Dual language pathways associate with attention and language deficits in high-functioning autism: a diffusion spectrum imaging (DSI) study

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Objective Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders with language-communication deficit as one of the core symptoms. Patients with high-functioning autism show worse performance than neurotypicals in complex language tasks such as comprehension and inference. In our previous study [1], we found altered structure-function relations in autism suggesting involvement of the dorsal (including arcuate fasciculus and superior longitudinal fasciculus Ⅲ) and ventral pathways (including Inferior frontal-occipital fasciculus and inferior longitudinal fasciculus) in compensating for the deficient semantic processing in autism (Figure 1). Keehn and colleagues [2] proposed that attention impairments are the key cognitive deficits leading to autism symptomatology, including language deficits. In light of these studies, we hypothesized that the dual pathways in autism may play a role not only in language processing but also in attention.

Methods Forty right-handed male youths with ASD and 40 matched neurotypical participants (aged 8 to 21) were recruited in the study. All participants underwent clinical assessments, the Chinese ADI-R interview (the autism group only), the Chinese K-SADS-E interview, Wechsler Intelligence Scale for Children-3rd edition (WISC–III), and Continuous Performance Test (CCPT-II). 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 bmax = 4000 s/mm^2 were sampled on the grid points in a half sphere of the 3D q-space with $|q| \leq 3.6$ units [3]. DSI analysis was performed based on the Fourier relationship between the echo signal S(q) and the diffusion probability density function P(r) [4]. 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, and 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 in terms of SD(ODF)/RMS(ODF) [1]. The GFA values were projected onto a single mean path of a specific white matter tract to analyze local changes in white matter integrity along the individual tract bundles.

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. We found significant differences in full-scale IQ (FIQ), verbal IQ (VIQ), and verbal comprehension index (VCI) between ASD and neurotypicals. There was a significant difference in GFA of left dorsal pathways between two groups, and left-greater-than-right asymmetry was absent in ASD. In ASD, CCPT-II measures were correlated with GFA of right dorsal pathways and GFA of left ventral pathways (see Table 1). Moreover, CCPT-II measures were correlated with omissions errors and VIQ/VCI (r=-0.420, p=0.008; r=-0.341, p=0.033, respectively).

Conclusion In this study, we used DSI to measure white matter property of the dual language pathways, and investigated its relationships with language and attention processing in youths with ASD. Reduced white matter integrity and less leftward lateralization of dual pathways were found. The correlations among CCPT-II measures, IQ, and white matter integrity also revealed unique characteristics in autism. The GFA values in left ventral and right dorsal pathways were associated with sustained attention and vigilance. Moreover, sustained attention performance was associated with VIQ and VCI. In conclusion, dual pathways involved not only language but also attention in ASD, suggesting that the roles of the dual pathways differ between neurotypicals and ASD.

Reference [1] Y.C. Lo, et al., 2013; [2] B. Keehn, et al., 2013; [3] L.W. Kuo, et al., 2008; [4] V.J. Wedeen, et al., 2005.

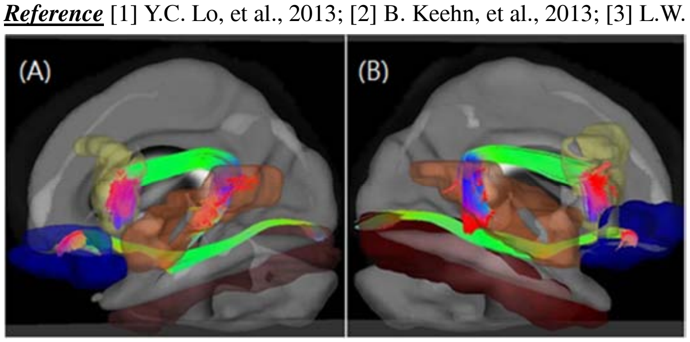

Figure 1 (A) Left dorsal pathway with the ROIs at the opercular part of the inferior frontal gyrus (yellow), and superior temporal gyrus (orange). Left ventral pathway with the ROIs at the orbital part of the inferior frontal gyrus (blue), and fusiform gyrus (red). (B) Right dorsal pathway with the ROIs at the opercular part of the inferior frontal gyrus (yellow), and superior temporal gyrus (orange). Right ventral pathway with the ROIs at the orbital part of the inferior frontal gyrus (blue), and fusiform gyrus (red).

	AUTISM (n=40)		
	Sustained attention	Vigilance	
	Hit SE BC	Hit RT ISI	Hit SE ISI
Left dorsal GFA	r=-0.269, p=0.098	r=-0.064, p=0.697	r=-0.245, p=0.133
Right dorsal GFA	r=-0.329, p=0.041	r=-0.325, p=0.043	r=-0.385, p=0.016
Left ventral GFA	r=-0.210, p=0.199	r=-0.406, p=0.010	r=-0.216, p=0.186
Right ventral GFA	r=-0.194, p=0.237	r=0.181, p=0.271	r=0.005, p=0.974

Table 1 There were negative correlations between CCPT-II measures and GFA of right dorsal pathways and GFA of left ventral pathways in ASD.