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Aberrant resting-state functional brain networks in dyslexia: Symbolic mutual information analysis of neuromagnetic signals

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ABSTRACT

Neuroimaging studies have identified a variety of structural and functional connectivity abnormalities in students experiencing reading difficulties. The present study adopted a novel approach to assess the dynamics of resting-state neuromagnetic recordings in the form of symbolic sequences (i.e., repeated patterns of neuromagnetic fluctuations within and/or between sensors).

Participants were 25 students experiencing severe reading difficulties (RD) and 27 age-matched non-impaired readers (NI) aged 7–14 years. Sensor-level data were first represented as symbolic sequences in eight conventional frequency bands. Next, dominant types of sensor-to-sensor interactions in the form of intra and cross-frequency coupling were computed and subjected to graph modeling to assess group differences in global network characteristics.

As a group RD students displayed predominantly within-frequency interactions between neighboring sensors which may reflect reduced overall global network efficiency and cost-efficiency of information transfer. In contrast, sensor networks among NI students featured a higher proportion of cross-frequency interactions. Brain-reading achievement associations highlighted the role of left hemisphere temporo-parietal functional networks, at rest, for reading acquisition and ability.

1. Introduction

1.1. Cortical connectivity in reading and reading disability

There is accumulating evidence that the degree of myelination in left hemisphere cortico-cortical tracts correlates positively with reading skill (Hoeft et al., 2011; Niogi and McCandliss, 2006). Moreover, there is evidence (using Diffusion Tensor Imaging; DTI) of reduced myelination in left hemisphere white matter tracts connecting inferior frontal, temporal, occipital, and parietal regions among adults with a history of reading disability (Vandermosten et al., 2012). Both increased and decreased anatomical (using DTI) and functional connectivity (using task-related fMRI) within a network of dorsal and ventral brain regions have been reported in struggling readers compared to typically achieving readers (Richards et al., 2015). Other task-related fMRI studies reported reduced connectivity within the reading network in adults with a history of reading difficulties compared to non-impaired readers (Schurz et al., 2014; van der Mark et al., 2011). fMRI evidence of a less integrated brain network has also been found in Chinese dyslexic children compared to typically achieving readers which was characterized by reduced long-range communication and increased local processing (Liu et al., 2015).

Studies on functional connectivity patterns at rest (i.e., independent of task performance) in dyslexia are scarce. Previous fMRI studies detected a strong association between functional connectivity in reading networks and reading ability in both children and adults (Koyama et al., 2011, 2013; Schurz et al., 2014; Zhang et al., 2014). Moreover, the strength of resting-state connectivity between the ventral visual word form area and the dorsal attention network was significant linked to individual reading skill (Vogel et al., 2014). Resting-state data may be particularly useful to assess aberrant modes of information exchange both within and between key reading-related cortical regions which

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may, in turn be associated with suboptimal cortico-cortical integration during reading acquisition and performance of reading tasks.

1.2. Cross-frequency coupling as a measure of resting-state functional connectivity

Magnetoencephalography (MEG) is uniquely suited to address functional connectivity because it possesses adequate temporal resolution to describe the real-time dynamics of fine-grained interactions between neuronal populations. By adopting a dynamic functional connectivity analysis of resting-state neuromagmetic data we identified abnormal temporal correlations between time series recorded over left temporo-parietal brain areas in students experiencing severe reading difficulties (RD) as compared to age-matched typical readers (Dimitriadis et al., 2013b). A more recent report using resting-state data from the same cohort focussed on cross-frequency coupling between neuromagnetic time series (Dimitriadis et al., 2016c). Sensor interactions in the form of phase-to-amplitude coupling were quantified though the phase-locking index which is thought to represent the degree to which slower brain rhythms in a given neuronal population can reset ongoing neurophysiological processes in a different neuronal population operating at higher frequencies (Buzsáki, 2010; Canolty and Knight, 2010; Buzsáki et al., 2013). Results indicated that resting-state activity in typical readers was characterized by more stable cross-frequency interactions than in RD students. One interpretation of these findings is that temporally stable cross-frequency information exchange reflects a typical and, presumably, optimal working level ensuring efficient neuronal transmission (Deco and Corbetta, 2011; Deco et al., 2013) available to support typical reading acquisition and performance.

