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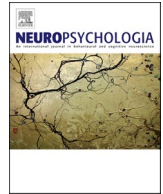
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# Resting-state EEG reveals global network deficiency in dyslexic children

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## ABSTRACT

Developmental dyslexia is known to involve dysfunctions in multiple brain regions; however, a clear understanding of the brain networks behind this disorder is still lacking. The present study examined the functional network connectivity in Chinese dyslexic children with resting-state electroencephalography (EEG) recordings. EEG data were recorded from 27 dyslexic children and 40 age-matched controls, and a minimum spanning tree (MST) analysis was performed to examine the network connectivity in the delta, theta, alpha, and beta frequency bands. The results show that, compared to age-matched controls, Chinese dyslexic children had global network deficiencies in the beta band, and the network topology was more path-like. Moderate correlations are observed between MST degree metric and rapid automatized naming and morphological awareness tests. These observations, together with the findings in alphabetic languages, show that brain network deficiency is a common neural underpinning of dyslexia across writing systems.

## 1. Introduction

Reading is an indispensable cognitive ability in our daily life. Unfortunately, learning to read can be challenging for many children, and approximately 5–17% of them are afflicted by developmental dyslexia, a severe learning disability that emerges despite normal intelligence and a normal socio-cultural environment (Sun et al., 2013; Ziegler et al., 2003). Neuroimaging studies have greatly advanced our understanding of the neural underpinnings of dyslexia and may eventually help to identify biomarkers that can be used for early diagnosis and intervention (Posner and Rothbart, 2005). As a complex cognitive activity, reading requires the coordination of multiple neural substrates (Beaulieu et al., 2005), and the field has seen a growing effort in examining abnormalities of brain networks in dyslexia, with task-based functional MRI data (Bullmore and Sporns, 2009; Feng et al., 2016; Greicius et al., 2009). For instance, a significant disruption of functional connectivity between the visual word form area (VWFA) and left inferior frontal and left inferior parietal language areas was seen in German dyslexic readers when performing continuous reading tasks (Van der Mark et al., 2011) and

phonological and lexical decision tasks (Schurz et al., 2015; Van der Mark et al., 2009). Decreased connectivity between the left middle occipital gyrus and left inferior frontal gyrus was also seen in dyslexic children when they performed lexical and perceptual tasks (Cao et al., 2018). With a whole-brain functional connectivity analysis, Finn et al. (2014) revealed reduced connectivity in the VWFA, as well as divergent connectivity within the visual pathway and between visual association areas and prefrontal attention areas. With EEG recordings, a recent study showed that the connection from the left-central to right inferior-temporal and occipital sites was weaker in dyslexic readers when processing visual word forms (Žarić et al., 2017).

In addition to task-evoked neural activity, the spontaneous neural activity in resting state (i.e., when no cognitive task is being performed) can also be used to reveal the intrinsic functional architecture of the brain in dyslexia and other neurodevelopmental disorders (Deco et al., 2011; Fox et al., 2005; van Diessen et al., 2015). With resting-state fMRI data, Koyama et al. (2013) found that the connectivity between the left intraparietal sulcus and the left fusiform gyrus is weaker in English-speaking dyslexic children, regardless of whether they had been

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## 2.2. Screening tools

### 2.2.1. Standard Combined Raven's test

The Standard Combined Raven's Test (Li and Chen, 1989) was used to assess the non-verbal intelligence of the children.

### 2.2.2. Chinese character recognition test

This test was developed by Shu et al. (2003) and it has been widely used for screening dyslexia in Mandarin-speaking Chinese children (Ding et al., 2016; Lei et al., 2011; Shu et al., 2006; Zhang et al., 2012). This test requires the child to read out a list of 150 Chinese characters, which are presented in order of increasing difficulty. The maximum possible score on this test is 150. Scoring one standard deviation below the grade average is a good indication of severe reading difficulty or dyslexia.

## 2.3. Reading-related cognitive tests

### 2.3.1. Phonological awareness test

A phoneme deletion test was used to assess the phonological processing skill of the children who participated in the present study (Li et al., 2012). In this test, children are asked to produce a new syllable by removing the first phoneme from a monosyllabic Chinese word. For example, given the syllable/cha1/, children are asked to delete the/ch/sound. The answer, in this case, is/a1/. This test consisted of four practice trials and 22 experimental trials. Among the experimental trials, there are fourteen trials for one-syllable words and four trials for two-syllable and three-syllable words.

