Altered structural brain networks in children with Asperger syndrome: a DTI-based connectome study

Haoxiang Jiang[1,2], Yanni Chen[2], Qinli Sun[1,3], Xianjun Li[3], Mengye Lv[3], Yang Song[1], and Jian Yang[1,3]

[1]*Department of Diagnostic Radiology, The First Hospital of Medical School,Xi'an Jiaotong University, Xi'an, Shannxi, China,* [2]*Department of Diagnostic Radiology, Xi'an Children Hospital, Xi'an, Shannxi, China,* [3]*Department of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, Shannxi, China*

INTRODUCTION

Asperger syndrome (AS) is a chronic neurodevelopmental disorder with social interaction, communication, and the restricted range in behaviors or interests. It was deemed to be a subtype of autistic spectrum disorder (ASD) in previous study[1]. However, the children with autism exhibit a language delay whereas those with AS do not[2]. Although the brain anatomical variations of autism have been detected by structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) [3,4]. But the brain variations of AS, especially in the structural connectivity, remains unclear. This study aimed to investigate the structural brain networks in AS children using the graph theoretic analysis.

MATERIALS AND METHODS

The 22 boys with AS (age: 3.45±0.67years) and 18 typically developing(TD) boys with matched age (age: 3.82±0.69years) were recruited. This study was approved by the local Institutional Review Board. All parents of participants were informed with the goals and risks of MR scanning and requested written consent before enrollment. The boy with AS were diagnosed by two pediatric neurologists using ICD-10 research diagnostic criteria. All patients fulfilled criteria for autism but without a history of language delay. In this study, 3D-MPRAGE T1WIs, FSE-T2WIs and DTIs were performed in a 3T scanner (GE, Signa HDxt) with 8-channel head coil. Technical parameters of DTI were as follows: TR/TE=5500/95ms, slice thickness=4mm without gap, field of view = 220×220mm^2, matrix = 256×256, b =1000 s/mm^2 with 35 gradient directions. The DTI data was automated processing in MATLAB toolbox named "Pipeline for Analyzing braiN Diffusion imAges" (PANDA)[5] .The process mainly included extracting brain images, correcting eddy current, calculating the DTI metrics, defining network nodes, constructing networks using deterministic tractography. We constructed the FN-weighted white matter (WM) network for each participant, which was represented by a symmetric 90×90 matrix. In order to characterizing the topological organization of WM structural networks, parameters of network graph analysis were acquired by clustering coefficient (C), local efficiency (E_{loc}), shortest path length (L), betweenness centrality (N_{bc}) and small worldness(σ). Meanwhile, the network-based statistic (NBS) approach was used to analyze the altered structural connectivity among brain regions in AS[6]. The differences between AS and TD group in network measures and regional nodal connectivity were determined by using two-sample t statistic. All tests were considered to be significant with P<0.05.

RESULTS

The comparison of graph measures between AS and TD group were shown in Table.1. The AS group showed significant reduction of σ and L, and a trend of reduction in N_{bc}. However, The AS group showed significant increment of C and E_{loc}. The difference of node N_{bc} was shown in Fig.1. In AS group, there were 7 nodes with significant reduction of N_{bc}, including left middle frontal gyrus (MFG), bilateral hippocampus (HIP), left postcentral gyrus (PoCG), right supramarginal gyrus (SMG), right pallidium (PAL), right superior temporal gyrus (STG), and there were 2 nodes with significant increase of N_{bc}, including right inferior frontal gyrus (IFGoperc) and right supplementary motor area (SMA). The connected network showed partly impaired connectivity in the right hemisphere of AS group by NBS method (Fig.2). The involved nodal regions mainly included PoCG, Precuneus (PCUN), Thalamus (THA), putamen (PUT), lingual gyrus (LING), HIP, parahippocampal gyrus (PHG), olfactory cortex (OLF), fusiform gyrus (FFG).

