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Chapter

Effects of a Phonological Intervention on EEG Connectivity Dynamics in Dyslexic Children

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Abstract

We examined the brain networks and oscillatory dynamics, inferred from EEG recordings during a word-reading task, of a group of children in grades 4 and 5 (ages 9–11), some of whom were dyslexic. We did this in order to characterize the differences in these dynamics between typical and dyslexic readers, and to begin to characterize the effect of a phonological intervention on those differences. Dyslexic readers were recorded both before and after they participated in a FastForWord (FFW) reading training program for approximately six months and typical readers were recorded once during this period. Before FFW dyslexic readers showed (i) a bottleneck in letter recognition areas, (ii) expansion in activity and connectivity into the right hemisphere not seen in typical readers, and (iii) greater engagement of higher-level language areas, even for consonant string stimuli. After FFW, dyslexic readers evinced a significant reduction in the engagement of language processing areas, and more activity and connectivity expanding to frontal areas, more resembling typical readers. Reduction of connectivity was negatively correlated with gains in reading performance, suggesting an increase in communication efficiency. Training appeared to improve the efficiency of the alternative (bilateral) pathways already used by the dyslexic readers, rather than inducing them to create new pathways more similar to those employed by typical readers.

Keywords: dyslexia, EEG, interregional connectivity, oscillatory dynamics, phonological intervention

1. Introduction

Having a reading disability, as seen in dyslexic children, is a very serious issue and often causes secondary emotional and cognitive consequences for the individual, as well as their family and their society [1]. Therefore, understanding the detailed underlying neurophysiological mechanisms of reading and their oscillatory brain network dynamics is of most importance.

Given the prevalence of phonological deficits in people with dyslexia [2, 3], it follows that training in phonological processing (and the underlying auditory processing therein) should improve reading ability. Indeed, there is evidence supporting this idea although there is some disagreement in the literature. Training and remediation programs that emphasize phonics and phonemic awareness have

been shown to improve fluency and comprehension [4–8]. Neuroimaging results reflect these findings, showing increases of cortical activity in reading-related areas including left fusiform, IFG, and temporo-parietal cortex, as well as right STG and IFG areas following training [8, 9].

Although the aforementioned neuroimaging results are useful, the exact underlying brain dynamics across local and large-scale networks are largely unknown. In particular, previous studies have not addressed the way information flows throughout reading networks during the process of reading words, and how this might be changed by an intervention designed to improve reading performance. The present study concerns the brain-regional connectivity dynamics of reading before and after an interventional reading training program. Of particular interest is the relationship between improvement in reading performance and changes in connectivity. Understanding this relationship may offer new insights into reading disabilities as well as ideas about how to further optimize reading training programs to elicit the highest performance gains. In what follows, we describe an experiment that compared the connectivity dynamics of a typical-reading group of children with that of a group of same-aged children who are significantly reading-impaired. The typical readers were measured once (given limitation of EEG measurements in school environment), and the challenged readers were measured twice: once before a reading training program in which the latter children had been enrolled, and once after those children had experienced the training program for a period of 6 months.

Despite a growing literature on the development of impaired reading-related brain regions in dyslexia [8, 10], it is much less understood just how the communication between these regions also changes as a function of time on a millisecond scale. In what ways does the reading network become more or less efficient throughout development, and which connections are being utilized more or less effectively? These emergent local and large-scale brain network dynamics are very critical at the age of these children, with known developmental stabilization but also plasticity and vulnerability [11]. To that end, this study sought to investigate the development of reading-related brain connectivity in dyslexic children by comparing functional and effective connectivity measures prior to intervention and after 6 months of schooling supplemented by a phonologically-based reading training program.

Despite the evidence as to how specific brain sites develop or alter in response to this training, it remains unclear how the overarching reading networks develop as a function of this training. Moreover, with regard to laterality of reading functions in the brain, it is unclear as to whether connectivity in dyslexic children shifts to include more traditional left-hemispheric engagement, or if their reading networks instead continue to emphasize right-hemisphere networks [9, 12].

Importantly, some researchers have argued that neural oscillations – particularly in theta- and gamma-bands – play a critical role in the processing of written language [13–15]. In particular, these neural network oscillations are said to be perturbed in atypical brains such as those of dyslexic readers [16]. Thus, in our study we focused on oscillatory activity and functional and effective connectivity in theta- and gamma-bands.

We first needed to establish a “baseline” of brain network behaviour prior to the reading intervention program. The readers in the present experiment were in grades 4 and 5. Although children typically learn to read in grade 1, we chose this older group to study, reasoning that an additional three to four years of brain development – and particularly years of reading training – can produce very different reading network patterns from those just learning to read. Moreover, if children are still struggling to read in grade four, it is clear that they have a severe deficit that requires remediation. Finally, we reasoned that the additional years of brain development (potentially without reading improvement or intervention) would produce brain

network behaviours in older children that were both different from those of typical readers, and also perhaps somewhat more resistant to change.

1.1 What happens 220 milliseconds after word presentation?

The temporal resolution of EEG affords the examination of brain activity at millisecond precision. Using such techniques, researchers have found specific moments in processing that reflect critical steps in the cognitive processing of words. Perhaps the most-commonly reproduced finding in reading is the N170 ERP component above the left fusiform gyrus in adult readers, in which a prominent negative peak is observed in the averaged EEG approximately 170 ms after word presentation [17–19]. This moment represents the orthographic processing step in word reading, where visual inputs are classified as orthography (written language) to then be passed along to higher-level language areas for further evaluation (e.g. extracting phonological information; [20]). In young children, this same processes is delayed somewhat to ~220 ms, as they are still developing the skills necessary to decode orthographic information [21–23]. So, when studying the neural dynamics of reading in children, this moment becomes critical in enhancing our understanding.

In this paper we focus our connectivity analyses on a specific window of time, 200–250 ms after word presentation, to capture the 5-dimensional brain oscillatory connectivity dynamics (across 3D space, time and frequency) of orthographic processing and the propagation of the reading information thereafter in the reading networks of dyslexic and typically-developing children. The lateralization of the connectivity, as well as the engagement of language areas in this time window may offer critical insights as to the neural underpinnings of dyslexia.

We hypothesized that, prior to intervention, children with reading difficulties would show altered and greater functional and effective connectivity in the theta and gamma frequency bands among reading-related sites compared to grade appropriate readers of the same age. These differences would arise because of the greater difficulty the impaired readers would have in decoding the orthographic symbols into language. We expected that these differences would be reduced after the intervention, at least to the extent the intervention ameliorated the reading difficulties and resulted in more fluid and effortless orthographic processing.

2. Methods

2.1 Participants

Twenty-eight students attending elementary schools in the Burnaby school district (BC, Canada) participated. In partnership with the school district, students in grades 4 and 5 were targeted to be a part of this study, making up a total potential pool of approximately 135 students. Parents of these students received information about the study and our consent forms through the schools. All eventual participants received parental consent and also gave verbal assent to participate. The protocol of the experiment was approved by the Behavioural Research Ethics Boards at the University of British Columbia and Simon Fraser University as well as by the Burnaby School Board in accordance with the provisions of the World Medical Association Declaration of Helsinki. Prior to our study, a subset of all grade 4 and grade 5 students had already been assessed by the schools as having specific reading difficulties and were already selected to be placed in an intervention program using FastForWord software (FFW; Scientific Learning, USA; see also [6, 7]) to practice core language skills such as phonemic awareness, auditory

discrimination, and spelling. Thus, our sample of this group was an opportunity sample, granting us an opportunity to study the neurodynamics of challenged readers as they experienced this targeted intervention. Selection into the intervention program was determined over time, using a multi-tiered approach developed by the teachers and administrators prior to the start of our study. Selection criteria for the FFW program by the schools included apparent auditory processing deficits, difficulty in associating letters with sound, and reading 1.5–2 years below grade level—observations often further assessed by Woodcock-Johnson standardized achievement tests (Word Attack, Letter-Word Identification, and Passage Comprehension sub-tests), the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Digit Span and Symbol Search sub-tests), and the Test of Auditory Processing Skills – Third Edition (TAPS-III; Word Discrimination, Phonological Blending, and Phonological Segmentation sub-tests). Guided by the district’s selection criteria, Language Support Services (LSS; e.g. speech and language pathologists) were also involved as part of the process and aided in the admission into the FFW program. The FFW program was never used as the initial point of intervention; rather, students were only admitted into the targeted reading training if no other intensive strategies had worked or if students were showing very small gains with other methods. These LSS professionals eventually conducted the training during school hours. Ultimately, through this vetting process, 15 FFW-eligible students were given consent forms.

A set of typically developing readers (TYP, control sample), not enrolled in the interventional reading training programs, were selected at random, from among those students whose parents gave consent and also who gave verbal assent, from the classrooms of the dyslexic pre/post-FFW students to control for effects of teacher and general curriculum received. All participants had English as their first and primary language, and had normal or corrected-to-normal visual acuity. FFW students had been in the program for less than one month at the time of the initial experimental session. This effort was made to record a baseline measure before any targeted reading intervention occurred. In total, 11 FFW readers and 17 TYP readers were recruited for this experiment.