### 2.3.2. Rapid number naming test

The rapid number naming test was used to assess the rapid naming ability of readers (Li et al., 2012). Five numbers (2, 4, 6, 7, and 9) are pseudo-randomly repeated eight times on a paper. Children are asked to name the numbers as accurately and rapidly as possible. Children are instructed to name the sheet twice. The score is the average naming time across those two trials.

### 2.3.3. Morphological awareness test

A morphological construction test (Lei et al., 2011; McBride-Chang et al., 2003) was used to assess morphological awareness. In each trial, children are required to construct a new compound word to represent the objects or concepts described by the experimenter. For example, the experimenter asks, "if a sun that is red in color is called red sun (/hong3 tai4 yang3/), what should we call a sun that is yellow?" The correct answer is "yellow sun (/huang3 tai4 yang3/)". There are 2 practice trials and 27 testing trials on this test.

## 2.4. EEG recording and analysis

EEG recordings were collected in a dimly lit and quiet room. In order to record stable and ocular artifact-free EEG data, all participants were instructed to refrain movements and to close their eyes. Two minutes of resting-state (eyes closed) EEG data were recorded using a 32-channel system. Horizontal eye movements (HEOG) were recorded using an electrode placed at the outer canthi of the right eye. Electrode for recording vertical eye movements (VEOG) was placed just under the left eye. All channels were amplified with a DC-100 Hz band-pass filter and then digitized at 1000 Hz using the BrainVision Recorder software (Brain Products GmbH, Gilching, Germany). Electrode impedance was kept below 5 k $\Omega$ .

Continuous EEG data were imported into EEGLAB (Delorme and Makeig, 2004) for analysis. Channels with excessive artifacts (e.g., eye blinks, eye movements, body movements, and muscle contractions) were removed and reconstructed from nearby channels with spline interpolation. Channel reconstruction was performed on the EEG data of 22 subjects (7 from the DD group), and a maximum of four channels was

allowed for an EEG recording. The EEG data were digitally filtered (0.5-30 Hz band-pass), downsampled to 512 Hz, and segmented into 2-s long epochs after re-referencing to the average of all scalp channels. The data from each participant were then converted to 20 artifacts free epochs, each containing 1024 times samples and saved in plain text files. To examine the various MST metrics, subsequent analyses were performed separately for the delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz) bands, with the BrainWave software developed by Cornelis Jan Stam (version 0.9.76; freely available from <http://home.kpn.nl/stam7883/brainwave.html>).

### 2.4.1. Power spectral analysis

The power in different frequency bands can be used to assess the drowsiness or alertness of the subjects. More relevantly, power is known to affect the estimation of connectivity and network metrics. Thus, the power spectrum of the 30 EEG scalp channels was first examined with a frequency resolution of  $1/2\text{ s} = 0.5\text{ Hz}$  in BrainWave.

### 2.4.2. Functional connectivity: the phase lag index (PLI)

The Phase Lag Index (PLI) is a measure of asymmetry for the distribution of phase differences between two signals. It is less affected by the influence of volume conduction, common sources, and montage (Stam et al., 2007). PLI is obtained from time series of phase differences,  $\Delta\phi(t_k)$ ,  $k = 1 \dots N$ ,  $PLI = \frac{1}{N} \sum_{k=1}^N |\langle \text{sign}[\sin(\Delta\phi(t_k))] \rangle|$ . The PLI ranges between 0 and 1. A PLI of zero suggests no coupling or coupling with a phase difference centered around  $0 \text{ mod } \pi$ . A PLI of 1 indicates perfect phase locking at a value of  $\Delta\phi$  from  $0 \text{ mod } \pi$ . A larger PLI suggests stronger phase locking. The PLI analysis in the present study generated  $30 \times 30$  weight adjacency matrices, which were later used in the MST analysis in each frequency band.

