Structural networks in children with autism spectrum disorder with regression: A graph theory study

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ABSTRACT

Background: Regression is frequently described in Autism spectrum disorder (ASD). Limited comprehensive studies have been conducted in patients with ASD with regression.

Purpose: To explore the network topological properties in ASD children with (ASD-R) and without (ASD-NR) regression.

Methods: In this study, 29 ASD-R, 68 ASD-NR, and 40 children with developmental delay (DD) were recruited. We utilized graph theory to characterize the white matter structure networks by using diffusion tensor imaging and T1-weighted imaging on a 3-T magnetic resonance system. Statistical analyses were performed using IBM SPSS (version 23).

Results: ANCOVA showed significant differences in global efficiency, characteristic path length and sigma among the ASD-R, ASD-NR and DD groups, but the difference was not significant between the ASD-R and ASD-NR groups. There were 10 common hubs based on regional degree and regional efficiency in all groups. The hubness of the left superior frontal gyrus-dorsolateral, left middle occipital gyrus and right precuneus were enhanced (by regional degree) and that of the right thalamus was reduced (by regional efficiency) in the ASD-R relative to the ASD-NR group. After controlling for the course of regression, the CARS scores were significantly correlated with the regional efficiency of the right precuneus in the ASD-R group.

Conclusions: The ASD-R children were different from the ASD-NR children in the distribution of hub regions, although there were no global network property differences between them. In ASD-R children, the right precuneus (PCUN.R) might play an important role and relate to autism symptom severity.

1. Introduction

Autism spectrum disorder (ASD) is one of the most common neurodevelopmental disorders, causing functional impairments in social, educational, and occupational domains. The core symptoms of ASD are impairments in social communication and interactions and repetitive and restricted behaviors, which include sensory abnormalities [1]. The high degree of heterogeneity among patients with ASD, in its etiology, clinical diagnosis, or treatment, is a very large challenge. With the wide application of neuroimaging technology in the field of ASD, there have been studies on the brain imaging of biological markers. Recent studies have made progress in identifying relevant brain network connections. However, these findings need to be further confirmed. In one study, children with ASD showed hyper-connectivity within large-scale brain networks and decreased between-network connectivity compared with typically developing individuals [2]. Another finding showed a pattern of overall brain under-connectivity and local over-connectivity [3]. There remains inconsistencies regarding the nature of connectivity impairments in autism, i.e., under-connectivity or over-connectivity [4]. To solve such a complex situation, examining brain connectivity within populations with specific clinical phenotypes may be one of the research strategies to be explored.

Regression is frequently described in ASD. Reports about behavioral regression in children with autism emerged in the 1960s [5,6], and many studies focused on regression in ASD have been published since that time. A meta-analysis of 85 articles representing over 29,000 people with ASD showed that the overall prevalence rate of regression was 32.1%, with an average onset of regression at 1.78 years [7]. Former studies demonstrated that ASD children with regression were more likely to have cognitive deficiencies compared to ASD children.
without regression, as well as higher levels of autistic symptomology [8,9]. The occurrence of regression is higher in children with ASD than in children with other idiopathic developmental conditions, such as specific language impairment and developmental delay [10]. In general, it is thought that regression in ASD could form one clinically characterized phenotype. Although some of the genetic syndromes have a high incidence of regression (e.g., RTT- and SHANK3-related disorders), there is not enough evidence to conclude that regressive ASD is solely driven by genetic factors [11]. Some studies have indicated that immunological factors might be associated with regression in some children with ASD [12,13]. Regression in ASD children might related to epilepsy and atypical epileptiform electroencephalograms [14]. The field is far from identifying precise biomarkers. Noninvasive imaging might provide opportunities for a better understanding of the neurobiological pathways [15]. Regarding neuroimaging findings, abnormal brain enlargement was found in boys with regressive autism, but not in boys without regression autism [16]. Abnormal white matter connectivity in children with ASD has been detected, and how the brain networks in those with ASD with regression function remains unknown.