Table 1 Comparison of the graph measures between AS group and TD group($\bar{x} \pm S$)

group	n	C	E_{loc}	L	N_{bc}	σ
AS	22	0.014±0.002	0.728±0.010	2.398±0.114	0.049±0.004	3.157±0.210
TD	18	0.011±0.001	0.720±0.013	2.503±0.088	0.050±0.003	3.435±0.182
t		3.529	2.155	-3.251	-1.030	-4.522
p		0.001**	0.038*	0.002**	0.310	0.000**

P values were generated from two-sample t -tests performed on each metric averaged over a range of sparsity thresholds(* P<0.05, **P<0.01). C, clustering coefficient; E_{loc} , local efficiency; L , shortest path length; N_{bc}. , betweenness centrality; σ, small worldness.

DISCUSSIONS

In this study, the graph theoretic analysis based on DTI data demonstrated the topological alterations of WM networks in AS group compared to the TD group. The reduced σ and N_{bc} reflect disrupted organization of the WM network in AS group . The increased C and E_{loc} and reduced L reflect local over-connectivity. Previous neuroimaging studies on autism have reported the similar results[7]. However, the brain abnormal connections of autism were mainly located in fronto-frontal and fronto-occipital regions[8], and more in the left hemisphere than the right hemisphere[7]. While the NBS result displayed impaired connected components in the right hemisphere in AS group, especially those long-range connections within the posterior part of the brain cortex and THA and limbic system. The involved nodal regions may be correlated with the attenuate sense ,cognition and social reciprocity, especially the FFG that was directly correlated with the face discrimination. Due to the frontal lobes were seldom implicated, the AS children manifest normal language development.

Conclusions

DTI-based brain network analysis can provide more objective estimation of brain abnormal connectivity, which will bring us more evdiences to further analyze the pathologic mechanism in AS children.

References1. Woodbury-Smith MR et al .Volkmar FR Eur Child Adolesc Psychiatry. 2009;18(1):2-11. **2.**Lugnegård T et al Res Dev Disabil. 2011;32(5):1910-7. **3.**Camacho LP et al. Research in Autism Spectrum Disorders 2013;7(2):333–343. **4.**Mak-Fan KM et al. Autism. 2013;17(5):541-57. **5.**Cui Z et al Front Hum Neurosci.2013;7:42. **6.**Zalesky A et al Neuroimage. 2010;53(4):1197-207. **7.**Li H et al Hum Brain Mapp. 2012. **8.**Barttfeld P et al Neuropsychologia 2011;49(2): 254–63

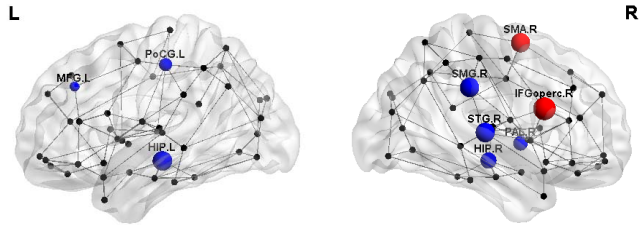

Figure1. The distribution of brain regions with significant group effects in N_{bc} between AS group and TD group at P<0.05. The node sizes indicate the significance difference of between-group . The nodes of AS>TD are colored in red, while the nodes of AS<TD are colored in blue. The other nodes are colored in black.

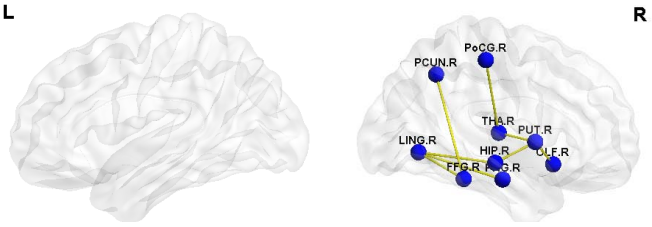

Figure2. The comparison of structural connectivity between AS group and TD group by NBS. The nodal regions (blue) showing decreased connections in AS group. These connections formed a single connected network with 9 nodes and 8 edges in right hemisphere (P< 0.035,corrected).