### 2.4.3. Network topology: MST analysis

MST allows no recurrent connections, and networks are constructed with the weight adjacency matrices generated from the PLI analysis. When examining brain networks across different populations, the MST analysis allows the construction of graphs of the same number of nodes and connections. Moreover, an MST network has a much simpler configuration as it focuses on the most significant sub-graph and thus avoids bias (van Diessen et al., 2015). Based on the PLI adjacency matrices, MST networks were constructed using the Kruskal algorithm (Kruskal, 1956). The weights (defined as  $1/PLI$ ) of all possible connections were first sorted in ascending order; the strongest connections were then added to the network one-by-one until all 30 nodes were linked in a loopless sub-graph. As noted, the topological properties of an MST network can be characterized by eight metrics: degree, leaf fraction, diameter, eccentricity, betweenness centrality (BC), Kappa, degree correlation, and tree hierarchy ( $T_h$ ) (Stam et al., 2014). A detailed description of these MST metrics is presented in Table S1 in Supplementary Material.

## 2.5. Statistical analysis

We compared the non-verbal IQ, the Chinese character recognition score, the cognitive test scores, and the various EEG metrics (spectrum power, PLI values, and MST metrics) between the DD and CA children. The PLI and MST metrics were log-transformed to meet the statistical assumption of normal distribution. Correlation analyses were performed to reveal the associations between network metrics (PLI values and MST metrics) and the various reading-related cognitive skills. Permutation tests were also performed on the correlations with the PERMUTOOLS toolbox in MATLAB (<https://github.com/mickcrosse/PERMUTOOLS>).



### 3. Results

#### 3.1. Behavioral tests

Scores from the CRT test (non-verbal IQ), the character recognition test, and the three reading-related cognitive tests are presented in Table 1. Not all children completed all behavioral tests, and the means reported in Table 1 are based on those who completed each of the tests (see notes below Table 1). The non-verbal IQ was not statistically different across the two groups (DD and CA),  $t(64) = 1.10, p = 0.276$ , *Cohen's d* = 0.275. Not surprisingly, DD children made more errors on the Chinese character recognition test,  $t(65) = 25.12, p < 0.001$ , *Cohen's d* = 6.257. The DD children also performed worse on the morphological awareness test,  $t(29) = 2.63, p = 0.013$ , *Cohen's d* = 0.946, the phonological awareness test,  $t(55) = 3.73, p < 0.01$ , *Cohen's d* = 0.993, and the rapid number naming test,  $t(64) = 4.894, p < 0.001$ , *Cohen's d* = 1.225.

#### 3.2. Power spectrum

As shown in Fig. 2, the power spectrum was similar between the DD and CA children, and no significant group difference was found in the four-frequency bands (see Table S2 in Supplementary Material). One of the reasons to examine the spectral power in different frequency bands was to reveal the attentional state of the participants (e.g., if they were drowsy). Following the practice of Fraga González et al. (2016), a participant was considered as an outlier if the power was 1.5 quartile range outside the upper or lower quartile (Tukey, 1977). For the delta band analysis, one subject from the DD group was excluded from further analysis. For the theta band analysis, one subject from the CA group was excluded.<sup>1</sup>

#### 3.3. Functional connectivity (PLI)

For PLI, no statistically significant group difference was observed in any frequency bands (see Table 2).

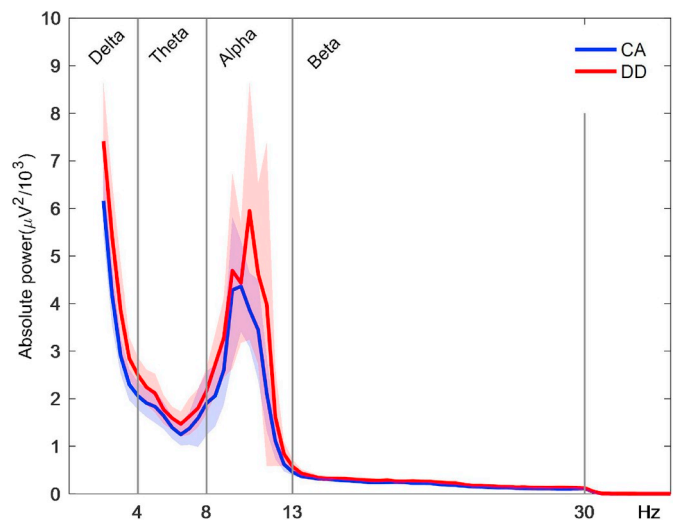
**Table 1**

Demographical data and scores on various behavioral tests for dyslexic children (DD) and healthy controls (CA). CCR- Chinese Character Recognition test; CRT- Combined Raven's Test; MA- Morphological Awareness test; PA- Phonological Awareness test; RAN- Rapid number Naming test.