2.2 Experimental procedures

The experiment was conducted on-site at elementary schools in the Burnaby school district (Vancouver, Canada). A quiet room at each school was set aside for each session. First, children were asked to simply sit in a relaxed position for five minutes while their brainwaves were recorded using EEG during resting state. Participants then performed a lexical decision task in which they were asked to decide whether a letter string was a real word or not (i.e., “Is this a real word?”). Stimuli were classified into three conditions: real words (e.g., ‘bread’), pseudowords (e.g., ‘croll’), and consonant strings (e.g., ‘rplcg’). A fixation cross was presented for 500 ms followed by a jittered inter-stimulus interval lasting between 800 and 1200 ms (**Figure 1**). Then a letter string was presented for 1500 ms or until the participant pressed a response, whichever occurred first. After a 1000 ms inter-trial interval, the next trial began. For the Word condition, single-syllable words were aggregated from lists found at <https://www.ontrackreading.com>. These lists have been assembled to be accessible to children and to represent a wide range of vowel sounds. Pseudowords were derived from the pool of real word stimuli by taking a word and changing a single letter (e.g. *bread* to *bream*). All participants, both pre-FFW ($n = 11$) and TYP ($n = 17$) students, participated in Session 1, but only the post-FFW ($n = 9$) student group

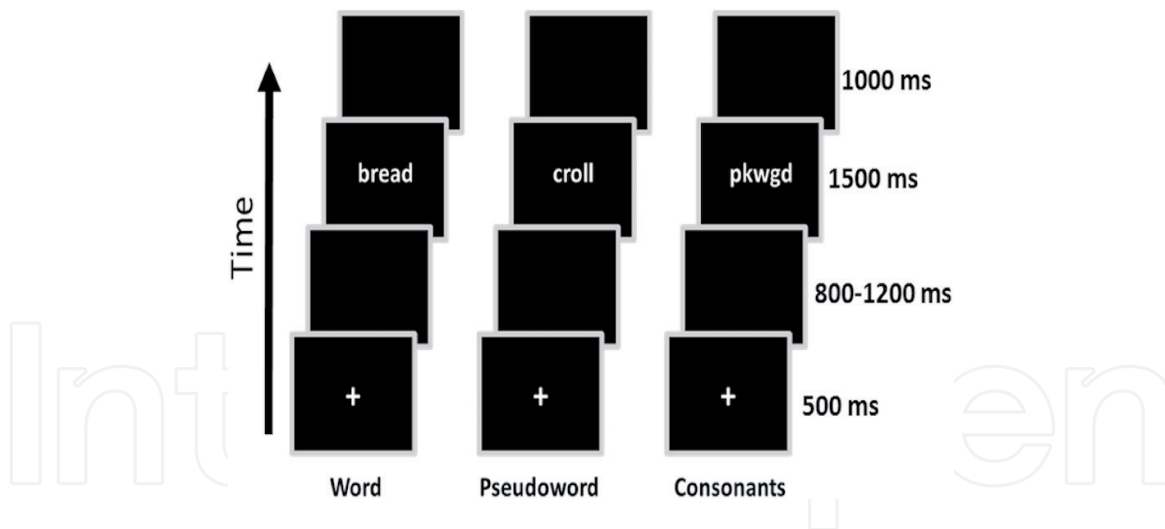


Figure 1.
Schematic of phonological lexical decision task. Participants were required to judge whether or not a letter string was a real word.

(also recorded in session 1) participated also in Session 2, which occurred about 6 months after Session 1. Unfortunately only the 9 post-FFW dyslexic students finished their training among the 11 who began it.

Stimuli from each condition consisted of 4- and 5-letter strings (60 trials each), each presented randomly for a total of 360 trials (120 trials per condition). Blocks of 40 trials were separated by self-timed rest breaks. Participants had the option to continue to the next block immediately upon reaching a break or they could rest as long as necessary before continuing. The task was performed on a laptop while sitting at a desk. A height-adjustable chin rest was used to reduce the possibility of head movements.

Presentation software (Neurobehavioral Systems, USA) was used to present stimuli in white font on a black background. All stimuli were centered on a 17-inch computer monitor placed 45 cm in front of the participants. All participants used their right hand to respond on the keyboard; however, the response buttons used for “Yes” and “No” were counterbalanced across subjects.

2.3 EEG acquisition

A portable BioSemi system, provided by the Behavioral and Cognitive Neuroscience Institute (BCNI), was used to record continuous EEG from 64 active electrodes at equidistant locations based on the International 10–10 system of electrode placement, referenced to the average of all scalp signals (except I_z). EEG signals were amplified and sampled at 512 Hz through an analog passband of 0.16–100 Hz. Eye muscle activity was recorded by electro-oculogram (EOG) from two periocular electrodes. All electrode impedances were below 20 k Ω .

All further offline processing and analysis was performed using MATLAB software (Mathworks, Natick, USA). All signals were re-referenced to an average reference, resampled to 256 Hz, and digitally filtered from 1 to 100 Hz using EEGLAB software [24], an open source MATLAB toolkit, and custom scripts. A digital notch filter from 55 Hz to 65 Hz was applied to reduce line noise. The continuous data were epoched into 3500 ms bins time-locked to the presentation of the letter strings, capturing 1500 ms before and 2000 ms after word presentation. In Session 1 each of the 28 participants contributed an average of 256.12 trials (SD = 73.41), for a total of 6659 trials for the experiment. In Session 2, each of the 9 participants

from the FFW group contributed an average of about 250 trials for a total of 2250 trials. All further processing and analysis was performed using MATLAB software (Mathworks, Natick, USA).

2.4 Current source density

To reduce the impact of volume conduction on subsequent analyses, the EEG signals were first converted to current source density (CSD). CSD, the second spatial derivative of the scalp potential, acts as a spatial filter, emphasizing shallow sources close to each recording electrode thus reducing volume conduction and increasing confidence that the channels being analyzed did in fact represent predominantly activity of the brain regions over which the corresponding electrodes sat. Furthermore, CSD acts as a form of artifact rejection or attenuation, particularly of muscular artifacts that can heavily contaminate EEG signals [25]. CSD Toolbox for MATLAB with default parameter values for spline flexibility (spline interpolation constant $m = 4$) and smoothing (smoothing constant $\lambda = 0.00001$) was used to compute the CSD values the continuous EEG data from each individual participant [26–28].

Cortical regions of interest (ROIs) for further analysis were selected based on reading-related brain areas as revealed in previous research (**Table 1**; [29]). The cortical Talairach coordinates of these sites were then cross-referenced to anatomical locations of electrodes based on the 10–10 system [30]. The nearest electrodes to these sites, as measured by Euclidean distance, were then selected for further analysis. The subset of electrodes selected in this manner were CP5, CP6, F5, F6, FT7, FT8, O1, O2, P7, P8, TP7, and TP8 (**Figure 2**). For ease of exposition the ROIs will be referred to by their closest cortical locations, but it must be remembered that in fact the data to be analysed are the CSD values computed for the electrode locations nearest those cortical locations and not the activation levels of cortical sources inferred through localization analysis.

EEG channel	Talairach coordinates			Corresponding Brain Region
	x	y	z	
F5	-51	27	25	L. IFG
F6	51	27	25	R. IFG
FT7	-59	3	-2	L. PreCG
FT8	59	3	-2	R. PreCG
CP5	-62	-46	23	L. AG/SMG
CP6	62	-46	23	R. AG/SMG
TP7	-64	-45	-4	L. MTG/STG
TP8	64	-45	-4	R. MTG/STG
P7	-56	-65	0	L. vOT
P8	56	-65	0	R. vOT
O1	-26	-93	8	L. Occip
O2	26	-93	8	R. Occip

Table 1.

EEG channels and their corresponding brain regions. EEG channels were selected for further analysis based on their proximity to previously established ROIs (Jobard et al., 2003) and their cross-hemispheric counterparts. Anatomic locations of EEG channels in Talairach space were derived from Koessler et al. (2009).

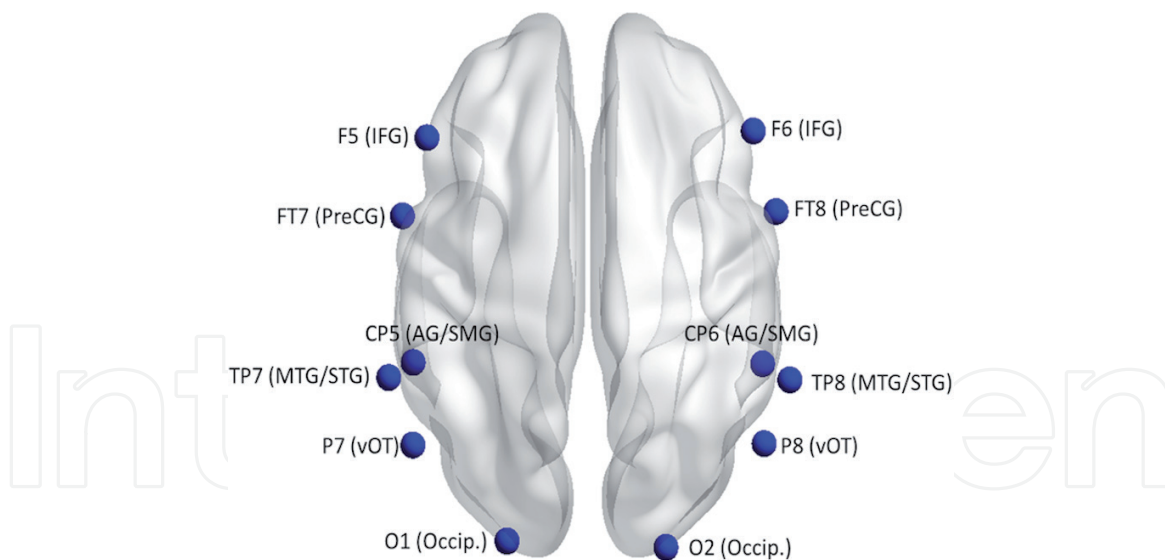


Figure 2.
Selected electrodes that overlap with reading-related brain areas. Visual representation of anatomical locations of channels as described in **Table 1**.