In MRI, morphological measures are known to have the highest reliability, while the reliability of functional MRI approaches tends to be lower and more variable [17]. Diffusion tensor imaging (DTI) is a magnetic resonance imaging technique that enables the measurement of the restricted diffusion of water in tissue in order to produce neural tract image. The reliability of DTI was high [18] and the DTI metrics were reliable in neonates [19]. A research of graph theory analysis of structural brain networks suggested that fractional anisotropy (FA) weighting schemes were more suited for DTI connectome studies in adolescents [20]. Graph theory-based analyses have been applied to the connectivity matrices for the extraction of important network characteristics, such as node degree (the number of connections of a node), characteristic path length (the average number of steps between nodes), average clustering coefficient (a measure of regional connectivity) and other quantifiable measures of network connectivity (for a review, see Rubinov and Sporns) [21]. Studying the human connectome using graph theory offers a unique opportunity to better understand interindividual differences in neural connectivity.

Based on previous research, we predicted that ASD children with and without regression may have no differences in global topology characteristics as they have similar clinical symptoms and that they may show differences in regional brain network features related to the different forms of onset. Therefore, we recruited ASD children with definite regression (ASD-R) and non-regression (ASD-NR) as different clinical subtypes, acquired diffusion tensor imaging data, and utilized graph theory to examine the global topological characteristics of the hub regions associated with ASD-R, ASD-NR and developmental delay (DD).

2. Materials and methods

2.1. Participants

All participants were recruited from April 2010 to March 2015 at the Child Mental Health Research Center of the Nanjing Brain Hospital affiliated to Nanjing Medical University. Written informed consent was obtained from each participant’s parents. The study was approved by the Institutional Review Board of Nanjing Brain Hospital of Nanjing Medical University in accordance with the ethical principles outlined in the Declaration of Helsinki.

We calculated the total sample size using G*Power3.1 and set the effect size 0.30, α 0.05, power 0.80. We grouped ASD-R, ASD-NR and DD in a 1:2:1 ratio, and matched sex and age. The study sample consisted of 29 ASD-R children (male/female: 21/8; age: 40.24 ± 12.78 months), 68 ASD-NR children (male/female: 60/8; age: 35.65 ± 11.25 months), and 40 DD children (male/female: 29/11; age: 39.98 ± 12.32 months). The diagnoses of ASD (autistic disorder) and DD (mental retardation or expressive language disorder) were conducted by two licensed child psychiatrists and based on the Diagnostic and Statistical Manual of Mental Disorders, 4th ed., text revision (DSM-IV-TR). The inclusion criteria of ASD were children with autistic disorder (according to DSM-IV-TR), aged 24–72 months and with their parents’ agreement. The ASD group excluded individuals with Rett’s syndrome or childhood disintegrative disorder. The inclusion criteria of DD were children with mental retardation or expressive language disorder (based on DSM-IV-TR), aged 24–72 months and with their parents’ agreement. The DD group excluded chromosome abnormalities or gene defects such as 21-trisomy syndrome and fragile X syndrome based on genetic tests. Patients in the ASD or DD groups with a history of head injury, neurological disorders, other major medical problems, other developmental disorders or psychiatric disorders were also excluded from the study. All ASD children were assessed by the childhood autism rating scale (CARS) [22].

Developmental regression was assessed via parent’s report of a history of loss of language (items 11–19) and other skills (items 20–28) according to the Autism Diagnostic Interview-Revised (ADI-R) [23]. Developmental quotients (DQs) were obtained using the Bayley Scales of Infant Development-Chinese Version (BSID-C) (DQ = ((motor age + cognitive age)/(chronological age × 2) × 100) [24] and Peabody Picture Vocabulary Test (PPVT) [25].

2.2. Image acquisition

MRI images were acquired by a 3.0 T Siemens Medical Systems Verio instrument at Nanjing Brain Hospital using a standard quadrature head coil. In this study, we acquired high-resolution images with a T1-weighted 3-D spoiled gradient-echo sequence with the following parameters: repetition time (TR) = 2530 ms, echo time (TE) = 3.34 ms, flip angle = 7°, field of view (FOV) = 256 × 256 mm2, in-plane resolution = 256 × 192, inversion time = 1100 ms, and slice thickness = 1.33 mm. Image orientations parallel to the anterior commissure–posterior commissure (AC–PC) plane were used. Diffusion tensor imaging (DTI) was obtained with single-shot echo-planar (SE-EPI) sequences with diffusion gradients applied in 30 noncollinear directions and b = 1000 s/mm2. The thickness of each slice was 2.5 mm without gap. The sequence parameters for DTI were TE = 104 ms, TR = 9000 ms, FOV = 230 × 230 mm2, and acquisition matrix = 128 × 128. The total DTI scanning time was 5 min 8 s. Before MRI scanning, each participant was sedated using chloral hydrate (0.5 g in 10 ml) with parental consent.