	DD	CA	Stats		
	M (SD)	M (SD)	t	p	Cohen's d
N	27	40			
Sex (M/F)	13/14	17/23			
Age (years)	9.22 (0.58)	9.38 (0.49)	1.16	0.249	0.290
CRT <sup>a</sup>	119.21 (11.93)	122.45 (11.69)	1.10	0.276	0.275
CCR	67.04 (10.85)	122.33 (7.19)	25.12	< 0.001	6.257
MA <sup>b</sup>	21.81 (3.29)	24.47 (2.17)	2.63	0.013	0.946
PA <sup>c</sup>	15.65 (3.36)	18.55 (2.49)	3.73	< 0.001	0.993
RAN <sup>d</sup>	18.46 (4.35)	14.11 (2.88)	4.89	< 0.001	1.225

Notes: <sup>a</sup> One child in the CA group did not complete this test. <sup>b</sup> Eleven children in the DD group and 16 children in the CA group did not complete this test. <sup>c</sup> One child in the DD group and 9 children in the CA group did not complete the test. <sup>d</sup> One children in the CA group did not complete this test.

<sup>1</sup> The PLI and MST metrics were also analyzed without excluding any participant. The statistical results are presented in Table S3 in Supplementary Material.



**Fig. 2.** Power averaged across all scalp electrodes. CA, chronological age-matched controls; DD, developmental dyslexia. The strips represent 95% confidence intervals.

#### 3.4. Network topology (MST metrics)

For illustration purposes, the MST trees constructed from the group average PLI are presented in Fig. 1B. Compared to age-matched controls, dyslexic children showed a more path-like (i.e., lacked interconnections) network topology. The statistical results for all MST metrics in all frequency bands are presented in Table S3 in Supplementary Material. For brevity, only significant or marginal group differences are discussed here; full details are summarized in Table 2.

In the beta band, the eccentricity metric was higher in the DD group ( $M = 0.283, SD = 0.010$ ) than that in the CA group ( $M = 0.278, SD = 0.009$ ),  $t(65) = 2.176, p < 0.05$ , *Cohen's d* = 0.542 (see Fig. 3A). The diameter score (the largest distance between any two nodes) was marginally higher in the DD group ( $M = 0.359, SD = 0.013$ ) than that in the CA group ( $M = 0.354, SD = 0.012$ ),  $t(65) = 1.842, p = 0.070$ , *Cohen's d* = 0.459 (see Fig. 3B). The betweenness centrality (BC) score, i.e., the fraction of all shortest paths that pass through a node was lower in the DD group ( $M = 0.697, SD = 0.017$ ) than that in the CA group ( $M = 0.707, SD = 0.015$ ),  $t(65) = 2.568, p < 0.05$ , *Cohen's d* = 0.640 (see Fig. 3C). These results all suggest a deficit in information integration in dyslexic children.

A marginal group difference was observed on degree in the theta band, with lower degree score observed in the DD ( $M = 0.222, SD = 0.015$ ) than in the CA group ( $M = 0.228, SD = 0.013$ ),  $t(64) = 1.810, p = 0.075$ , *Cohen's d* = 0.453 (see Fig. 4A).

The EEG epochs of the present study were 2-s long, shorter than that in Fraga González et al. (2016); however, the results reported here were unlikely confounded by the length of the epochs. The MST network metrics derived from PLI are less affected by epoch length, and reliable results can be obtained with even shorter epochs (Fraschini et al., 2016).