2.5 Event-related potentials (ERPs)

ERPs were computed by averaging each participant's epoched EEG activity in signal space and across trials. This was done separately for each condition. ERPs were baseline corrected relative to a 100 ms pre-stimulus window and low-pass filtered at 20 Hz. ERPs from each group were then compared using independent samples *t*-tests at each time point. Instances of significant differences between conditions sustained across multiple time points then informed the subsequent connectivity analyses as to which moments might provide insights into important network differences.

2.6 Event-related spectral perturbations (ERSPs)

ERSPs ($10 \log [\text{power at time point } t / \text{average baseline power}]$; in dB units) allow us to observe the moment-to-moment fluctuations in oscillatory power at various oscillatory frequencies relative to a 100 ms pre-stimulus baseline. The powers at different frequencies were computed in 1.5 Hz increments from 3 Hz to 50 Hz using a sliding cosine wavelet (Hanning-windowed) with linearly increasing cycles from 1.8 cycles at 3 Hz to 30 cycles at 50 Hz. ERSPs were computed by EEGLab's *newtimef()* function across trials for each subject separately. This technique produced an output 400 time points in length, capturing ERSPs from -940 to 1440 ms of the original epoch.

Each ERSP output was then collapsed across each selected frequency band (i.e. theta and gamma) at each time point, such that the maximum absolute value of ERSP at any individual frequency in the band was used [31, 32]. This produced a time series for each channel that reflected its most prominent level of activation in a region at each time point. ERSPs from each condition were then compared using pairwise *t*-tests at each time point. Sustained instances of significant differences between groups then informed the eventual connectivity analyses as to which moments might provide insights into important network differences.

2.7 Phase synchrony

Phase synchrony analyses were conducted in order to assess inter-regional functional connectivity, or the degree to which two brain areas are sharing information,

in theta- (3–8 Hz) and gamma- (30–50 Hz) bands. This was done by computing the phase-locking values (PLVs) between pairs of electrodes located over reading-related brain regions. PLVs were computed using the following formula [24]:

$$PLV_{1,2}(f,t) = \frac{1}{N} \sum_{k=1}^N \frac{W_{1,k}(f,t)W_{2,k}^*(f,t)}{|W_{1,k}(f,t)W_{2,k}(f,t)|} \quad (1)$$

where $W_{i,k}(f,t)$ are the wavelet coefficients for each time point, t , and frequency, f , for each EEG channel, i , and $k = 1$ to N is the index of epochs. The PLVs produced by these computations indicate the degree of constancy of the phase differences between signals at a specific oscillatory frequency across trials. PLVs range from 0 to 1, where 0 indicates the absence of any phase locking, and 1 indicates perfect phase locking, such that the phase difference between two channels at a given time point remains constant across all trials. Only stochastic phase locking, with $0 < PLV < 1$, is expected from any time series of brain activity because of neural noise [33].

PLVs were computed by EEGlab's *newcrossf()* function across subjects separately and for each time point for all channel pairs. This technique produced an output 400 time points in length, capturing ERSPs from –940 to 1440 ms of the original epoch. The phase lags of the significant PLVs were always significantly different from zero (as determined by circular t -tests, $p < 0.001$), indicating that volume conduction, which can cause spurious zero-phase-lag synchronization, could not have been responsible for any significant PLVs.

PLVs were baseline corrected by subtracting the mean of PLVs in the 100 ms window immediately preceding stimulus presentation from the dataset. Each output was then collapsed across each frequency band at that time point (theta and gamma bands), such that the maximum absolute value of PLV at any individual frequency in the band was used, identical to the process used for ERSPs. This consolidated the time series for each channel pair so that it reflected their degree of functional connectivity in this pair of regions at each time point. In order to differentiate PLV connectivity patterns between groups, two-tailed independent t -tests ($\alpha = 0.01$) were used.

In order to assess the connectivity patterns with each group, two-tailed one-sample t -tests ($\alpha = 0.001$) were employed to determine the statistical significance of these PLVs relative to zero at each time point. As a means to differentiate PLV connectivity patterns between groups, two-tailed independent t -tests ($\alpha = 0.01$) were used, comparing FFW and TYP groups at each time point.

To assess the statistical reliability of these t -tests, time points from 0 to 900 ms following the stimulus onset were divided into non-overlapping 50 ms time bins (i.e., 18 such bins). To control for multiple comparisons, and to exclude meaningless interactions, we adopted a conservative criterion and considered a 50 ms bin to contain meaningful evidence of greater functional connectivity for one group than for the other if at least half (5 or more of 9) of the time points in that bin reached the statistical threshold described earlier for either TYP > pre/post-FFW, or vice versa, and none did for the opposite comparison. To assess the experiment-wise error of this procedure, we used $p = 0.01$ ($q = 1 - p = 0.99$) as the probability of a success in a single binomial trial to compute the binomial probability of getting 5 or more significant time points by chance out of the total of 9 time points in each 50-ms bin [36]. This probability is 1.21×10^{-8} if all of the time points in a bin represented independent tests. This assumption of independence is probably not precisely correct as using consecutive time points will lack complete independence, although it is not too unreasonable because the tests were made across subjects, who were independent of each other. Since we made 66 (inter-regional) comparisons

(each possible pairing of 12 different brain ROIs) for 18 time bins, there were 1188 such tests. At most ($p = 0.01$, with the minimum 5 of 9 significant data points per bin), the experiment-wise error probability for each set of t-tests, assuming independence, was $1188 \times 1.21 \times 10^{-8} = .0000144$.

2.8 Transfer entropy

Whereas measures of functional connectivity show which brain areas are engaged and sharing information (i.e. functionally connected), these measures do not indicate the directional flow of the information. That is, a measure such as phase synchrony does not indicate which site is *sending* the information, and which site is *receiving* the information, or if a bi-directional relationship exists. In order to understand such relationships, effective connectivity analyses must be employed. To address this, we employed transfer entropy, a recently developed technique for revealing directed information flow without needing to specify or fit a model [34]. Transfer entropy from time series J to time series I is defined [34] as the (asymmetric) Kullback-Liebler entropy between two time series at a specified, non-zero, lag ($k-l$):

$$T_{J \rightarrow I} = \sum p(i_{n+1}, i_n^{(k)}, j_n^{(l)}) \log \frac{p(i_{n+1} | i_n^{(k)}, j_n^{(l)})}{p(i_{n+1} | i_n^{(k)})}. \quad (2)$$

Transfer entropy measures the extent to which the transition probabilities (dynamics) between states within one time series (say J) are *not* independent of the past states of another time series (say I). It is larger the greater the influence of the state of I on the transition probabilities of J . Both the influence of J on I and that of I on J can be computed in this way. With regard to information transfer between neural sources, transfer entropy computes the additional information predicted by one region that is not already predicted by another region's prior activity. Narrow-band transfer entropy (NBTE) is a variant of this, whereby transfer entropy is computed *within a specific frequency band* rather than over the broadband signal [35]. The TIM toolbox, developed by German Gomez-Herrero and Kalle Rutanen, for MATLAB (<http://www.cs.tut.fi/~timhome/tim/tim.htm>) was employed to compute theta- and gamma-band NBTE.

Theta-band (3–8 Hz) and gamma-band (30–50 Hz) oscillatory time series were obtained by filtering the CSD activations in the epochs using EEGlab's digital FIR filter. NBTE was then computed across trials for each subject at 30 ms and 50 ms lags. The lags used here span the range of lags found to contain significant NBTE in previous similar investigations [13, 35].

In order to assess the connectivity patterns within each group, two-tailed one-sample t -tests ($\alpha = 0.05$) were employed to determine the statistical significance of these NBTE values relative to zero at each time point. As a means to differentiate NBTE connectivity patterns between groups, two-tailed independent t -tests ($\alpha = 0.01$) were used, comparing FFW and TYP groups at each time point.

To assess the experiment-wise error of this procedure, we used $p = 0.05$ ($q = 1 - p = 0.95$) as the probability of a success in a single binomial trial to compute the binomial probability of getting 7 or more significant time points by chance out of the total of 13 time points in each 50-ms bin [36]. This probability is 9.85×10^{-7} if all of the time points in a bin represented independent tests. This assumption of independence is probably not precisely correct as using consecutive time points will lack complete independence, although it is not too unreasonable because the tests were made across subjects, who were independent of each other. Since we made

132 (inter-regional) comparisons (each possible pairing of 12 different brain ROIs in both directions) for 18 time bins, there were 2376 such tests. At most ($p = 0.05$, with the minimum 7 of 13 significant data points per bin), the experiment-wise error probability for each set of t-tests, assuming independence, was $2376 \times 9.85 \times 10^{-7} = 0.00234$.

2.9 Connectivity correlations

Measuring the brain activity from FFW participants at two distinct time points (pre-FFW and post-FFW) gave us the opportunity to examine the relationship between gains in reading performance and changes in network connectivity. Correlations were computed, both before and after the FastForWord intervention, between FFW participant assessment scores (WJ-WA and WJ-LW tests) and connectivity measures (PLVs and NBTE) for the nine post-FFW participants who participated at both times (session 1 and session 2). This process followed the exact set of methods in the synchrony and transfer entropy analyses, but used the difference in assessment scores (POST – PRE) and the differences in connectivity values (POST – PRE).

