

White Matter Microstructure Abnormality in Autism Spectrum Disorders : A DTI based Subdivided Corpus Callosum Study

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Introduction

Autism spectrum disorders (ASD) is a heterogeneously neurodevelopmental disorder. It is characterized by impaired social reciprocity, communication difficulties, and restricted interest or stereotyped behavior. Many studies have supported the hypothesis that the ASD result from disconnection of brain regions that are highly evolved and that are involved in higher-order associations; that is, in other words, ASD form a “development disconnection syndrome” [1]. The fibers from different cortical areas are distributed on corpus callosum (CC), the main tract dominating interhemispheric information transfer in the brain (Figure A). Diffusion tensor imaging has become a popular noninvasive method for studying white matter structure and pathology of human brain *in vivo* [2]. Fiber tracking has also provided a reconstructed method from DTI for mapping the white matter fibers connections in the brain [3]. To observe the abnormal brain connectivity in ASD, the investigation of subdivision CC using DTI fiber tracking with the anisotropy index, fractional anisotropy (FA), can directly and easily indicate the integrity of the fiber tracts in connection with each cortical region.

Materials and Methods

Twenty healthy subjects (20M, mean age 13.64 ± 0.96 y/o) and twenty individuals with ASD (20M, mean age 13.61 ± 2.52 y/o) diagnosed with DSM-IV and the Autism Diagnostic Interview-Revised (ADI-R) [4] were recruited. None had a history of major psychiatric disorder or medical illness affecting brain function (e.g., psychosis or epilepsy). All subjects were scanned on a 1.5T Signa GE Excite-II MR scanner in TPE-VGH with an 8-channel head coil using a single shot diffusion spin-echo EPI sequence with TR/TE = 17000/68.3 msec, the voxel size = $2 \times 2 \times 2.2$ mm. The diffusion gradients were applied in 13 non-collinear directions with b-value = 900 s/mm² and NEX = 6. FA images were calculated and aligned into a standard space using the nonlinear registration tool FNIRT [5] which is implemented in FSL (FMRIB Software Library) [6]. The contours of CC mask were defined on the midsagittal slices and bilateral parasagittal slices in mean FA image. The CC mask was subdivided to 8 subregions [7] by the in-house program developed in Borland C++. The 8th subregion was defined as a circle area divided manually from the splenium to analyze the fibers connected with the inferior temporal lobe [8]. The CC Mask was then transformed into each subject’s native space using the inverse of the original warping transform and the fiber tracking performed on native space [9]. The mean FA of all fibers comprised by each voxel was determined. Regional differences of fibers mean FA between the ASD-control groups were explored through one-way analysis of covariance (ANCOVA) controlling for age with a statistic threshold of p-value < 0.05.

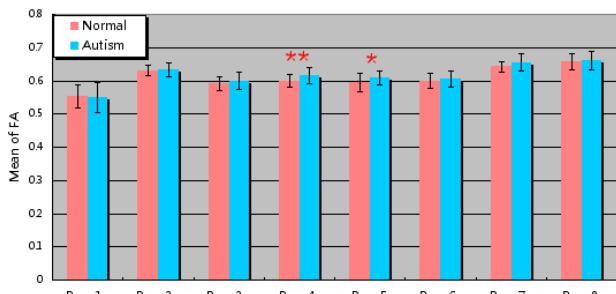


Figure B. The mean FA of the CC in Region 4, and 5 were significantly larger in ASD than healthy controls under statistic threshold of * $P<0.05$ and ** $P<0.01$.

Results

The ASD subjects had greater FA in the Region 4 and 5 than healthy subjects, as showed in Figure B. Region 4 and 5 relate to the motor-related communication areas and somaesthetic area (Table 1). Greater FA reflected the abnormal neural overconnection. The result indicated that the communication between bilateral hemispheres was abnormal in motor, somaesthetic related areas in ASD subjects.

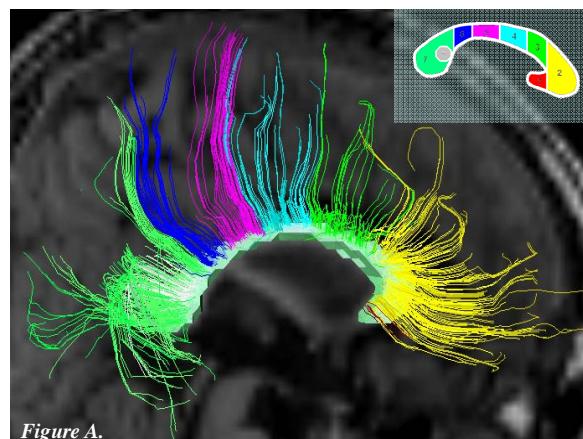
Discussions

Previous studies indicated abnormal regulation of brain growth in ASD results from early overgrowth followed by abnormally slowed growth. It also disturbed enrich local connections but retarded long connections. CC, an important marker for bilateral interhemisphere connection, was evaluated in this study. There are no distinct differences in white matter content except Region 4 and 5, which were inferred to motor-related and somaesthetic areas respectively. Higher FA in ASD may be relate to overgrowth local connection. It is worth to have further study to understand the pathological meaning of FA increase in ASD.

Region	Anatomical label	Cortical region
1	Rostrum	Caudal/orbital prefrontal, inferior premotor
2	Genu	Prefrontal
3	Rostral body	Premotor, supplementary motor
4	Anterior midbody	Motor
5	Posterior midbody	Someaesthetic, posterior parietal
6	Isthmus	Superior temporal, posterior parietal
7	Splenium	Occipital, inferior temporal
8	Splenium	Inferior temporal

Table A. The 8 subregions with the anatomic labels and a rough topography of callosal fibers in relation to cortical regions were listed in the table [7].

Figure A. The fibers from different cortical areas are distributed on corpus callosum and the relative cortical regions were listed in Table A.



Acknowledgements

This study was supported in part by National Science Council grant NSC 97-2752-H-010 -004 –PAE.

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