#### 3.5. MST metrics and reading-related cognitive skills

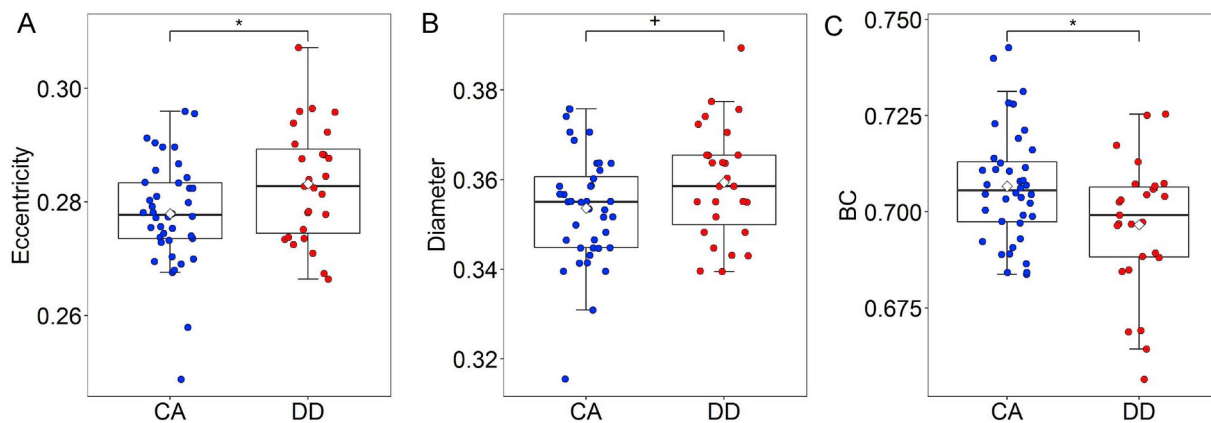
Correlation analysis was performed to examine the association between the MST network metrics and the reading-related cognitive skills assessed in the present study. For brevity, only statistically significant results are reported here (see Fig. 4).

In the theta band, a negative correlation was observed between rapid number naming speed and degree in the CA group (see Fig. 4B),  $r = 0.328, p = 0.044$ . In the DD group, morphological awareness positively correlated with degree (see Fig. 4C),  $r = 0.631, p = 0.009$ . No significant correlation was found between the other network metrics and reading-

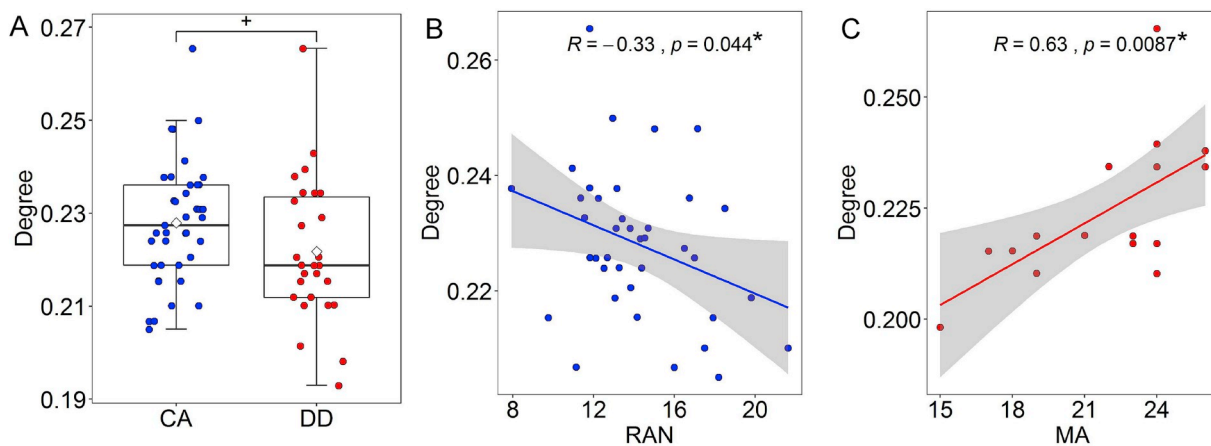
**Table 2**  
The PLI value and network topology metrics in dyslexic children (DD) and normal developing children (CA).