Correlations were employed to determine the statistical significance of these associations between brain connectivity and assessment scores at each time point ($\alpha = 0.01$ for PLVs, 0.05 for NBTE). To assess the experiment-wise error of this procedure, we used $p = 0.01$ ($q = 1 - p = 0.99$) as the probability of a success in a single binomial trial to compute the binomial probability of getting 5 or more significant time points by chance out of the total of 9 time points in each 50-ms bin for correlations with PLVs. This probability is 1.21×10^{-8} if all of the time points in a bin represented independent tests. This assumption of independence is probably not precisely correct as using consecutive time points will lack complete independence. Since we made 66 (inter-regional) comparisons (each possible pairing of 12 different brain ROIs) for 18 time bins, there were 1188 such tests. At most ($p = 0.01$, with the minimum 5 of 9 significant data points per bin), the experiment-wise error probability for each set of t-tests, assuming independence, was $1188 \times 1.21 \times 10^{-8} = .0000144$.

The experiment-wise error for the NBTE correlations required 7 or more significant time points out of 13 time points ($p = 0.05$) to consider a 50 ms to be significant. This probability is 9.85×10^{-7} if all of the time points in a bin represented independent tests. Since we made 132 (inter-regional) comparisons (each possible pairing of 12 different brain ROIs in both directions) for 18 time bins, there were 2376 such tests. At most ($p = 0.05$, with the minimum 7 of 13 significant data points per bin), the experiment-wise error probability for each set of t-tests, assuming independence, was $2376 \times 9.85 \times 10^{-7} = .000234$.

3. Results

3.1 Comparison of TYP and pre-FFW groups

3.1.1 Behavioural performance

Woodcock-Johnson tests (Word Attack and Letter-Word Identification) were conducted on a subset of all participants (9 pre-FFW (those who were tested twice), 11 TYP) by the experimenters to validate the differentiation of groups with regard to reading difficulties initially appraised by the schools (**Figure 3A**). The pre-FFW group showed significantly lower scores compared to the TYP group

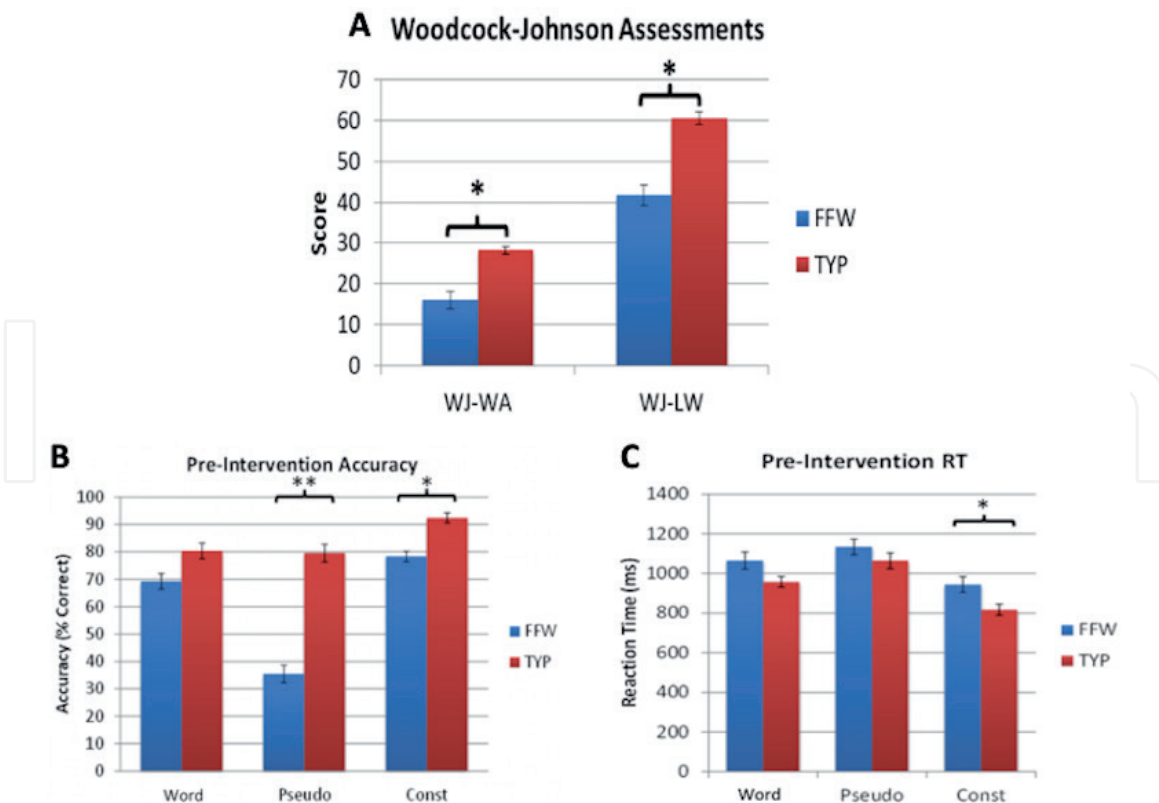


Figure 3. (A) Reading assessments of typical readers (TYP) and atypical (FFW) readers before starting the Fast Forward training program in both the Word Attack (WJ-WA) and Letter-Word Identification (WJ-LW) tests. $*p < 0.0001$. (B) Pre-FFW lexical decision task accuracy before starting training. Word = Word, Pseudo = Pseudoword, Const = Consonant Strings. $*p < 0.05$, $**p < 0.0001$. (C) Pre-FFW lexical decision task reaction times before starting training. Word = Word, Pseudo = Pseudoword, Const = Consonant Strings. $*p < 0.05$.

in both the Word Attack subtest, $t(18) = 6.64$, $p < 0.0001$, and the Letter-Word Identification subtest, $t(18) = 5.14$, $p < 0.0001$.

Accuracy in each experimental task condition was measured as percentage of correct trials. The pre-FFW group was significantly less accurate than the TYP group in the Consonant condition, $t(23) = 2.15$, $p = 0.04$ (**Figure 3B**). The FFW was also significantly less accurate than in the TYP group in the Pseudoword condition, $t(23) = 5.37$, $p < 0.0001$. The accuracy difference between groups in the Word condition was not statistically significant ($t(23) = 1.83$, $p = 0.08$), although the 11% difference was in the direction of TYP > pre-FFW as for the other conditions.

With respect to reaction time, the pre-FFW group was significantly slower than the TYP group in the Consonant condition, $t(23) = 2.54$, $p = 0.02$ (**Figure 3C**). There was no significant difference in reaction time between groups in the Pseudoword condition, $t(23) = 1.11$, $p = 0.28$, or the Word condition, $t(23) = 1.49$, $p = 0.15$, although the TYP group was faster than the pre-FFW group in all conditions.

3.1.2 ERPs

ERPs from TYP and pre-FFW groups were compared at each time point for each condition using two-sample t -tests (**Figure 4A**). The pre-FFW group showed a more pronounced N170/220 component (early negative peak) at R.vOT and R.AG sites in all three conditions 200–250 ms following stimulus presentation ($p < 0.05$, uncorrected) as well as from L.AG in the Pseudoword condition. In the Pseudoword and Word conditions, the pre-FFW group also generated a larger P1 component at R.vOT 100–150 ms after stimulus presentation, as well as greater activation in

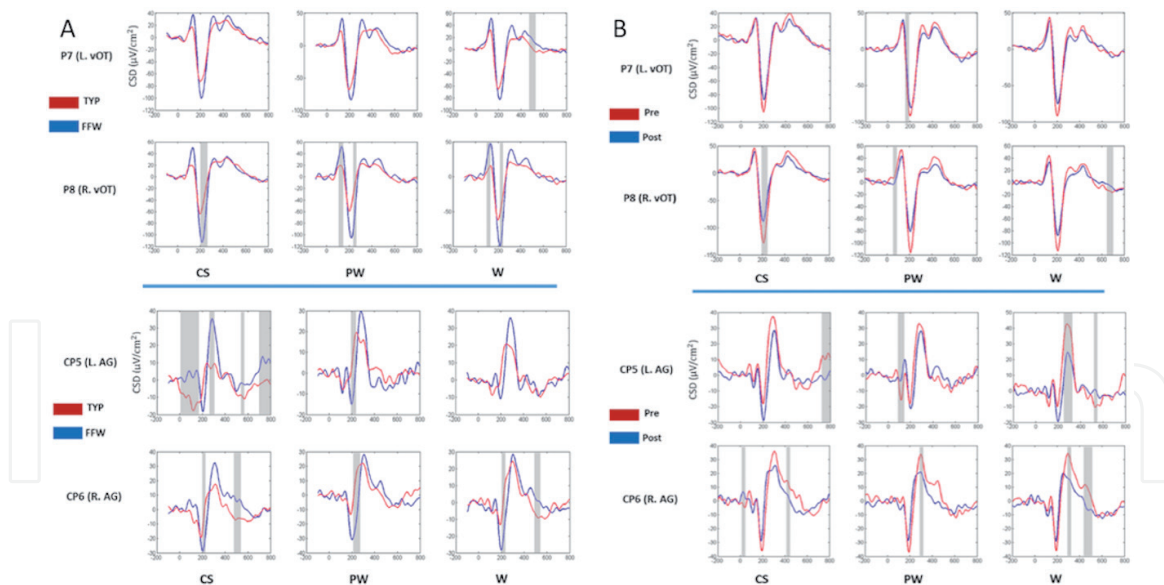


Figure 4.