2.3. Data processing

The DTI data were processed with PANDA (a pipeline toolbox for analyzing brain diffusion images) [26] in MATLAB that included the following steps: converting DICOM files into NIfTI images, estimating the brain mask, cropping the raw images, correcting for the eddy current effect, correcting for head motions, estimating the diffusion tensor models by using the linear least-squares fitting method on each voxel, tracking whole-brain fiber in the native diffusion space via the fiber assignment by continuous tracking algorithm, and averaging multiple acquisitions and calculating diffusion tensor metrics.

2.4. Network construction

Nodes and edges are the two basic elements needed to form a network. The nodes of the structural networks were delimited according to an automated anatomical labeling (AAL) algorithm template [27]. This algorithm scheme parcellated the entire cerebral cortex, except the cerebellum, into 90 anatomical regions (AAL-90), which resulted in 90 nodes covering the noncerebellar brain with 45 nodes in each hemisphere. The structural networks were constructed by deterministic
tractography using the PANDA toolbox. Matrix_FA (90 × 90) generated from PANDA was thresholded into different levels to create an adjacency matrix. The FA threshold was set from 0.2 to 1, and the angle threshold was set as 45°. Each matrix represented the white matter network of the cerebral cortex, in which each row or column represented a brain region from the AAL template. For each child, the Matrix_FA was used for subsequent graph analyses.

2.5. Graph analysis

Network analyses of the graph analysis were calculated by the Matrix_FA with routines from the GRETNNA toolbox (graph theoretical network analysis toolbox) [28]. Several network topological properties were used to characterize the white matter structural network derived from each participant.

The network topological properties included (1) properties that implied network segregation of the brain, including the weighted clustering coefficient (Cp) and local efficiency (Eloc). (2) Properties that indicated network integration of the brain, including the characteristic path length (Lp) and global efficiency (Eg). The characteristic path length was used to characterize the optimal routing of information transmission. Eg was defined as the average inverse shortest path length, and Eloc was defined as the mean of the global efficiencies of subgraphs consisting of the immediate neighbors of a particular node. (3) Small-worldness (sigma, σ), which evaluates the balance of segregation and integration.

Nodal efficiency was calculated to measure the characteristic path length of a node to other nodes in the network. Nodal efficiency represents the position of the node in the network information transmission. The degree is one of the most common measures of centrality. Nodes with a high degree interact with many other nodes in the network. Nodes were identified as ‘hubs’ in the network if the values of nodal degree or efficiency were one standard deviation (SD) greater than the average nodal degree or efficiency of the entire network. The hub regions were depicted by the BrainNet Viewer toolbox [29].

2.6. Statistical analysis

Statistical analyses were performed by using IBM SPSS (version 23). Sex data were examined with a chi-square test. Group differences in age and DQ were examined with one-way ANCOVA. T-test analyses were employed to compare the CARS scores between the ASD-R and ASD-NR groups, and p-values less than 0.05 were considered statistically significant. For group effects in the global network, comparisons were performed among the three groups using one-way ANOVA. Post hoc pairwise t-tests with Bonferroni correction for multiple comparisons were performed if ANOVA yielded significant results at p < 0.05. Partial correlations were performed between the CARS scores and nodal degree or efficiency with enhanced or weakened hubness by controlling for the course of regression in the ASD-R group, with a statistical significance level of p < 0.05.

3. Results

3.1. Demographics and clinical assessment results

There were no significant differences in age, sex, or DQ among the three groups. The CARS scores of the ASD-R children were significantly higher than those of the ASD-NR children. The demographic details of the participants are summarized in Table 1.

3.2. Global topology of the white matter connectome

All three groups presented small-world organization (σ > 1) (Table 2). ANCOVA showed significant differences in global efficiency, characteristic path length and sigma. Following Bonferroni corrections, ASD-R and ASD-NR groups demonstrated increased global efficiency and shorter characteristic path lengths than the DD group. There were no significant differences between the ASD-R and ASD-NR groups for all global network properties.