In this study we extend these findings by examining both same-frequency and cross-frequency interactions in the same cohort of RD and typical readers. The novelty of the present report entails computing sensor interaction metrics based on the concept of *symbolic dynamics*, wherein neuromagnetic signals are first transformed into symbolic sequences consisting of a finite set of substrings (Janson et al., 2004; Dimitriadis et al., 2012a; Robinson and Mandell, 2015). Sensor interactions were then quantified using a variant of Mutual Information (King et al., 2013; Robinson and Mandell, 2015), a rather popular approach in the search for aberrant patterns of functional connectivity based on EEG and MEG recordings in a variety of clinical conditions (Colclough et al., 2016; Uhlhaas and Singer, 2006). The original Mutual Information algorithm was adapted here to accommodate symbolic time series and to compute an undirected weighted connectivity estimator (i.e., Symbolic Mutual Information). Surrogate data analyses were then used to identify the dominant type of intra- or cross-frequency coupling for each pair of sensors and construct a weighted, integrated functional connectivity graph characteristic of the resting-state recordings of each participant. Finally, estimated functional networks were spatially filtered through bootstrapping and submitted to graph analyses in order to assess both sensor-specific and overall network efficiency and cost-efficiency (Stam, 2014).

The present study had three aims: First, to identify aberrant spectral (intra- and cross-frequency coupling) and spatial characteristics of functional brain networks in RD students; Second, to assess the value of features associated with sensor-level brain network metrics in discriminating between RD and age-matched typical readers using machine learning techniques. Finally, to establish the functional significance of these metrics for basic reading skills through correlational analyses. We hypothesized that RD children would demonstrate reduced efficiency of information flow compared to non-impaired readers and sensor interactions that operate predominantly in same-frequency oscillations. Conversely, cross-frequency interactions would be more prominent in typical readers and their relative predominance will serve as a significant predictor of basic reading skill.

2. Material and methods

2.1. Participants

Participants were two age-matched groups of students aged 7–14 years. The RD group included 25 children (12 boys) with reading difficulties (RD group) as indicated by scores below the 16th percentile level (standard score of 85) on the Basic Reading composite index (Word Attack and Letter–Word Identification subtest scores of the Woodcock–Johnson Tests of Achievement-III; Woodcock et al., 2001; WJ-III). These scores are consistent with the presence of dyslexia and is lower than in previous studies (Rezaie et al., 2011; Simos et al., 2011) of this cohort because we focused on studying severely impaired children. They were recruited from a larger Grade 6–8 intervention study (Vaughn et al., 2010) involving students at-risk for further academic failure because they failed to pass the school-administered Texas Assessment of Knowledge and Skills (TAKS).

Twenty-seven children (9 boys) who had never experienced difficulties in reading (NI group) served as a comparison group. These students had standard scores > 90 on the Basic Reading Composite (corresponding to the 36th percentile) and were recruited from the same schools as the RD group in an attempt to control for educational history, ethnicity, and SES factors. All participants had Full Scale IQ scores > 80 on the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999).

Detailed psychoeducational and demographic data are provided in Table 1. The two groups were comparable on age, ethnicity, handedness (there was one left handed student in each group), and Performance IQ ($p > 0.1$ in all cases). As expected the RD group demonstrated significantly lower scores than the NI group on measures of reading, Verbal IQ and spelling. Additionally, participants were selected for inclusion in either group only if they had T scores below 65 on the Attention Problems scale of the Child Behavior Checklist (Achenbach, 1991), as indicators of low risk for ADHD (Chen et al., 1994). Written informed assent and consent forms were signed by all participating children and their parents or guardians, respectively. The study had been approved by the Health Science Center-Houston and University of Houston Institutional Review Boards.

2.2. MEG recordings

Three minutes of continuous brain activity was acquired with a

Table 1
Demographic and psychoeducational data for typical (NI) and students with severe reading difficulties (RD).

	Group	Mean	SD	Range
Age (years)	NI	11.35	2.8	7–14
	RD	12.20	2.1	7–14
LWID**	NI	99.55	8.9	90–126
	RD	80.73	8.2	62–85
WA**	NI	99.44	9.6	91–130
	RD	84.78	7.2	68–85
Composite**	NI	99.70	9.7	90–130
	RD	81.78	6.9	65–85
Spelling	NI	103.86	9.91	88–128
	RD	78.33	11.24	56–103
VIQ*	NI	104.04	16.6	80–141
	RD	90.76	13.3	81–128
PIQ	NI	100.29	11.2	80–117
	RD	95.39	12.6	80–129
FSIQ	NI	102.34	12.4	80–124
	RD	93.48	13.2	80–129

Group differences: $^*p < 0.01$, $^{**}p < 0.001$. Abbreviations, LWID, WA, Composite, Spelling: Woodcock-Johnson III Letter-Word Identification, Word Attack, Reading composite, and Spelling subtests, respectively; VIQ, PIQ, FSIQ: WASI Verbal IQ, Performance IQ and Full Scale IQ scores, respectively.