(A) Event-related potentials (ERPs) during word reading for selected electrodes before Fast Forward training for typical readers (TYP) and atypical readers (FFW). Sections highlighted in grey indicate significant differences between groups ($p < 0.05$, uncorrected). CS = Consonant String; PW = Pseudoword; W = Word; vOT = ventral Occipito-Temporal cortex; AG = Angular Gyrus. (B) ERPs comparing engaged reading-related brain regions between sessions (pre-FFW vs. post-FFW). Sections highlighted in grey indicate significant differences between groups ($p < 0.05$, uncorrected). CS = Consonant String; PW = Pseudoword; W = Word; vOT = ventral Occipito-Temporal cortex; AG = Angular Gyrus.

L.vOT at 475–540 ms. At area L.AG, the pre-FFW group produced a significantly larger ERP immediately following stimulus presentation, as well as a more pronounced peak from 260 to 310 ms. The pre-FFW group produced late ERP components (>500 ms) in both L.AG and R.AG sites in the Consonants condition, while R.AG showed this effect in the Word condition, as well.

3.1.3 ERSPs

Spectral power dynamics were investigated at reading-related sites at theta (3–8 Hz) (**Figure 5A**) and gamma (30–50 Hz) (**Figure 5B**) frequency bands. Between-subjects t -tests revealed greater theta power for the pre-FFW group in the Consonants condition at L.AG from 210 to 280 ms, R.AG from 650 to 800 ms, and R.AG from 100 to 260 ms and 360–410 ms ($p < 0.05$, uncorrected). The pre-FFW group showed greater theta power at R.vOT in the Pseudoword condition from 180 to 240 ms. In the Word condition, the pre-FFW group showed greater theta power at R.AG from 195 to 300 ms and at R.vOT from 175 to 290 ms. These results highlight not only the greater amount of resources engaged by the pre-FFW group for written language, but also the bilateral nature of this processing, such that they utilize regions of the right hemisphere to an extent that TYP readers do not.

Between-subjects t -tests revealed greater gamma power for the pre-FFW group in the Consonants condition at R.vOT from 110 to 385 ms and 595–780 ms ($p < 0.05$, uncorrected). The pre-FFW group showed greater gamma power in the Pseudoword condition at R.AG from 270 to 305 ms, and at R.vOT from 300 to 405 ms. The TYP group showed greater gamma power in the Consonant condition at R.AG from 585 to 630 ms, in the Pseudoword condition at L.AG from 440 to 510 ms, and in the Word condition at R.vOT from 475 to 580 ms. Overall, The TYP group showed more gamma power later in the trial (>400 ms) in the right-hemispheric regions during Consonant and Word trials, as well as in L.AG during Pseudoword trials.

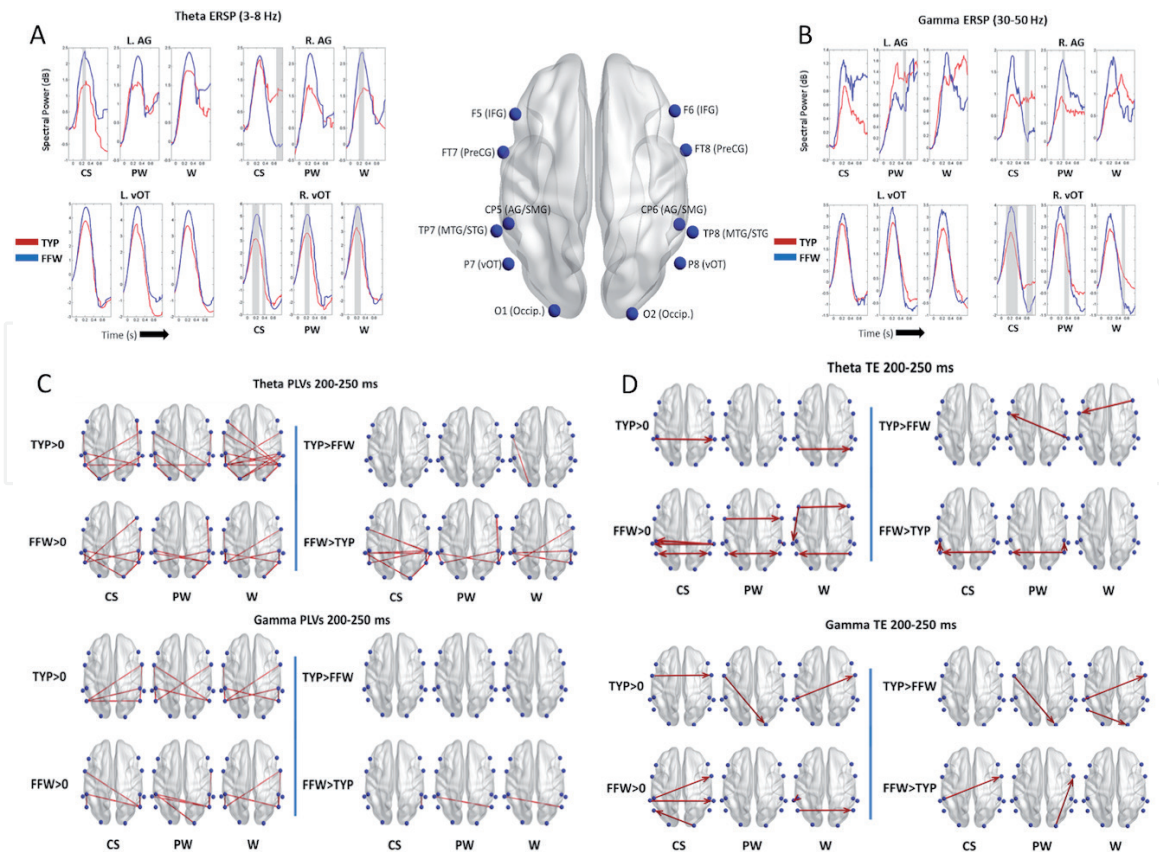


Figure 5. (A) Theta-band ERSs for both groups before training. Sections highlighted in grey indicate significant differences between groups ($p < 0.05$, uncorrected). (B) Gamma-band ERSs for both groups before training. Sections highlighted in grey indicate significant differences between groups ($p < 0.05$, uncorrected). (C) (Top) Theta-band phase synchrony from 200 to 250 ms. (Left) Red lines between areas indicate significant changes in PLV compared to zero ($p < 0.001$); (Right) Red lines between areas indicate significant differences between groups ($p < 0.01$). (Bottom) Gamma-band phase synchrony from 200 to 250 ms. (Left) Red lines between areas indicate significant changes in PLV compared to zero ($p < 0.001$); (Right) Red lines between areas indicate significant differences between groups ($p < 0.01$). (D) (Top) Theta-band (3–8 Hz) NBTE from 200 to 250 ms. (Left) Red arrows between areas indicate significant changes in TE compared to zero; (Right) Red arrows between areas indicate significant differences between groups. (Bottom) Gamma-band (30–50 Hz) NBTE from 200 to 250 ms. (Left) Red arrows between areas indicate significant changes in TE compared to zero; (Right) Red arrows between areas indicate significant differences between groups. CS = Consonant String; PW = Pseudoword; W = Word; vOT = ventral Occipito-Temporal cortex; AG = Angular Gyrus.

3.1.4 Phase synchrony

As mentioned earlier, we focused our connectivity analyses on the time window 200–250 msec after word onset, as this window is critical for orthographic processing and transmitting the resulting information to areas downstream of the vOT cortex. Both groups showed distributed theta-band network functional connectivity relative to baseline across all conditions ($p < 0.001$; **Figure 5C**). Comparing groups, the TYP group show no instances of greater theta-band phase synchrony ($p < 0.01$) in any condition. The pre-FFW group showed greater theta-band PLVs between R.AG and L.PreCG, L.STG, L.vOT, and R.vOT in the Consonant condition, and between R.IFG and R.vOT in the Pseudoword condition. The pre-FFW group showed greater theta-band PLVs between L.STG and R.vOT, L.vOT and R.PreCG, and R.vOT and R.AG in the Word condition. Especially notable is the significant engagement of the vOT and AG regions in the right hemisphere across all conditions in the pre-FFW group.

Both groups showed distributed gamma-band network functional connectivity relative to baseline across all conditions ($p < 0.001$). Comparing groups, the TYP group did not yield any instances of greater gamma-band synchrony in any

condition ($p < 0.01$). The pre-FFW group showed greater gamma PLVs between R.vOT and R.AG in the Consonant condition, and between R.vOT and L.STG in the Pseudoword and Word conditions. Again, especially notable is the engagement of the vOT region in the right hemisphere across all conditions.

3.1.5 Transfer entropy

The TYP group showed significant theta-band NBTE from L.STG to R.STG in the Consonant condition, as well as from L.vOT to R.vOT in the Word condition ($p < 0.05$; **Figure 5D**). The pre-FFW group showed significant NBTE from R.STG to L.STG and L.AG sites, in addition to a bi-directional relationship between L.vOT and R.vOT in the Consonant condition. The bi-directional relationship was present in the Pseudoword condition, accompanied by theta-band NBTE from L.PreCG to R.PreCG. In the Word condition, the pre-FFW group showed NBTE from L.IFG to L.STG and R.IFG, as well as from R.vOT to L.vOT. Comparing groups, the TYP group showed no instances of greater theta NBTE ($p < 0.01$) in the Consonant condition, although this group showed greater connectivity from R.STG to L.PreCG in the Pseudoword condition, and from R.IFG to L.PreCG in the Word condition. The pre-FFW group showed no instances of greater theta NBTE in the Word condition, but showed greater connectivity from R.vOT to L.vOT and from L.vOT to L.AG in the Consonant condition, and from R.vOT to L.vOT and from R.vOT to R.AG in the Pseudoword condition.