3.3. Hub regions

We identified ‘hubs’ as nodes with regional degree and efficiency values at least one standard deviation higher than the average for the network. The hub regions identified in each group are shown in Fig. 1. By nodal degree, the ASD-R, ASD-NR and DD groups had 10 hubs in common (bilateral insula, hippocampus, caudate nucleus and putamen, left precuneus and right superior frontal gyrus-dorsolateral). The left superior frontal gyrus-dorsolateral gyrus, left middle occipital gyrus and right precuneus were hub regions only in the ASD-R group. Regarding nodal efficiency, there were 11 common areas (bilateral superior frontal gyrus-dorsolateral, insula, hippocampus, caudate nucleus, putamen and left precuneus) in the ASD-R, ASD-NR and DD groups. The right precuneus was a hub only in the ASD-R group, and the right thalamus was a hub only in the ASD-NR group.

We controlled for the course of regression to perform partial correlation analysis on the CARS scores and regional degree and efficiency of the left superior frontal gyrus-dorsolateral, left middle occipital gyrus, right precuneus and right thalamus in children with regression. The results are shown in Table 3. The CARS scores were significantly correlated with the regional efficiency of the right precuneus.

4. Discussion

The incidence of regression in the children with ASD was 32.1%, with an average onset at 1.78 years [7]. ASD children with regression were more likely to have severe autistic symptoms compared to those without regression [8]. There was no difference in DQ between the ASD-R and ASD-NR groups, indicating that the severe differences in core autistic symptoms between those with ASD-R and ASD-NR were not due to intelligence levels. That is, the ASD-R children had more serious autistic symptoms regardless of DQ. This finding was consistent with the results of previous studies showing that regression was associated with higher levels of autistic symptoms [8,9].

Previous studies have shown that ASD individuals had brain connectivity dysfunction [2–4]. Lp is used to characterize the optimal routing of information transmission. Eg is a global measure of the parallel information transfer ability of the whole network. Both the ASD children with and without regression showed increased global efficiency and shortened characteristic path length, indicating that the ASD children had hyper-connectivity. These data were consistent with the study of Li SJ et al., which demonstrated that ASD children had increased global efficiency and shortened characteristic path length [30]. There was no significant difference between the ASD-R and ASD-NR groups for all the global network properties. Small-worldness is an important characteristic of a network because it represents an optimal balance between segregation and integration, which is essential for high synchronizability and fast information transmission in a complex network [31,32]. Our results were consistent with previous studies in which both the normal control and ASD groups exhibited small-world properties [33]. This finding also confirmed a previous theory that neonatal anatomical brain networks displayed the clear presence of a small-world modular organization before term birth [34].

Hubs, which are nodes occupying central positions for the coordination of global communication in the overall organization of a network, are usually densely connected or highly centralized [35]. Here, we identified ‘hubs’ as having a nodal degree or nodal efficiency that was at least one standard deviation higher than the average nodal degree and nodal efficiency for the network. As shown in Fig. 1, there were 10 hubs in common based on both regional degree and regional efficiency in the three groups of ASD-R, ASD-NR, and DD children. The
hub regions were mainly concentrated in primary visual and sensorimotor networks and the limbic system, which was consistent with previous studies. Analyses of brain structural subnetworks have shown that the primary visual and sensorimotor networks mature first. Structural hubs emerge early within the dorsal medial frontal, hippocampal, precuneus and insula regions [36]. The caudate and putamen, as parts of basal ganglia, harbor components of both motor and association systems.

The precuneus, a part of the medial posterior parietal cortex, has been reported to be correlated with integrated tasks, including visuospatial imagery, episodic memory retrieval, self-related processing, awareness and conscious information processing [37,38]. The prefrontal cortex is thought to contribute to higher cognitive functions, such as executive processing and spatially oriented processing [47]. Another study by Chen ZX et al. indicated that the left superior frontal gyrus played a vital role in the executive aspects of feigned memory impairments, restricted, repetitive patterns of behavior or interests and sensory processing abnormalities. Individuals with autism showed decreased functional connectivity between the amygdala and bilateral thalamus [50]. In another study, individuals with ASD showed stronger thalamus cluster connectivity with auditory, somatosensory, motor, and interoceptive cortices than neurotypical individuals [51]. Dysregulation of the thalamus might play an important role in the development of autism.

