NeuroImage 124 (2016) 63–74

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

More bilateral, more anterior: Alterations of brain organization in the large-scale structural network in Chinese dyslexia

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ARTICLE INFO

Article history:
Received 17 November 2014
Accepted 5 September 2015
Available online 10 September 2015

Keywords:
Cortical thickness
Dyslexia
Graph theory
Structural network
Surface area

ABSTRACT

Abnormalities in large-scale brain networks have been recently reported in dyslexia; however, it remains unclear whether these abnormalities are congenital (due to dyslexia per se) or arise later in development. Here, structural magnetic resonance imaging data of 17 Chinese reading disabled (RD) and 17 age-matched typically developing (TD) children were used to construct cortical thickness (sensitive to postnatal development) and surface area (sensitive to prenatal development) networks. In the thickness network, compared to TD, RD showed reduced nodal network properties (e.g., degree and betweenness) in the left hemisphere along with enhanced nodal properties mainly in the right hemisphere. As for the surface area network, compared to TD, RD demonstrated lower nodal properties in the posterior brain regions and higher nodal properties in the anterior brain regions. Furthermore, hubs in both the thickness and surface area networks in RD were more distributed in frontal areas and less distributed in parietal areas, whereas TD showed the opposite pattern. Altogether, these findings indicate that the aberrant structural connectivity in the dyslexic individuals was not only due to a late developmental effect reflected in the altered thickness network, but may also be a congenital effect during prenatal development, reflected in the altered surface network.

Introduction

Reading, as a high-level brain function, involves interactive collaboration of brain regions that are essential to the reading process. Therefore, brain connectivity, concerned with the integration among different brain regions, has been widely assessed in studies of reading and dyslexia. To date, functional connectivity studies have typically focused on dyslexia in alphabetic languages. These studies have converged on the view that dyslexia is a disconnectivity syndrome, as dyslexic individuals have shown weaker or absent connectivity between crucial reading regions (Cao et al., 2008; Horwitz et al., 1998; Pugh et al., 2000; van der Mark et al., 2011).

Traditional connectivity studies such as those mentioned above have tended to focus on the seed regions selected based on previous findings, frequently ignoring interactions with the rest of the brain; as a result, it is possible that these studies fail to capture the complexity of the organization of the brain (Corbetta, 2012). Compared with traditional connectivity studies, the recent extensive application of graph theory in neuroscience makes understanding the functional and structural connectivity among the entire brain possible. Briefly, graph theory is a valuable framework for investigating the organization of functional and structural networks in the brain (Bullmore and Sporns, 2009). Based on graph theory, brain networks can be considered as graphs that contain abstract representations such as nodes corresponding to neural elements (i.e., brain regions) and edges corresponding to the physical connections or functional synchrony (Bullmore and Sporns, 2009). In general, graph theoretical analysis makes it possible, from an entire brain point of view, to examine the topological principles of the functional and structural networks, which are more vulnerable to cognitive disorders (Bassett and Bullmore, 2009).

To date, based on graph theory, one study investigated the functional brain network in English dyslexia using functional magnetic resonance imaging (fMRI) (Finn et al., 2014). This study revealed divergent connectivity within the visual pathway and between visual association areas and prefrontal attention areas in dyslexics compared with normal controls. Additionally, the authors reported increased right-hemisphere connectivity and persistent connectivity to inferior frontal gyrus, reflecting a compensatory mechanism for poor reading in dyslexics. Another study (Dimitriadis et al., 2013), applying a magnetoencephalography (MEG) approach to investigate resting state brain networks, demonstrated that global and local network measures were

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http://dx.doi.org/10.1016/j.neuroimage.2015.09.011
1053-8119/

significantly reduced in dyslexic individuals. In particular, local efficiency in the parietotemporal region was reduced in dyslexia. This region has frequently been reported as dysfunctional in previous neuroimaging studies of dyslexia (Hoeft et al., 2007; Shaywitz et al., 2002; Shaywitz and Shaywitz, 2005).

Structural connections constrain and shape functional interactions among the cerebral areas, giving rise to diverse functional networks, while functional connectivity patterns reflect the structural connectivity of the cerebral cortex (Wang et al., 2015). Given this relationship between structural and functional networks, we were therefore interested in whether whole-brain structural networks in dyslexia would also show similar patterns of aberrant connectivity. This has been rarely investigated; to date, only one study has investigated structural networks in Chinese dyslexia (Liu et al., 2015). This study defined a structural network based on gray matter volumetric covariance and reported that compared to controls, the structural network of dyslexic children exhibited significantly increased local efficiency combined with a tendency of decreased global efficiency, thus reflecting a more locally specialized topological organization (Liu et al., 2015).