The TYP group showed significant gamma-band NBTE (relative to baseline) from L.PreCG to R.PreCG in the Consonant condition, from L.PreCG to R.Occipital cortex in the Pseudoword condition, and from L.STG to R.PreCG in the Word condition ($p < 0.05$, **Figure 5D**). The pre-FFW group showed significant gamma-band NBTE from L.AG to R.PreCG, from L.STG to R.STG, and from R.Occipital cortex to L.vOT in the Consonant condition, from L.vOT to R.vOT in the Word condition, and no gamma-band NBTE in the Pseudoword condition. Comparing groups, the TYP group showed greater gamma-band NBTE from L.PreCG to R.Occipital cortex in the Pseudoword condition ($p < 0.01$), from L.STG to R.PreCG and from L.vOT to R.Occipital cortex in the Word condition. The pre-FFW group showed greater gamma-band NBTE from L.AG to R.PreCG in the Consonant condition and from R.Occipital cortex to R.PreCG in the Pseudoword condition.

3.2 Pre-post FFW intervention comparison

3.2.1 Behavioural performance

Whereas both WJ-WA and WJ-LW reading assessments revealed slight improvements after training in the post-FFW group, these improvements were overall not statistically significant. Participants showed increased scores for WJ-WA in the second session ($M = 18.73$, $SD = 4.34$) compared to session one ($M = 16$, $SD = 6.54$), though these gains were not statistically significant, $t(8) = 0.14$, $p > 0.05$. In the WJ-LW assessment, participants showed increased scores in the second session ($M = 44.64$, $SD = 6.86$) compared to session one ($M = 41.67$, $SD = 7.75$), although again not reaching statistical significance, $t(8) = 0.15$, $p > 0.05$. No significant difference in accuracy or reaction time on the experimental task was observed between sessions for the post-FFW group (**Tables 2 and 3**).

3.2.2 ERPs

In L.vOT, the POST session (post-FFW) yielded a less pronounced N170/220 negative peak from 170 to 190 ms in the Pseudoword condition ($p < 0.05$, **Figure 4B**).

Condition	Pre		Post		<i>t</i> (8)	<i>p</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>		
Consonant	78.36	23.69	73.16	29.49	0.59	0.57
Pseudoword	35.47	27.67	44.60	26.09	1.02	0.34
Real Word	69.24	18.77	53.90	27.77	1.98	0.08

Table 2.

Dependent sample *t*-tests revealed no significant differences in accuracy (percent correct) between sessions. *M* = Mean; *SD* = Standard Deviation.

Condition	Pre		Post		<i>t</i> (8)	<i>p</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>		
Consonant	943	132	871	123	1.69	0.13
Pseudoword	1134	130	1045	136	1.99	0.08
Real Word	1064	146	1012	128	1.14	0.29

Table 3.

Dependent sample *t*-tests revealed no significant differences in reaction times (in milliseconds) between sessions. *M* = Mean; *SD* = Standard Deviation.

In R.vOT, the POST session yielded a less pronounced negative peak from 195 to 240 ms in the Consonant condition, as well as a smaller ERP from 70 to 110 ms in the Pseudoword condition, and greater activation in the Word condition from 640 to 715 ms. In L.AG, the PRE session (pre-FFW) showed greater activations from 730 to 800 ms in the Consonant condition, while the POST session (post-FFW) showed greater activations from 95 to 140 ms in the Pseudoword condition. The PRE session showed greater activity from 290 to 315 ms in the Word condition, with the POST session showing greater activity from 525 to 550 ms. In R.AG, the POST session showed greater activity from 10 to 40 ms in the Consonant condition, while the PRE session showed greater activity from 415 to 435 ms. The PRE session yielded a greater response from 280 to 310 ms in the Pseudoword condition. In the Word condition, the PRE session showed greater activity from 290 to 315 and 425–505 ms. Although not always significant, there is a general trend of post-intervention ERP peaks being less pronounced compared to the same peaks in the first session, especially around ~210 ms at vOT sites. As well, the left and right AG regions tend to show more prominent positive peaks after ~300 ms in the first session.

3.2.3 Phase synchrony

Both sessions showed distributed theta-band network functional connectivity relative to baseline across all conditions ($p < 0.001$; **Figure 6A**). Comparing sessions, the POST session (post-FFW) showed greater theta-band phase synchrony between L.STG and R.IFG in the Pseudoword condition, and between left and right PreCG regions and left and right STG sites in the Word condition ($p < 0.01$). The PRE session (pre-FFW) showed greater theta-band PLVs between R.vOT and R.AG sites, as well as between R.vOT and R.PreCG in the Consonant condition. The PRE session displayed greater PLVs between R.AG and R.IFG for Pseudowords. In the Word condition, the PRE session showed greater PLVs between L.vOT and R.PreCG, between R.vOT and R.AG, and between L.PreCG and right occipital cortex.

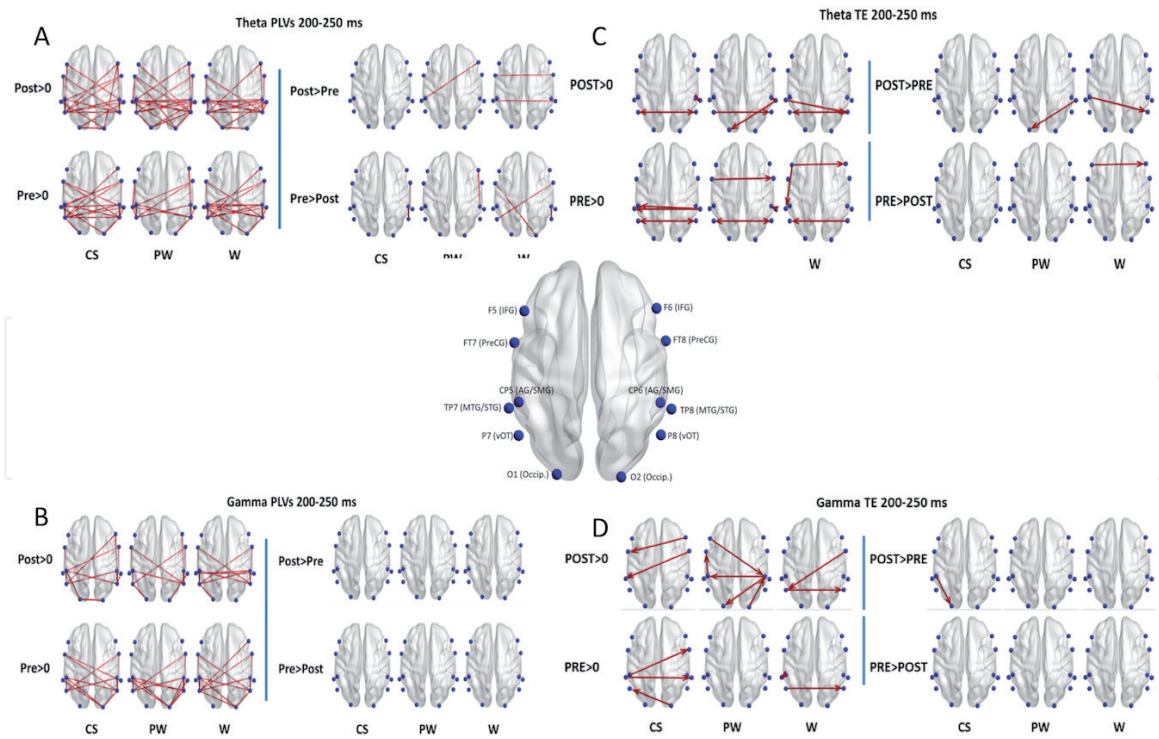


Figure 6.

(A) Theta-band phase synchrony from 200 to 250 ms before and after training for the FFW group. (Left) Red lines between areas indicate significant PLV compared to zero ($p < 0.001$); (Right) Red lines indicate significant differences comparing PRE- versus POST-training ($p < 0.01$) (greater connectivity in the PRE session suggests a significant decrease in the POST session). (B) PRE- and POST-training gamma-band phase synchrony from 200 to 250 ms. (Left) Red lines between areas indicate significant PLV compared to zero ($p < 0.001$); (Right) Red lines indicate significant differences comparing PRE- versus POST-training ($p < 0.01$). (C) Theta-band NBTE from 200 to 250 ms. (Left) Red arrows between areas indicate significant TE compared to zero ($p < 0.001$); (Right) Red arrows indicate significant differences in TE comparing PRE- versus POST-training ($p < 0.01$). (D) Gamma-band NBTE from 200 to 250 ms. (Left) Red arrows between areas indicate significant TE compared to zero ($p < 0.001$); (Right) Red arrows indicate significant differences in TE comparing PRE- versus POST-training ($p < 0.01$). CS = Consonant String; PW = Pseudoword; W = Word.

Both sessions (pre-FFW and post-FFW) showed distributed gamma-band network functional connectivity relative to baseline across all conditions ($p < 0.001$; **Figure 6B**). When comparing across sessions, however, neither showed any instances of greater gamma-band network functional connectivity.