5. Limitations

There are several limitations in this study. First, regression in our study was based on interviews with parents, which might have been influenced by retrospective bias; in the future, some prospective studies are needed. Second, the analysis of node definitions was limited to the AAL template-based brain networks. Future studies are needed to clarify the effect of various node definitions. Third, the sample size in the ASD-R group limited us regarding additional grouping comparisons.

6. Conclusions

In conclusion, the graph theory analysis of DTI data demonstrates no significant difference in global and local properties between the ASD-R and ASD-NR groups. There were 10 hubs in common based on either regional degree or regional efficiency in the three groups of ASD-R, ASD-NR, and DD children. The right precuneus was a hub region only in the ASD-R group. In the ASD-R group, the function of the right precuneus (PCUN.R) might play an important role and relate to autistic severity.

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Fig. 1. The distribution of hub regions.
The distribution of hub regions in the ASD-R, ASD-NR and DD groups. Hub regions were visualized with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/) (Xia et al., 2013). The regions were mapped in an axial view. SFGdor, superior frontal gyrus-dorsolateral. INS, insula. HIP, hippocampus. CAU, caudate nucleus. PUT, putamen. PCUN, precuneus. MOG, middle occipital gyrus. THA, thalamus. L, left. R, right. Red, common areas. Green, areas only in the ASD-R group. Blue, areas only in the ASD-NR group.

Table 3
Partial correlations between the regional characteristics and CARS scores.

| Region         | Regional degree | Regional efficiency |
|----------------|-----------------|---------------------|
|                | R          | p         | R          | p        |
| SFGdor.L       | −0.115     | 0.559     | −0.016     | 0.935    |
| MOG.L          | −0.165     | 0.402     | −0.196     | 0.317    |
| PCUN.R         | −0.351     | 0.067     | −0.381     | 0.046    |
| THA.R          | −0.110     | 0.579     | −0.136     | 0.491    |

SFGdor, superior frontal gyrus-dorsolateral. MOG, middle occipital gyrus. PCUN, precuneus. THA, thalamus. L, left. R, right. Significant differences: $p < 0.05$.

References

[1] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders (DSM-5), 5th ed., American Psychiatric Association Publishing, Washington, DC, 2013, https://doi.org/10.1176/appi.books.9780890425596.

[2] J.S. Nomi, L.Q. Uddin, Developmental changes in large-scale network connectivity in autism, Neuroimage Clin. 7 (2015) 732–741, https://doi.org/10.1016/j.nicl.2015.02.024.

[3] C. Lord, M. Elsabbagh, G. Baird, J. Veenstra-Vanderweele, Autism spectrum disorder, Lancet 392 (2018) 508–520, https://doi.org/10.1016/S0140-6736(18)31129-2.

[4] C. Ecker, S.Y. Bookheimer, D.G. Murphy, Neuroimaging in autism spectrum disorder: brain structure and function across the lifespan, Lancet Neurol. 14 (11) (2015) 1121–1134, https://doi.org/10.1016/S1474-4422(15)00050-2.

[5] S. Wolff, S. Chess, A behavioural study of schizophrenic children, Acta Psychiat. Scand. 40 (1964) 438–466, https://doi.org/10.1111/j.1600-0447.1964.tb07496.x.

[6] V. Lotter, Epidemiology of autistic conditions in young children, Soc. Psychiatry 1 (1966) 124–137, https://doi.org/10.1007/BF00578950.

[7] B.D. Barger, J.M. Campbell, J.D. McDonough, Prevalence and onset of regression within autism spectrum disorders: a meta-analytic review, J. Autism Dev. Disord. 43 (4) (2013) 817–828, https://doi.org/10.1007/s10803-012-1621-a.

[8] N. Al Backer, Developmental regression in autism spectrum disorder, Sudanese J. Paediatric 15 (1) (2015) 21–26 PMID: 27493417.

[9] K.D. Gadow, G. Perlman, R.J. Weber, Parent-reported developmental regression in autism: epilepsy, IQ, schizophrenia Spectrum symptoms, and special education, J. Autism Dev. Disord. 47 (4) (2017) 918–926, https://doi.org/10.1007/s10803-016-3004-1.

