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Research article

Altered topological organization of brain structural network in Chinese children with developmental dyslexia

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HIGHLIGHTS

- We investigated the Chinese DD's brain using structural network analysis.
- Chinese DD's brain showed higher local specialization in topological organization.
- A tendency of lower E_{glob} and prolonged characteristic path length was noted in DD.
- Increased regional network property was found in the left precentral gyrus.
- A series of Chinese-related hub regions were found unpresented in DD's network.

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ABSTRACT

Increasing evidence indicates that developmental dyslexia (DD) is a "disconnection syndrome", and new probes of connectome were applied to investigate the "disconnection" in DD. However, there is a lack of brain connectome studies of Chinese dyslexics, who may have a different neural impairment pattern due to the logographic nature of Chinese. The aim of this study was to investigate the topological organization characteristics of the DD brain using a structural network based analysis on the volumetric covariance, which is a method with the advantage of reflecting brain developmental changes. Twenty-five children diagnosed with DD and twenty-five typically developing controls were included. The structural networks based on the pair-wise correlation of gray matter volume from 90 brain regions were constructed for the two groups and compared. Compared to controls, the structural network of dyslexic children exhibited significantly increased local efficiency combined with a tendency of decreased global efficiency and prolonged characteristic path length, thus reflecting a more locally specialized topological organization. Two brain areas showed significantly altered local regional network properties: the left precentral gyrus with increased b_i, and the right Heschl's gyrus with decreased b_i and k_i. Moreover, a series of hub regions

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(especially the right fronto-temporal regions) identified in the network of typically developing children were not presented in the brain of DD. To our knowledge, this is the first whole-brain structural network study on Chinese dyslexics. This study provides evidence of brain topological organization changes in Chinese children with DD, and thus may help shed light on its neurobiological basis.
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1. Introduction

Developmental dyslexia (DD) is a neurodevelopmental disorder with an incidence of 5–18% [1], and is the most common form of learning disability. Although many theories have been established to explain the biological mechanism of DD, its neurobiological etiology remains controversial. Due to the logographic nature, Chinese language processing involves a more complex, unsystematic, and semantics-related mapping compared with alphabetic language processing [2]. To date, most neuroimaging studies of Chinese patients with DD support a unique pattern of neural impairment [3–6].

Increasing evidence has suggested that DD is a "disconnection syndrome" among a series of language processing regions, instead of isolated changes, and applying new probes of the connectome to investigate the "disconnection" in the brains of patients with DD has become an important area of research and provided novel findings [7,8]. Based on topological quantitative methods [9], research has shown that the structural network organizes data based on regional brain morphometry (volume [10], cortical thickness, or surface area [11,12]) to describe the whole-brain level topological organization patterns using volumetric covariance (i.e., the association between regional morphometry), and could reflect the anatomical connections among brain neurocircuits [13,14].

In this study, we planned to investigate the topological organization characteristics of the brain structural network in Chinese dyslexics. Although the neurophysiological significance of this method may be debated, we performed this study based on three considerations. (1) Recent work has confirmed the advantage of the network of structural covariance in reflecting synchronized brain developmental changes [14]. (2) Coincidentally, the original inspiration for introducing the structural network was motivated by investigating the hypothetical association between cortical thickness of Broca's area and Wernicke's area [13], with strikingly consistent results to previous tractography findings. On the other hand, this underlies the feasibility of using this method to investigate language-related disorders. (3) Since there is evidence of brain morphometric alteration in both alphabetic and Chinese DD populations [4,15], it is possible that the interregional associations between brain areas engaged in language processing are changed as well.

To date, we have found only one whole-brain structural network study of normal children with a familial risk for DD [12], and no study of Chinese individuals with DD. The results of this study would not only provide evidence for topological organization changes in the brains of individuals with DD, but also help to better understand the differences between alphabetic and Chinese type DD and thus shed light on their neurobiological basis.

2. Materials and methods

2.1. Subjects

This study was approved by the joint Chinese university of Hong Kong (CUHK) and new territories east cluster (NTEC) clinical research ethics committee (CREC). Informed consent was obtained from each subject and his/her parents before experiment. Twenty-five children (15 boys and 10 girls; mean age, 8.65 ± 0.90 years; range, 7.58–10.83 years) diagnosed with DD were included in this study. Only individuals <12 years old were included because the diagnosis of DD in children >12 years of age is less valid with the instrument used. The diagnosis of DD was established using the Hong Kong test of specific learning difficulties in reading and writing (HKT-SpLD) [16]. Children were referred by the local education authority, child assessment centers, and a parent association (Hong Kong association for specific learning disabilities). The HKT-SpLD instrument contains 12 subtests which were designed to generate five composite scores in the aspects of literacy, phonological awareness, phonological memory, rapid naming and orthographic skills. A diagnosis of DD was established if a child's literacy composite score and any one of the other composite scores were below the average of their respective ages in the HKT-SpLD by one standard deviation. In this study, 11 children were included without recording their test results because they could not cooperate to finish the test but were found to be below average in enough subtests by the psychologist. Another twenty-five typically developing controls (NC group; 14 boys and 11 girls; mean age, 8.69 ± 0.95 years; range, 7.12–10.53 years) matched for age ($p = 0.88$), gender ($p = 0.77$), and intelligence quotient (IQ) ($p = 0.21$) with normal reading ability (screened using their language examination results at school being above the 90th percentile [3,4,6]) were included (Table S1). All the participants were right-handed native Chinese-speaking students from primary schools. Children with neurological diseases or psychiatric disorders, head injuries, abnormal hearing/corrected vision, a history of taking medication affecting the central nervous system, an IQ < 80, and attention deficit hyperactivity disorder (ADHD) were excluded.

2.2. Magnetic resonance imaging (MRI) acquisition

Subjects in dyslexia group were scanned using a clinical 3T MRI scanner (Achieva, Philips Medical Systems, Best, The Netherlands) with a quadrature head coil. For each subject, whole brain high resolution three-dimensional T1-weighted (3DT1) images were acquired using a turbo field echo (TFE) sequence with the following parameters: TR/TE = 6.9/3.2 ms, FOV = 240×240 mm, flip angle = 8°, slice thickness = 1 mm, voxel size = $1 \times 1 \times 1$ mm^3. Data of normal subjects were acquired on a 1.5T MR scanner (Achieva, Phillips Medical Systems, Best, The Netherlands) with an eight-channel Philips SENSE head coil. A 3D fast field echo (FFE) sequence was applied with the following parameters: TR/TE = 525/4.6 ms, FOV = 256×256 mm, flip angle = 15°, slice thickness = 1 mm, voxel size = $1 \times 1 \times 1$ mm^3.

2.3. Structural data processing

All acquired 3DT1 MR images were processed utilizing Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology), and calculated for a gray matter (GM) volume of 90 cortical and subcortical regions of interest (ROI) with parcellation in accordance with automatic anatomical labeling (AAL). After visual inspection of the images of each subject to exclude the cases with

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