3.2.4 Transfer entropy

The POST session (post-FFW) showed significant theta-band NBTE from R.AG to R.STG, as well as bi-directional connectivity between left and right vOT sites in the Consonant condition ($p < 0.05$; **Figure 6C**). In the Pseudoword condition, the POST session further showed significant connectivity from R.AG to R.STG, from L.vOT to R.vOT, and from R.STG to right occipital cortex. In the Word condition, the POST session showed theta NBTE from L.STG to R.vOT, as well as bi-directional connectivity between left and right vOT regions. The PRE session (pre-FFW) showed significant connectivity from R.STG to L.AG and L.STG, and between left and right vOT sites in the Consonant condition. For Pseudowords, the PRE session showed theta-band NBTE from L.PreCG to R.PreCG, and between L.vOT and R.vOT. In the Word condition, connectivity was observed from R.vOT to L.vOT, and from L.IFG to R.IFG and L.STG. Comparing groups, the POST session (post-FFW) showed greater theta-band NBTE from R.STG to left occipital cortex in the Pseudoword condition, and from L.AG to R.vOT in the Word condition ($p < 0.01$). The PRE session (pre-FFW) showed greater connectivity from L.IFG to R.IFG in the Word condition.

The POST session (post-FFW) showed significant gamma-band NBTE from R.PreCG to L.STG, and from R.IFG to L.PreCG in the Consonant condition ($p < 0.05$; **Figure 6D**). In the Pseudoword condition, the POST session showed significant connectivity from L.AG to L.PreCG, from L.IFG to R.AG, from R.AG to L.AG and left occipital cortex, and from right occipital cortex to R.AG. In the Word condition, the POST session showed gamma NBTE from R.PrecCG to L.vOT and from L.vOT to R.vOT. The PRE session (pre-FFW) showed significant connectivity from L.AG to R.PreCG, from L.STG to R.STG, and from right occipital cortex to L.vOT in the Consonant condition. For Pseudowords, the PRE session showed gamma-band NBTE from L.PreCG to R.PreCG, and between L.vOT and R.vOT. In the Word condition, connectivity was observed from R.vOT to L.vOT, and from L.IFG to R.IFG and L.STG. Comparing sessions, the POST session (post-FFW) showed greater gamma-band NBTE only from R.AG to left occipital cortex in the Consonant condition ($p < 0.01$).

3.3 Correlations between connectivity and assessment scores

Gains in performance (POST-PRE scores) on two reading assessments – WJ-WA and WJ-LW – were correlated with changes in brain connectivity. Increases in theta-band phase synchrony between R.vOT and R.IFG in the Pseudoword condition were significantly correlated with WJ-WA performance gains ($p < 0.01$, **Figure 7A**). Significant correlations were also observed between R.vOT and L.IFG for Words. Negative correlations in the Consonant condition were observed between R.AG and L.AG, between R.AG and L.STG, and between R.vOT and right occipital cortex. In the Word condition, correlations were observed between R.STG and L.PreCG, and between R.vOT and R.STG. Increases in theta-band synchrony between R.vOT and R.PreCG in the Consonant condition were significantly correlated with WJ-LW performance gains ($p < 0.01$). In the Pseudoword condition, correlations were observed between R.vOT and L.IFG and between L.vOT and R.STG. Correlations were also observed between R.vOT and L.IFG, between R.vOT and R.AG, and between R.AG and R.PreCG for Words. Negative correlations in the Pseudoword condition were observed between L.AG and R.STG, between R.AG and L.STG, and in the Word condition between L.IFG and R.IFG, and between right occipital cortex and R.STG, L.STG, and left occipital cortex.

Increases in gamma synchrony between L.vOT and R.PreCG in the Consonant condition were significantly correlated to WJ-WA performance gains ($p < 0.01$, **Figure 7B**). Negative correlations in the Consonant condition were observed between L.IFG and left occipital cortex. In the Word condition, negative correlations were observed between L.AG and right occipital cortex. Increases in gamma synchrony between L.IFG and left occipital cortex in the Pseudoword condition were significantly correlated to WJ-LW performance gains ($p < 0.01$). In the Word condition, correlations were observed between R.IFG and left and right vOT regions, as well as with left occipital cortex. Negative correlations in the Consonant condition were observed between R.PreCG and L.IFG, and between R.PreCG and R.IFG. In the Pseudoword condition, negative correlations were observed between R.PreCG and right occipital cortex. In the Word condition, negative correlations were observed between R.PreCG and left and right occipital cortex sites.

Increases in theta-band NBTE from L.AG and R.PreCG to right occipital cortex in the Pseudoword condition were significantly correlated to WJ-WA performance gains ($p < 0.05$, **Figure 7C**). Significant correlations were also observed from L.IFG to L.PreCG for Words. Negative correlations in the Consonant condition were observed from L.AG to L.vOT, and from left occipital cortex to right occipital cortex. In the Pseudoword condition, correlations were observed from left occipital

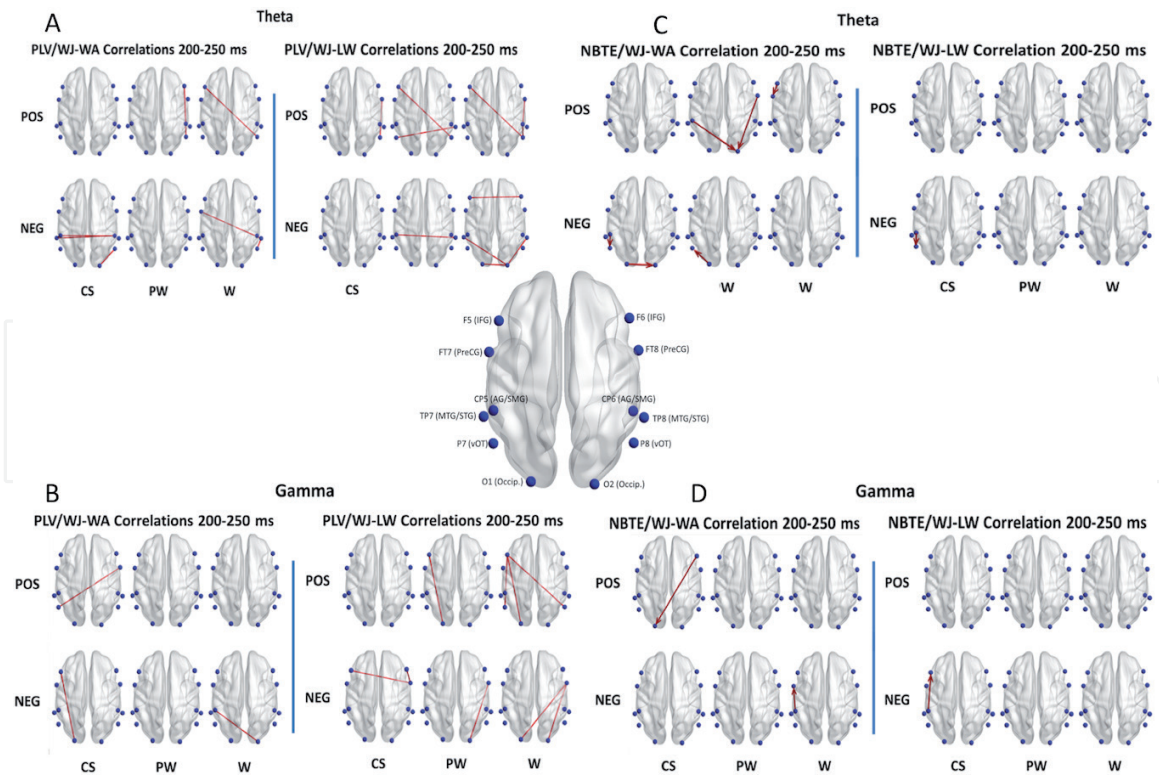


Figure 7.

(A) Significant correlations (red lines between areas) between changes in theta-band PLVs from 200 to 250 ms and gains in behavioural performance in WJ-WA (Left) and WJ-LW (Right) assessments after FFW intervention for the FFW group only. (B) Significant correlations between changes in gamma PLVs from 200 to 250 ms and gains in behavioural performance in WJ-WA (left) and WJ-LW (right) assessments post FFW intervention. (C) Significant correlations between changes in theta NBTE from 200 to 250 ms and gains in behavioral performance in WJ-WA (left) and WJ-LW (right) assessments following FFW intervention. (D) Significant correlations between changes in gamma-band NBTE from 200 to 250 ms and gains in behavioral performance in WJ-WA (left) and WJ-LW (right) assessments following FFW intervention. CS = Consonant String; PW = Pseudoword; W = Word.

cortex to L.vOT. Gains in theta NBTE from L.AG to R.IFG were significantly positive correlated to WJ-LW performance gains in the Pseudoword condition ($p < 0.05$), and from R.IFG to L.vOT in the Word condition. Negative correlations in the Consonant condition were observed from L.AG to L.vOT.

Increases in gamma-band NBTE from R.IFG to left occipital cortex in the Consonant condition were significantly correlated to WJ-WA performance gains ($p < 0.05$, **Figure 7D**). Significant negative correlations in the Word condition were observed from L.AG to L.PreCG. Changes in gamma-band NBTE did not show significant positive correlations with WJ-LW performance gains in any condition ($p < 0.05$). Negative correlations in the Consonant condition were observed from L.AG to L.IFG.