[10] K. Williams, A. Brignell, M. Prior, et al., Regression in autism spectrum disorders, J. Paediatr. Child Health 51 (1) (2015) 61–64, https://doi.org/10.1111/jpc.12805.

[11] K. Tamminimies, Genetic mechanisms of regression in autism spectrum disorder, Neuroni. Biobehav. Rev. 102 (2019) 208–220, https://doi.org/10.1016/j.neubiorev.2019.04.022.

[12] O. Scott, D. Shi, D. Andriashek, Clinical clues for autoimmunity and neuroinflammation in patients with autistic regression, Dev. Med. Child Neurol. 59 (9) (2017) 947–951, https://doi.org/10.1111/dmcn.13432.

[13] I.S. Heuer, L.A. Croen, K.J. Jones, et al., An exploratory examination of neonatal cytokines and chemokines as predictors of autism risk: the early markers for autism study, Biol. Psychiatry (2019), https://doi.org/10.1016/j.biopsych.2019.04.037.

[14] B.D. Barger, J. Campbell, C. Simmons, The relationship between regression in
autism spectrum disorder, epilepsy, and atypical epilepsyiform EEG: a meta-analytic review, J. Intell. Dev. Disabil. 42 (1) (2017) 45–60, https://doi.org/10.3109/
13668250.2016.1208812.
[15] A. Thurau, E.M. Powell, J.L. Neul, et al., Loss of skills and onset patterns in neu-
rodevelopmental disorders: understanding the neurobiological mechanisms, Autism
Res. 11 (2) (2018) 212–222, https://doi.org/10.1007/s11680.1903.
[16] C.W. Nordahl, N. Lange, D.D. Li, et al., Brain enlargement is associated with re-
gression in preschool-age boys with autism spectrum disorders, Proc. Natl. Acad.
Sci. U. S. A. 108 (50) (2011) 20195–20200, https://doi.org/10.1073/pnas.1107560108.
[17] X.N. Zuo, T. Xu, M.P. Milham, Harnessing reliability for neuroscience research, Nat.
[18] C. Lord, M. Rutter, A. Le Couteur, Autism diagnostic interview-revised: a revised
instrument for use in a nonclinical population, J. Autism Dev. Disord. 24 (5) (1994) 659
[19] E. Schopler, R.J. Reichler, R.F. DeVellis, et al., Toward objective classi-
fication of autistic developmental disorders, J. Autism Dev. Disord. 24 (10) (1994)
91–103, https://doi.org/10.1007/BF0240843b.
[20] C. Lord, M. Rutter, A. Le Couteur, Autism diagnostic interview-revised: a revised
version of a diagnostic interview for caregivers of individuals with possible per-
vasive developmental disorders, J. Autism Dev. Disord. 24 (5) (1994) 659–685,
https://doi.org/10.1007/BF02217245.
[21] Y. Shourng, L. Xuong, Y. Zhwei, et al., The revising of the bayley scales of infant
developmental assessment for use in a nonclinical population, J. Autism Dev. Disord. 24 (5)
1994) 91–103, https://doi.org/10.1007/BF0240843b.
[22] V. Shourng, L. Xuong, Y. Zhwei, et al., The revising of the bayley scales of infant
developmental assessment for use in a nonclinical population, J. Autism Dev. Disord. 24 (5)
1994) 91–103, https://doi.org/10.1007/BF0240843b.
[23] M. Xia, J. Wang, Y. He, BrainNet viewer: a network visualization tool for human
brain networks in infants with intrauterine growth restriction and its association with
later neurodevelopmental outcome, Neuroimage 60 (2012) 1352–1366, https://doi.org/10.1016/j.
nimage.2012.01.059.
[24] T. Babaishi, T. Yamada, H. Watanabe, et al., Altered network topologies and hub
organization in adults with autism: a resting-state fMRI study, PLoS One 9 (4) (2014) e94115,
https://doi.org/10.1371/journal.pone.0094115.
[25] M.P. Van den Heuvel, K.J. Kernsbergen, M.A. de Reus, et al., The neonatal con-
nectome during preterm brain development, Cereb. Cortex 25 (9) (2015) 3000–3013,
https://doi.org/10.1093/cercor/bhu095.