	DD		CA		Stats		
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>t</i>	<i>p</i>	<i>Cohen's d</i>
<b>Theta band</b>							
PLI	0.240	(0.014)	0.246	(0.013)	1.642	0.106	0.411
Degree	0.222	(0.015)	0.228	(0.013)	1.830	<i>0.072</i>	0.458
Eccentricity	0.284	(0.012)	0.281	(0.011)	1.049	0.298	0.263
BC	0.699	(0.016)	0.703	(0.015)	1.251	0.215	0.313
Kappa	2.920	(0.109)	2.945	(0.099)	0.986	0.328	0.247
R	-0.345	(0.028)	-0.340	(0.036)	0.721	0.473	0.181
Diameter	0.360	(0.016)	0.356	(0.015)	1.131	0.262	0.283
Leaf	0.544	(0.016)	0.545	(0.016)	0.245	0.807	0.061
T <sub>h</sub>	0.392	(0.010)	0.390	(0.012)	0.704	0.484	0.176
<b>Beta band</b>							
PLI	0.132	(0.006)	0.134	(0.007)	0.755	0.453	0.188
Degree	0.215	(0.016)	0.222	(0.015)	1.574	0.120	0.392
Eccentricity	0.283	(0.010)	0.278	(0.009)	2.176	<b>0.033</b>	0.542
BC	0.697	(0.017)	0.707	(0.015)	2.568	<b>0.013</b>	0.640
Kappa	2.863	(0.098)	2.907	(0.125)	1.563	0.123	0.389
R	-0.314	(0.037)	-0.313	(0.039)	0.187	0.852	0.047
Diameter	0.359	(0.013)	0.354	(0.012)	1.842	<i>0.070</i>	0.459
Leaf	0.531	(0.015)	0.538	(0.020)	1.499	0.139	0.373
T <sub>h</sub>	0.384	(0.012)	0.383	(0.014)	0.401	0.690	0.100

Notes: Bold text highlights significant results ( $p < 0.05$ ); italic text highlights results at trend level.



**Fig. 3.** In the beta band, the MST metrics eccentricity (A) and diameter (B) were higher in dyslexic children, whereas BC (C) was lower in dyslexic children. The group averages are represented by solid diamonds. \* $p < 0.05$ , + $p < 0.075$ .



**Fig. 4.** In the theta band, the MST degree metric were lower in dyslexic children (A). The correlation between the MST degree metrics and reading-related cognitive abilities in healthy controls (B) and dyslexic children (C). RAN, rapid number naming test; MA, morphological awareness test. The grey strips represent 95% confidence intervals. \* uncorrected  $p$ -values.

related cognitive tests. The permutation tests yielded consistent results (see Table S4 in Supplementary Material).

#### 4. Discussion

The present study used resting-state EEG data to examine the functional brain network in Chinese dyslexic children. Consistent with previous findings in alphabetic languages (Fraga González et al., 2016, 2018b), the MST network in dyslexic children had a higher eccentricity metric in the beta band, suggesting a more path-like network topology in dyslexic children. The BC metric, which reflects dysfunctional hub nodes, was lower in the beta band in Chinese dyslexic children, a network abnormality that was not seen in dyslexic children in alphabetic languages (Fraga González et al., 2016, 2018b). Importantly, the present work also revealed moderate associations between MST metrics and various cognitive skills that are critical to reading.

##### 4.1. Network topology in the theta band

Fraga González and colleagues (2018b) found several MST network metrics, including degree, leaf fraction, and Kappa, were lower in the theta band in dyslexic children, showing that the long-range connections in dyslexic children may be less efficient. The present observation of a less integrated network in dyslexic children, as reflected in the lower degree metric in the theta band, is consistent with this hypothesis. The present results, together with that from alphabetic languages (Fraga González et al., 2018; Jiménez-Bravo et al., 2017), clearly show that a less integrated network in the theta band is likely a common deficiency in dyslexia.

##### 4.2. Network topology in the beta band

Network deficiency in the beta band has not been seen in alphabetic languages (e.g., Dutch, see Fraga González et al., 2016, 2018b). Compared to normally developing children, in the beta band, the MST eccentricity metric was higher, and the BC metric was lower in Chinese dyslexic children. In addition, the diameter metric was marginally higher in dyslexics compared with healthy controls. The diameter metric is the maximum eccentricity (Stam and Straaten, 2012), and it is positively associated with the path length of brain networks (Tewarie et al., 2015). These results suggest an overall longer node path and a less integrated network in dyslexic children. Consistently, a recent MRI study also showed that Chinese dyslexic readers have prolonged node path and fewer hub regions in whole-brain structural networks (Liu et al., 2015).

