White Matter Abnormalities in Boys with Autism Spectrum Disorders: Preliminary evidence from Diffusion Tensor Imaging

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Introduction

Autism spectrum disorders (ASD) are characterized by qualitative impairments of reciprocal social interaction and deficits in communication, and stereotyped or repetitive pattern of behavior. ADS inclued autism, pervasive developmental not otherwise specified (PDD-NOS) and Asperger syndrome. The neurobiological pathogenesis of ASD is still unknown and unclear, but several neuroimaging studies have reported abnormalities in various regions of the brain associated with these severe and persistent conditions, including decreased gray matter volume in cerebellum [1] and decreased volume of medial temporal structures such as the amygdala and the hippocampus in non-mentally retarded autistic subjects [2]. Recent functional magnetic resonance imaging (fMRI) studies in the subjects with autistic disorder have suggested evidences of abnormal activation in brain area associated social cognition. In particular, the fusiform face area (FFA) which is known to be related to the key role in social perception is functionally activated less in the subjects with ASD compared with healthy control subjects while they perform the face perception tasks [3]. A few reports have shown the abnormalities of white matter in autism using diffusion tensor imaging (DTI), which is an MRI technique that is a non-invasive tool for in vivo mapping of human brain connectivity and might be useful for understanding the organization of axons and myelin sheath. There is still lack of evidence showing strong relation to abnormalities in white matter structural integrity with autism even though replicating study to support those abnormalities currently are increasing by using the DTI technique. In this study, we aimed to evaluate the structural integrity of white matter fiber in male children with high-functioning ASD compared to matched male control children by using DTI. We hypothesized that different white matter structures near "social brain" structure as well as corpus callosum would be abnormal in the ASD subjects.

		ASD (n=17) Mean±SD	Control (n=17) Mean±SD	p-value
AGE		11.00±2.06	10.18±2.04	.250
IQ	verbal IQ	115.13±10.13	111.44±10.92	.337
	performance IQ	106.40±16.21	109.75±13.45	.538
	Total IQ	112.67±12.73	114.2±511.22	.717
Handedness	Left/Right	1/17 (5.88%)	1/17 (5.88%)	1.00

Table1. Demographic data of the subjects.

	ASD (n=17) Mean±SD	Control (n=17) Mean±SD	p-value
Corpus callosum	0.589±0.064	0.664±0.041	.000**
Left Uncinate fasciculus	0.495±0.084	0.582±0.034	.001**
Right Uncinate fasciculus	0.534±0.062	0.553±0.050	.329
Left inferior longitudinal fasciculus	0.438±0.051	0.543±0.049	.000**
Right inferior longitudinal fasciculus	0.466±0.046	0.498±0.037	.037**
Left Anterior thalamic radiation	0.533±0.027	0.580±0.026	.000**
Right Anterior thalamic radiation	0.547±0.030	0.587±0.0297	.000**

Table2. Individual ROI based group comparison of FA in brain regions.

Materials and Methods

ASD and healthy normal subjects were recruited from a child and adolescent psychiatric clinical groups, well-defined community sources and schools in Koyang area in South Korea. We enrolled thirty four male subjects (17 ASD: mean age 11± 2.06 years old, 17 healthy control: mean age 10.18 ± 2.04 years old). We used SRS (Social Responsiveness Scale), ASSQ (Autism Spectrum Screening Questionnaire), ADI-R-K (Autism Diagnosis Interview-Revised-Korean version), and ADOS-K (Autism Diagnostic Observation Schedule-Korean version) to screening and diagnosis all ASD subjects. We performed MRI scans using a 1.5T clinical MRI scanner (Avanto 1.5T, Siemens, Erlangen, Germany) with a gradient strength of 40 mT/m. 12-channel head matrix coil was used for study. Diffusion weighted images were acquired using a spin-echo based single-shot echo-planar diffusion sequence. The specific MR imaging parameters used were as follows: TR = 6500 ms; TE = 86 ms; number of diffusion gradient directions = 30; b value = 900 s/mm2; number of excitation = 2; GRAPPA factor = 2. The in-plane resolution was 1.8 mm, and the slice thickness was 3 mm without gap. Preprocessing of MR images and caculate diffusion indicies map such as FA images were performed using FSL (FMRIB Software Library -www.fmrib.ox.ac.uk/fsl). For SPM group analysis we generated a WM (white matter) only FA (or MD) image. This study was approved by the institutional review board for human subjects at the Myong-Ji Hospital affiliated with Kwandong University College of Medicine in Kyunggi and Gacheron Neuroscinece Research Institute in Incheon, where all subjects were scanned, in South Korea.