Cortical gray matter volume is the combination of two morphological measurements, cortical surface area and cortical thickness, each of which can change independently of the other (Frye et al., 2010). From the perspective of development, cortical thickness is strongly age-related (Shaw et al., 2006; Tamnes et al., 2010) and is more sensitive to the development of cognitive ability (Sowell et al., 2004), while cortical surface area changes drastically in the prenatal periods (Kapellou et al., 2006), yet shows less developmental effects after birth in healthy subjects (Ostby et al., 2009). Therefore, exploring the structural network by separately analyzing cortical thickness and surface area can help us understand whether the abnormalities in structural networks that were observed in dyslexic readers are congenital or arise later in development. So far, only one similar study has taken this approach of differentiating gray matter volume into cortical thickness and surface area to investigate structural networks implicated in dyslexia (Hosseini et al., 2013); more specifically, the authors recorded measurements from preschool children with a familial risk of dyslexia. This study revealed that topological alterations in children with a risk of dyslexia manifested mostly in the surface area network rather than in the cortical thickness network (Hosseini et al., 2013). According to previous studies (Fisher and Francks, 2006; Pennington and Lefly, 2001), approximately only one-third of these high-risk dyslexic children were ultimately diagnosed with dyslexia. Therefore, studies are needed to take this same approach of looking at cortical thickness and surface area networks separately to investigate the topological properties in diagnosed dyslexia, which will allow for a better understanding of their neural basis.

In the current study, we aimed to investigate whether the changes in brain structural networks potentially observed in Chinese dyslexic readers are congenital (due to dyslexia per se) or arise later in development. We did this by examining abnormalities in cortical thickness and surface area networks obtained via graph theoretical analysis of a group of Chinese dyslexic children compared with a group of typically developing children. Specifically, structural co-variation in brain morphometric measurements (cortical thickness, and surface area) from MRI data was used to construct the structural networks. Structural co-variation has been proposed as a valid approach to infer the patterns of large-scale brain structural networks (Bernhardt et al., 2008; He et al., 2007; Lerch et al., 2006; Sanabria-Diaz et al., 2010). Although debate still remains, the biological significance of structural co-variance has been suggested to reflect developmental coordination or synchronized maturation between the connected brain regions (Alexander-Bloch et al., 2013). Additionally, structural networks constructed using the morphometry-based approach have been confirmed to have similar network properties with diffusion tensor imaging (DTI) networks (Gong et al., 2012), and even to show overlap with intrinsic brain activity as measured by fMRI (Kelly et al., 2012; Seeley et al., 2009; Segall et al., 2012; Zhang et al., 2011).

Materials and methods

Participants and materials

Forty children participated in this study; these children were recruited from two primary schools in Beijing. Six children were excluded from analysis due to head movement (two children) or failures in image processing (four children). Finally, the study included 17 reading disabled children (RD) (male: 13; ages ranged from 123 months to 157 months; mean age: 142 months, SD: 8.1 months) and 17 age- and gender-matched typically developing children (TD) (male: 12; ages ranged from 126 months to 145 months; mean age: 139 months, SD: 4.4 months). Inclusion criteria were as follows: (1) native Chinese speakers; (2) right-handed; (3) normal hearing and normal or corrected to normal vision; (4) no neurological disease or psychiatric disorders; (5) not taking medication affecting the central nervous system; and (6) no attention deficit hyperactivity disorder (ADHD). Written informed consent was obtained from the parent or legal guardian of each participant.

Two standardized tests were used to measure mental ability and reading achievement. Mental ability was measured by the Chinese version of the Wechsler Intelligence Scale for Children — Revised (WISC-R) (Wechsler, 1974). Reading achievement was estimated by the Character Recognition Measures and Assessment Scale for Primary School Children (CRM) (Wang and Tao, 1993). This test is a widely used standardized test to screen Mandarin-speaking Chinese children for reading disabilities.

RD was defined based on two criteria: (1) performance IQ above 90 in WISC-R and (2) 1.5 years below a subject's corresponding age in the CRM test. The detailed demographic characteristics of the two groups are shown in Table 1. The two groups were matched in age, gender, and performance IQ, but were significantly different in verbal IQ (t (32) = 4.254, $p < 0.001$) and CRM (t (32) = 9.791, $p < 0.001$), with lower scores in the RD group.

Image acquisition

All images were acquired with a 3-T Siemens scanner at Beijing Normal University. A high-resolution, three-dimensional volume of T1 weighted images was acquired with the following parameters: TR = 2300 ms; TE = 3.36 ms; TI = 900 ms; flip angle = 9°; axial slices = 160; slice thickness = 1 mm; FOV = 256 mm × 256 mm; matrix = 256 × 256 × 160; and voxel size = 1 mm × 1 mm × 1 mm. To allow for adaptation to the scanning procedure and minimization of subject motion, children were familiarized with the scanning environment in a simulated MRI scanner prior to data collection.

Data preprocessing

We used the CIVET pipeline to generate measurements of cortical thickness and cortical surface area, as previously described (Gong et al., 2012). Briefly, the T1-weighted MR images were linearly aligned in stereotaxic space using a 9-parameter linear transformation (Collins et al., 1994); subsequently, these images were corrected for non-

Table 1
Demographics, intelligence and reading performance of the typically developing (TD) and reading disabled (RD) groups.

	TD (mean (SD))	RD (mean (SD))	t/χ^2	p
Age (months)	139 (4.4)	142 (8.1)	−1.262	.216
Gender (M/F)	5/12	4/13	$\chi^2 = .151$	.698
Performance IQ	108 (14.7)	100 (9.1)	1.833	.078
Verbal IQ	116 (11.3)	98 (12.6)	4.254	<0.001
CRM	3015 (143)	2496 (165)	9.791	<0.001

CRM refers to the character recognition measure. CRM is the number of characters recognized out of 3500 commonly used Chinese characters.