[26] M. Cao, H. Huang, H. He, Developmental connectomics from infancy through early
childhood, Trends Neurosci. 40 (8) (2017) 494–506, https://doi.org/10.1016/j.
trends.2017.06.003.
[27] S. Zhang, C.R. Li, Functional connectivity mapping of the human precuneus by
resting state fMRI, Neuroimage 59 (4) (2012) 3548–3562, https://doi.org/10.1016/j.
nimage.2011.11.023.
[28] A.E. Cavanna, M.R. Trimble, The precuneus: a review of its functional anatomy and
behavioural correlates, Brain 129 (Pt 3) (2006) 564–583, https://doi.org/10.1093/
brain/awl004.
[29] A.V. Utevsky, D.V. Smith, S.A. Huettel, Precuneus is a functional core of the default-
mode network, J. Neurosci. 33 (4) (2013) 932–940, https://doi.org/10.1523/
JNEUROSCI.4227-13.2014.
[30] C.J. Lynch, L.J. Uddin, K. Supekar, et al., Default mode network in childhood
autism: posteroanterior cortex heterogeneity and relationship with social deficits,
Biol. Psychiatry 74 (3) (2013) 212–219, https://doi.org/10.1016/j.biopsycho.2012.
608.
[31] Q. Li, B. Becker, X. Jiang, et al., Decreased interhemispheric functional connectivity
rather than corpus callosum volume as a potential biomarker for autism spectrum
disorder, Cereb. Cortex (2019) 258–266, https://doi.org/10.1093/cercor/bjx003.
[32] W. Cheng, E.T. Rolls, J. Zhang, et al., Functional connectivity decreases in autism in
emotion, self, and face circuits identified by knowledge-based enrichment analysis,
Neuroimage 148 (2017) 169–178, https://doi.org/10.1016/j.neuroimage.2016.12.
686.
[33] X. Guo, H. Chen, Z. Long, et al., Atypical developmental trajectory of local spon-
taneous brain activity in autism spectrum disorder, Sci. Rep. 7 (2017) 39822,
https://doi.org/10.1038/srep39822.
[34] I. Simard, D. Luck, L. Mottron, et al., Autistic fluid intelligence: increased reliance
on visual functional connectivity with diminished modulation of coupling by task
difficulty, Neuroimage Clin. 18 (9) (2015) 467–474, https://doi.org/10.1016/j.nicl.
2015.09.007.
[35] A. Retico, A. Giuliano, R. Tancredi, et al., The effect of gender on the neuroanatomy
of children with autism spectrum disorders: a support vector machine case-control
study, Mol. Autism 7 (5) (2016), https://doi.org/10.1186/s13229-015-0067-3
eCollection 2016.
[36] F. Samson, L. Mottron, I. Soulères, et al., Enhanced visual functioning in autism: an
ALF meta-analysis, Hum. Brain Mapp. 33 (7) (2012) 1553–1581, https://doi.org/
10.1002/hbm.21307.
[37] F. du Boisgrosqueuen, R. Levy, E. Volle, et al., Functions of the left superior frontal
gyrus in humans: a lesion study, Brain 129 (Pt 12) (2006) 3315–3328, https://doi.
org/10.1093/brain/awi244.
[38] Z.X. Chen, L. Xue, C.Y. Liang, et al., Specific marker of feigned memory impairment:
the activation of left superior frontal gyrus, J. Forensic Leg. Med. 36 (2015)
164–171, https://doi.org/10.1016/j.jflm.2015.09.008.
[39] K. Hugdahl, M.K. Beyer, M. Brix, et al., Autism spectrum disorder, functional MRI
and MR spectroscopy: possibilities and challenges, Microb. Ecol. Health Dis. 23
(2012) 18960, https://doi.org/10.3402/mehd.v23i0.18960.
[40] X. Guo, X. Duan, Z. Long, et al., Decreased amygdala functional connectivity in
adolescents with autism: a resting-state fMRI study, Psychiatry Res. Neuroimaging
257 (2016) 47–56, https://doi.org/10.1016/j.pscychresns.2016.10.005.
[41] D. Tomasi, N.D. Volkow, Reduced local and increased long-range functional con-
nectivity of the thalamus in autism Spectrum Disorder, Cereb. Cortex 29 (2) (2019)
573–585, https://doi.org/10.1093/cercor/bhz340.

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