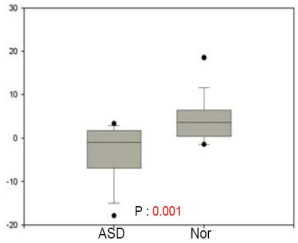

Fig.2. Comparison result of laterality between ASD and healthy control group in IFL.

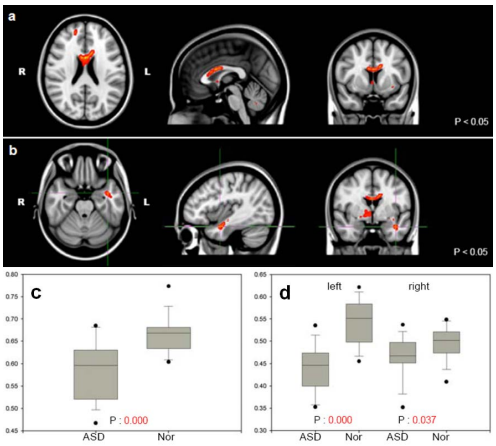

Fig.1. Group comparison results between ASD and normal healthy control group. (a-b) Results of VBM style group analysis of FA value. Activated area represent that ASD group have lower FA value than healthy control group. (c-d) Individual ROI based group comparison results. (Independent t-test, (c) Corpus callosum, (d) Inferior longitudinal fasciculus.)

Results

As shown in Table 1, the ASD group and healthy control group were group-matched on age, IQ, handedness. In Table 2 shows the results of individual ROI based analysis, ASD subjects showed significantly reduced FA values in corpus callosum (CC), both inferior longitudinal fasciculus (IFL) adjacent to facial fusiform area (FFA), left uncinate fasciculus (overlapped with inferior fronto-occipital fasciculus) and both anterior thalamic radiation compared to the control subjects. We did VBM style group analysis of FA value and the results are displayed in Fig.1(a) and (b). The activated area represent that ASD group have significantly ($p<0.05$) lower FA value than healthy control. In CC (a) and left IFL (b) we found significant difference of FA value between two groups. To confirm these VBM analysis results we did individual ROI data based independent t-test in CC and IFL regions. In both regions the differences are significant (Fig. 1(c-d)). We can find one more information in Fig.1(d), the difference between two groups are much significant at the left side. And compare with left and right hemisphere FA value in each group, healthy control group shows big difference however ASD group shows not much. So we calculated laterality (absolute value of (left-right)/(left+right)) in IFL and compare this value between two groups. The comparison result of laterality is shown in Fig.2.

Conclusions

Our preliminary findings which showed significant reduction of FA in white matter structure related social cognition in ASD subjects compared control subjects support previous findings that social brain structure may be disrupted in ASD. These findings will help on understanding of more advanced neurobiological basis underlying the social deficits in ASD. Nevertheless, we will still need to focus on evaluating the association between each symptom shown in ASD individuals and brain abnormalities in the future study.

References [1] Hashimoto et al., J Autism Dev Disord 1995;25(1): 1-18. [2] Aylward et al., Neurology 1999;53(9): 2145-50. [3] Schultz et al., Int J Dev Neurosci 2005 ; 23(2-3): 125-41.