$). There were commissural fibers connecting bilateral MPFC, bilateral IPL, and bilateral HF. Significant difference in mean GFA was only seen in the left PCC-IPL tract, with ASD having a higher mean GFA than TD. There was a tendency that long white matter fiber tracts (>100 mm) have lower mean GFA values in ASD compared to those of TD; and short white matter fiber tracts (<100 mm) have higher mean GFA values in ASD compared to those of TD (Table 1).

Discussion: Functional resting-state studies have demonstrated hypoconnectivity between anterior and posterior medial cortex, while hyperconnectivity between local cortical regions in ASD patients [5]. We postulate that this phenomenon is reflected through the mean GFA of white matter tracts of different lengths. The difference may not be significantly shown due to the small sample size. An increase in subject number can validate our assumption.

Conclusion: Our results suggest that the hypo- and hyperconnectivity between brain regions in ASD can be shown through the mean GFA value of the interconnecting white matter fiber tracts. Further work with a larger subject group is warranted.

References: [1] Broyd, S. J., et al. (2009) *Neurosci Biobehav Rev*. Mar; 33(3):279-96. [2] Wedeen, V. J., et al. (2005) *Magn Reson Med*. Dec; 54(6):1377-86. [3] Hsu, Y. C., et al. (2012) *Neuroimage*. Nov 1; 63(2):818-34. [4] Chiang, W. Y. et al. (2007). *Proc 16th ISMAR*. [5] Washington, S. D. et al. (2013). *Hum Brain Mapp*. Jan 18.

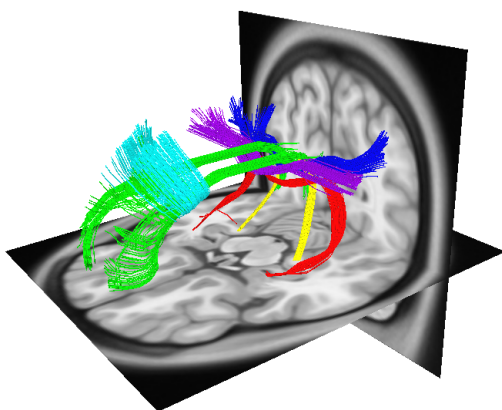


Figure 1. An image of the interconnecting fibers between brain regions of the default mode network. The green tracts are CB_{dorsal} , the yellow tracts are $CB_{ventral}$, and the blue tracts are PCC-IPL. The commissural fibers between MPFC, HF, and IPL are in light blue, red, and purple, respectively.

		Length (mm)	Mean GFA		p-value
			ASD	TD	
PCC-IPL	L	71.25	0.236	0.222	0.035
	R	73.75	0.227	0.220	0.345
$CB_{ventral}$	L	70	0.261	0.263	0.892
	R	78.75	0.256	0.251	0.7
CB_{dorsal}	L	142.5	0.308	0.314	0.341
	R	160	0.310	0.319	0.075
Commissural fibers					
MPFC		123.75	0.286	0.294	0.315
HF		193.75	0.323	0.340	0.089
SMG		187.5	0.300	0.308	0.168

Table 1. The statistical results of the difference in mean GFA of each white matter fiber tract. Short fiber tracts tend to have a higher mean GFA in ASD; long fiber tracts tend to have a lower mean GFA in ASD. The only significant difference is seen in the left PCC-IPL.