

## Structural connectivity of the default mode network in adolescents with autism spectrum disorders

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### Introduction

The default mode network (DMN) is a specific system which activates in the resting state and social tasks, and deactivates in performing the goal-oriented and cognitive demanding tasks [1]. Previous findings suggested that adults with autism spectrum disorders (ASD) failed to suppress the DMN activation in tasks and had weaker intrinsic functional correlation [2-3]. The evidence from functional imaging studies speculated that under-connectivity of the cortical systems existed in ASD and consequently caused the functional deficit [4-6]. This study aimed to investigate the structural connectivity of DMN in children with adolescents with ASD as compared to typically developing (TD) adolescents.

### Methods

We assessed 13 adolescents with ASD (high functioning autism and Asperger's syndrome, aged  $15.0 \pm 0.94$ ), who were formally diagnosed by child psychiatrists and confirmed by the ADI-R; and 13 age-, sex-, and handedness-matched TD adolescents, aged  $14.8 \pm 1.52$ . All the participants and their parents provided written informed consent. The DSI images were acquired on a 3T MRI system (TIM Trio, Siemens) with a 32-channel head coil and performed using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, FOV = 200 x 200 mm, image matrix size = 80 x 80, and slice thickness = 2.5 mm. 102 diffusion encoding gradients with the maximum diffusion sensitivity  $b_{\max} = 4000$  s/mm<sup>2</sup> were sampled on the grid points in the 3D q-space with  $|q| \leq 3.6$  units [7]. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction. The intravoxel fiber orientations were determined by decomposing the original ODF into several constituent ODFs. Further, those primary fiber orientations were used for tractography reconstruction. To reconstruct the 15 white matter tracts in DMN (Figure 1), we placed predefined regions of interest (ROI) based on previous DMN studies (e.g. medial prefrontal cortex, medial temporal lobe, posterior cingulate cortex, and inferior parietal lobule). The ROIs were transformed from Montreal Neurological Institute (MNI) space through the DSI template performed by large deformation diffeomorphic metric mapping (LDDMM) [8] to the individual native DSI. The mean generalized fractional anisotropy (GFA), an index for white matter integrity, of a specific tract was computed by calculating the weighted sum of the GFA sampled along the tract bundle. Asymmetric difference of left (L) and right (R) hemispheres in GFA values was also determined using a lateralization index (LI) =  $(L-R) / ((L+R) / 2)$  [9]. A repeated measures ANOVA with hemisphere (right and left) and tracts as the within-subjects factor and group (ASD and TD) as the between-subjects factor was performed.

### Results

Despite no significant group difference, the mean GFA of nine fiber bundles of DMN showed higher value in the ASD group than the TD group, especially the right superior fronto-occipital fasciculus (SFOF) ( $F(1, 24) = 3.611$ ,  $p = .069$ ) and the bilateral uncinate fasciculus (UF) ( $F(1, 24) = 3.284$ ,  $p = .082$  for the right and  $F(1, 24) = 3.423$ ,  $p = .077$  for the left) (Figure 2). The SFOF is one long range fiber connecting the frontal region to the parietal region to communicate the social cognition consciously, which was thought to present functional hypo-connectivity in ASD. The higher mean GFA might suggest compensatory mechanism of white matter for balancing the functional performance. It is known that the UF is the latest matured neural fiber in development. Its function has not been clearly identified but is believed to be correlated with some psychiatric symptoms. The commissural fibers were reported to be reduced in ASD in some studies [9-10], and the genu and splenium actually showed the similar tendency of reduction in our ASD group. There was neither significant group difference in all LIs nor correlations between the mean GFA of callosal fibers and LI for these six pairs of association fiber bundles.

### Conclusion

Using the LDDMM normalization and transformation procedure for the predefined ROIs, we successfully tracked the 15 fiber bundles of DMN in adolescents with ASD and TD. With a current small sample size, our study provides weak evidence showing that structural connectivity within DMN might be altered in adolescents with ASD.

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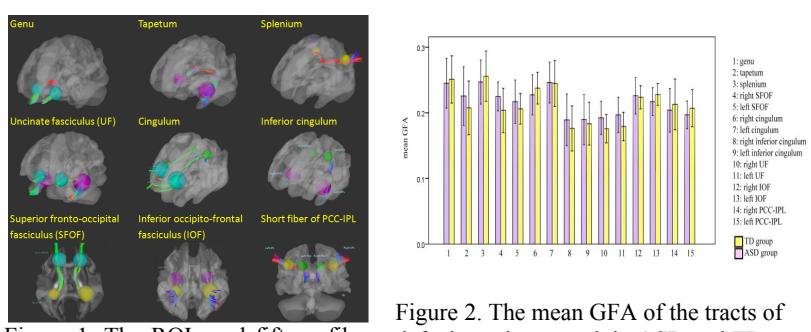


Figure 1. The ROIs and fifteen fiber bundles of default mode network

Figure 2. The mean GFA of the tracts of default mode network in ASD and TD groups.