Altered functional significance of structural connectivity for language processing in autism spectrum disorders

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Introduction Autism spectrum disorders (ASD) are a group of neurodevelopment disorders with language-communication deficit as one of the three core symptoms. Patients with high function autism or Asperger's syndrome showed worse performance than neurotypicals in complex language tasks such as comprehension and inference [1]. Despite the striking nature of the language phenotype in ASD, little is known about the brain basis of this fundamental feature [2]. In this study, we investigated the dorsal (including arcuate fasciculus and superior longitudinal fasciculus Ⅲ) and ventral (including Inferior frontal-occipital fasciculus and inferior longitudinal fasciculus) pathways responsible for language processing [3] [Fig. 1]. We hypothesized that the functional significance of structural connectivity for language processing was altered in adolescents with ASD.

Materials and methods Twenty right-handed male adolescents with ASD and 20 matched neurotypical participants were recruited in this study. Images were acquired on a 3T MRI system with a 32-channel head coil (Tim Trio, Siemens, Erlangen, Germany). DSI was performed using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, image matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm^2, and slice thickness = 2.5 mm. 102 diffusion encoding gradients with the maximum diffusion sensitivity b_{max} = 4000 s/mm^2 were sampled on the grid points in the 3D q-space with $|q| \leq 3.6$ units [4]. DSI analysis was performed based on the relationship that the echo signal S(q) and the diffusion probability density function P(r) were a Fourier pair, i.e., S(q)=FT{P(r)}. 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 [5], and those primary fiber orientations were used for tractography reconstruction. Tractography was reconstructed using a streamline-based algorithm adapted for DSI data and the targeted tracts were selected by specific regions-of-interest. Generalized fractional anisotropy (GFA) was quantified at each voxel based on the directional variance of the original ODF [6]. A method that projected the GFA onto a single mean path of a specific white matter tract, called mean path analysis, was used to analyze local changes in structural connectivity along the individual tract bundles [7].

Results The clinical assessment showed that patients' past symptoms fulfilled the criteria of the diagnosis of pervasive developmental disorders as defined by the DSM-IV and ICD-10. The Wechsler Intelligence Scale for Children-3rd edition was administered to all the 40 participants [Table 1]. We found significant differences in full-scale IQ (FIQ), verbal IQ (VIQ), and verbal comprehension index (VCI) between ASD and neurotypicals. There was no significant group difference in GFA of both dorsal and ventral pathways. However, left-greater-than-right asymmetry was absent in patients with ASD. An exploratory correlation analysis was performed between GFA of language pathways and IQ scores. The GFA of the left dorsal pathway was positively correlated with VIQ (r = 0.493, *p*=.0027) in neurotypicals, whereas the GFA of the left ventral pathway was positively correlated with VCI (r = 0.447, *p*=.0048) in patients with ASD [Fig. 2].

Discussion Fletcher *et al.* report no significant clinico-pathological relationship between microstructure of the arcuate fasciculus and language function in ASD [2]. Our study confirms their results and further shows that the left ventral pathway rather than the left dorsal pathway corresponds to better language performance. The atypical functional significance implies that language processing through the left dorsal pathway might be impaired in ASD, and the ventral pathway is resorted to compensate for language comprehension. In conclusion, altered structural connectivity of the language pathways and atypical functional significance might attribute to language-communication deficits in ASD.

References [1] D. L. Williams *et al*., Child Neuropsychol. 2006; 12(4-5): 279-98. [2] P.T. Fletcher *et al.*, NeuroImage 2010; 51:1117-25. [3] D. Saur *et al*., PNAS 2008 ; 105(46) :18035-40. [4] V.J. Wedeen, *et al*., Magn Reson Med. 2005; 54:1377-86. [5] F.C.Yeh, *et al*., Proc ISMRM, 2008. [6] D.S. Tuch, Magn Reson Med, 2004; 52, 1358-1372. [7] W.Y. Chiang, *et al*., Proc ISMRM, 2008.

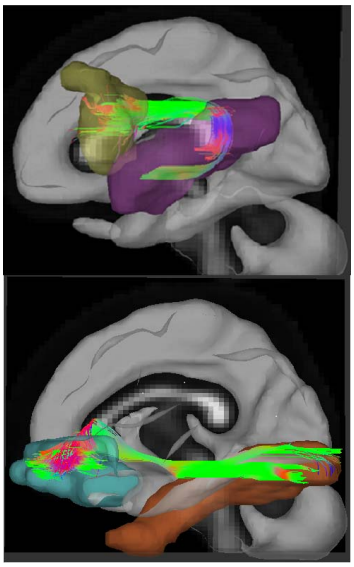

Fig.1 Upper panel: left dorsal pathway with the ROIs at the opercular part of the inferior frontal gyrus (yellow), and superior temporal gyrus (purple). Lower panel: left ventral pathway with the ROIs at the orbital part of the inferior frontal gyrus (blue), and fusiform gyrus (orange).

Table 1 Differences in IQ between ASD and neurotypicals

	Autism (n=20)		Neurotypical (n=20)		*p*
	Mean	SD	Mean	SD	
Age, in years	13.7	2.8	13.7	2.9	0.95
Full-scale IQ	101.3	13.8	112.1	13.1	0.016*
Verbal IQ	101.5	12.9	112.8	10.6	0.004*
Performance IQ	101.9	17.8	109.1	14.6	0.17
Verbal comprehension index	102.9	12.8	112.6	11.2	0.015*
Perceptual organization index	105.7	19.5	110.6	16.2	0.39
Freedom from distractibility index	97.8	12.4	110.8	13.2	0.004*

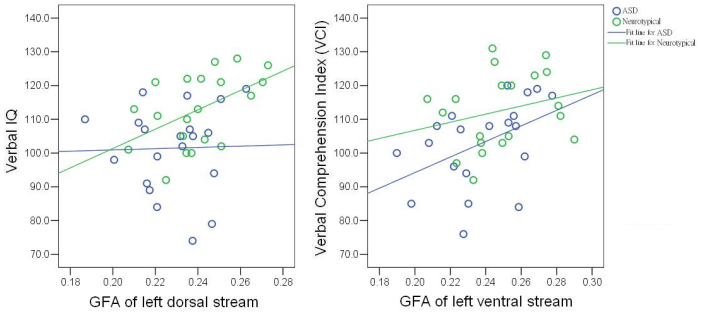

Fig. 2 Left: positive correlation between VIQ and GFA of the left dorsal pathway in neurotypicals. Right: positive correlation between VCI and GFA of the left ventral pathway in ASD.