Beta oscillations are related to motor control (Brovelli et al., 2004; Herrmann et al., 2016; Jenkinson and Brown, 2011) and visual perception (Quentin et al., 2015). For instance, synchronized activation has been observed in sensorimotor areas following voluntary movements and somatosensory stimulation (Neuper and Pfurtscheller, 2001). Classen et al. (1998) also reported a decrease in activation coherence in the beta band in a visuomotor force-tracking task but not in visual- or motor-only tasks, suggesting that beta oscillations are related to visuomotor integration (Classen et al., 1998; Kilavik et al., 2013; Müller et al., 2003). Visuomotor skills are particularly important to Chinese reading (Meng et al., 2018; Tan et al., 2005b), and deficits in visuomotor integration have been observed in Chinese dyslexic children in previous behavioral studies (Cheng-Lai et al., 2013; McBride-Chang et al., 2011). Visuomotor integration was not directly assessed in the present study. Whether the beta-band network deficiency in Chinese dyslexic children is related to visuomotor integration remains an open question for future investigations.

##### 4.3. MST metrics and reading-related cognitive skills

Frequently assessed with the rapid number naming task, rapid automatized naming (RAN) is a good predictor of reading ability (Kirby

et al., 2010; Liao et al., 2015; Norton and Wolf, 2012; Shum and Au, 2017), and recent studies have shown that RAN is related to Chinese orthographic processing (Liao et al., 2015; Wang et al., 2018). Morphological awareness is another reliable predictor of dyslexia in Chinese (Lei et al., 2011; Li et al., 2009; Shu et al., 2006). In the theta band, the present study revealed a negative correlation between RAN and the MST degree metric in the CA group, and a positive correlation between morphological awareness and the MST degree metric in the DD group. Children with lower network degree metrics are less efficient in information transfer; they are slower in automatized naming and make more errors in morphological processing. These correlations are consistent with previous findings that theta-band activity is related to speech processing (Luo and Poeppel, 2007), comprehension (Bastiaansen et al., 2008), and various cognitive skills that are indispensable to readings. A lower MST degree metric suggests a more path-like network topology. Network topology is likely a determinant of orthographic processing and automaticity in reading.

##### 4.4. Limitations of the present study

Before closing our discussion, we would like to note a few limitations of the present work. First, the epoch length was shorter in the current study (2 s) compared to previous work by Fraga González et al. (2016). Although an epoch of 2 s is sufficient for reliable MST analysis, especially for the eccentricity metric, some MST metrics (leaf and hierarchy) would require much longer epochs to estimate (Fraschini et al., 2016). Second, the electrode montage was smaller in the present study; further replication of the present findings is desirable. Thirdly, the correlation analysis was performed on various brain network metrics and reading skills, which are highly inter-correlated. Although permutation tests have been performed to control false-positive results, further study with a much larger sample is needed. Nevertheless, as an initial attempt in revealing network abnormalities in Chinese dyslexic children with resting-EEG recordings, the present work revealed a moderate correlation between the MST degree metric and rapid automatized naming and morphological awareness, suggesting network topology is likely a major constraint on reading ability.

#### Declaration of competing interest

The authors declare no conflict of interest.

#### CRediT authorship contribution statement

**Huidong Xue:** Investigation, Data curation, Formal analysis, Methodology, Resources, Software, Visualization, Writing - original draft. **Zhiguo Wang:** Conceptualization, Funding acquisition, Methodology, Resources, Software, Supervision, Validation, Writing - review & editing. **Yufei Tan:** Investigation, Resources, Writing - review & editing. **Hang Yang:** Investigation, Resources, Writing - review & editing. **Wanlu Fu:** Investigation, Resources, Writing - review & editing. **Licheng Xue:** Methodology, Resources, Writing - review & editing. **Jing Zhao:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Software, Project administration, Supervision, Validation, Writing - review & editing.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.neuropsychologia.2020.107343>.

## Compliance with ethical standards

This study was carried out following the guidelines listed in the Declaration of Helsinki. The research protocol was reviewed by a local ethics committee, and written informed consent was obtained from the parents of all children who participated in this study.

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