3.4 Comparing post-intervention dyslexic and typical reading networks

The FFW group's phase synchrony measures from both PRE and POST intervention sessions were compared to the networks of typical readers from Session 1 (TYP). Across all conditions in the PRE session, pre-FFW readers showed widespread occipito-temporal theta-band connectivity that was significantly greater than TYP readers (**Figure 8A**; $p < 0.05$). In the POST session, post-FFW readers showed occipito-temporal theta-band connectivity that was significantly greater than TYP readers in the pseudoword and word conditions, but show no differences in the consonant condition ($p < 0.05$). Following the interventional training program, the reading networks of dyslexic children more resemble those of

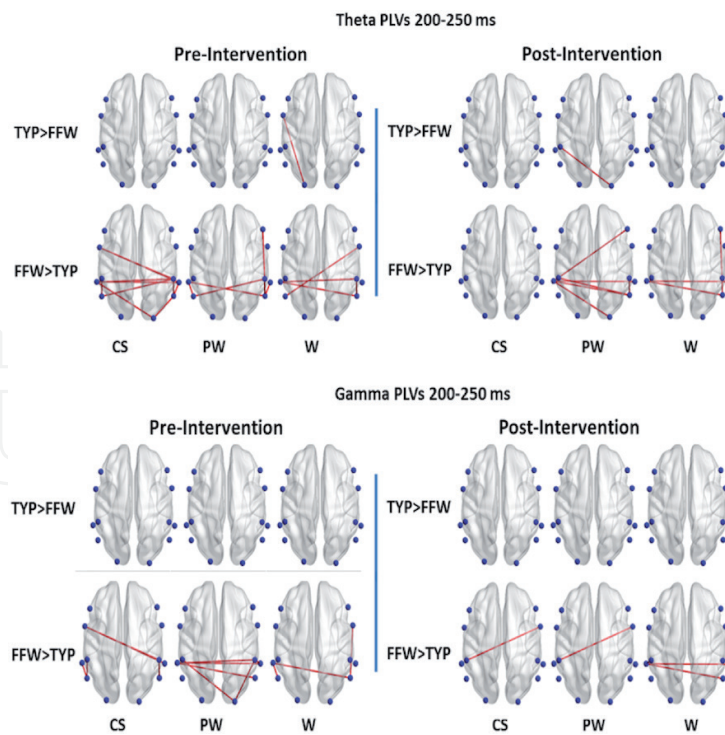


Figure 8.

(Top) Comparing dyslexic and typical theta-band network connectivity dynamics before and after intervention. (Left) Theta PLVs, comparing the dyslexic group (pre-FFW) to their typically-developing classmates prior to intervention. (Right) Comparing the dyslexic group after six months training (post-FFW) to the typical group (only session). (Bottom) Comparing dyslexic and typical gamma-band networks before and after intervention pre/post-FFW. (Left) Gamma PLVs, comparing the dyslexic group to their typically-developing classmates prior to intervention. (Right) Comparing the dyslexic group after six months to the typical group (only session). CS = Consonant String; PW = Pseudoword; W = Word.

typically-developing classmates when processing basic orthography (consonants). However, when processing pseudowords and words the post-FFW group continued to use pathways that were dissimilar to those used by typically-reading children when processing the same information.

Across all conditions in the PRE session, pre-FFW readers showed occipito-temporal gamma-band connectivity (**Figure 8B**), as well as occasional engagement of frontal sites, that was significantly greater than in TYP readers ($p < 0.05$). In the POST session, post-FFW readers showed single instances of greater gamma-band connectivity (than the TYP group) between L.AG and R.PreCG in the Consonant and Pseudoword conditions, as well as occipito-temporal connectivity in the Word condition. Comparing PRE and POST sessions, the gamma-band connectivity in the Pseudoword condition is much more sparse following intervention. Following the intervention program (post-FFW), however, the reading networks of dyslexic children, viewed from gamma-band connectivity, do more closely resemble those of typically-developing classmates, particularly in the Pseudoword condition.

4. Discussion

The present study examined the differences in neural processing dynamics between typically developing readers (TYP) and dyslexic readers who have been enrolled in a reading training program (FastForWord, FFW), prior to training (pre-FFW) and after the training (post-FFW). Our initial hypothesis of dyslexic readers generating more functional connectivity (phase synchrony) in response to words was supported. With regard to information flow connectivity (NBTE),

results supported the hypothesis for theta-band NBTE, but were somewhat ambiguous for the gamma band.

Both groups in this experiment showed pronounced N170/220 components at reading-critical sites in response to orthographic stimuli. However, the pre-FFW group showed more pronounced negative peaks across all conditions in the R.vOT region – a right-hemispheric analog to the so-called visual word-form area (VWFA, or L.vOT), which is thought to be critical to the processing of sub-lexical orthographic information [37, 38]. These results may reflect a similar specialization for orthographic processing that is leveraged by dyslexic readers to compensate for under-developed regions in the left hemisphere. Or it could reflect a less efficient (more effortful) bilateral form-processing response to orthographic stimuli, as the original function of these areas is visual form processing [37].

Observing underlying oscillatory activity at specific frequency bands allows for more nuanced examinations of neural oscillations that help to further characterize patterns observed in ERPs. To that end, we investigated the fluctuations in theta- and gamma-band power following the presentation of written words. Similar to the ERP results, the pre-FFW group showed significantly larger bursts of theta-band power from R.vOT at the same time as the N170/220 component, a relationship that has been documented in prior studies of the oscillatory dynamics of reading in the brain [13].

The connectivity results further corroborated this assertion of a right-hemispheric network at play in dyslexic children during reading. Neuroimaging studies have repeatedly identified regions in the right hemisphere producing stronger activations in dyslexic individuals in response to reading tasks [9, 10, 12, 39, 40]. Here we showed that, at the moment that orthographic information is first being processed, each group leverages distinct neurocognitive networks to carry out this process – such that dyslexic children display more inter-hemispheric connectivity, as well as right-sided intra-hemispheric connectivity in response to written language, not seen in typical readers.

Pre-FFW readers showed robust posterior (occipito-temporal) connectivity across all three conditions. Notably, this includes the Consonants condition, in which the stimuli lacked any linguistic content to be evaluated by the central question “Is this a real word?” Presumably, if dyslexia only involves processing beyond simple orthographic decoding, then the two groups should be identical until such processing is required. Our interpretation of the overactive connectivity in the Consonant condition is that there is a “bottleneck” in processing in early dyslexic language networks. Note that regardless of the actual linguistic content in the stimuli, the string still must be evaluated as though it *may* have linguistic content, which is enough to engage various aspects of the reading network to evaluate the content [20]. This window 200–250 ms after stimulus onset captures the moment in which orthographic decoding occurs and information is relayed to other sites to be further evaluated for content. For pre-FFW readers, a set of alternative processes and pathways is engaged to handle the consonants. First, as we saw with ERPs and ERSs, the right hemisphere plays a large role for dyslexic readers, particularly in posterior sites. In the decoding and transmission of orthographic information, the lack of expertise in dyslexic children means that they must spend more time processing the stimuli in order to make their judgement.

Theta-band NBTE results are consistent with this framing, with dyslexic readers showing greater effective connectivity from R.vOT to L.vOT, then from vOT sites to AG regions. Whereas pre-FFW network connectivity was constrained to occipito-temporal sites in posterior cortex, the TYP group showed greater engagement of frontal sites.

Across all behavioral scores – reading assessments (WJ-WA and WJ-LW), task accuracy, and reaction time – the pre-FFW vs. post-FFW comparison was not

significant for either task accuracy or reaction time. Despite the overall FFW group lacking significant gains in aggregate, however, some readers did improve their performance after intervention. This fortuitous result in turn informed the correlation analysis between changes in reading performance and changes in oscillatory connectivity. Between sessions (post-FFW vs. pre-FFW), localized brain activity (ERPs) at reading-related sites showed a general reduction in intensity, such that positive and negative peaks of interest (e.g. N170 component) were less pronounced in the POST session (post-FFW) [17, 18, 22, 23, 41]. These findings are in line with neuroimaging studies of other dyslexia interventions, whereby improved reading ability was linked to decreases in general activation due to more efficient and specialized processing, as well as a shifting in regional activations [42, 43].

Functional connectivity findings, as measured by phase synchrony, displayed several differences in connectivity patterns between sessions (post-FFW vs. pre-FFW) and across conditions. Theta-band phase synchrony has been shown to reflect network connectivity patterns over time during reading [13, 31]. In the present study, a reduction of theta synchrony was observed in the Consonant condition of the POST session (post-FFW) at the time window most critical for pre-lexical orthographic processing in children (200–250 ms). Interestingly, the Consonant condition requires no additional reading training to identify its semantic or phonological properties, and yet orthographic expertise seems to have had an effect even here. Just as with ERPs, this result suggests a reduction in executive engagement during orthographic processing, thus requiring fewer resources to accomplish the same task [20, 44].

Further supporting this account, the correlations between behavioral performance and brain network connectivity also showed significant negative correlations between occipito-temporal posterior connectivity and reading assessment scores. In other words, children who showed the lowest performance gains also tended to exert more resources among posterior sites involved in the early stages of reading, whereas individuals who showed the largest performance gains in their reading assessments instead tended to show brain connectivity patterns engaging more frontal sites, suggesting the engagement of higher-level language areas.

Price and Devlin [20] have argued for a framework of occipito-temporal cortical dominance in word reading that emphasizes the role of connectivity and communication between these and other regions, such that orthographic information is resolved by comparing bottom-up inputs with top-down expectations. In this framework, unfamiliar or difficult content would require substantially more frequent evaluations to resolve the perceptual inputs before sending that information to higher-level language-processing regions, resulting in slower overall performance. The results presented here indeed suggest that readers who showed the greatest behavioral improvements required fewer resources at earlier stages, allowing for earlier engagement of frontal sites.

In general, the most improved readers showed greater theta-band connectivity within frontal brain areas whereas the least improved readers showed greater posterior occipito-temporal connectivity patterns instead. Following Price and Devlin's framework, whereas poor readers are still resolving the orthographic and initial linguistic content, more developed readers are evaluating (or at least engaging with) higher-level linguistic content in the frontal language processing centers. In this case, we suppose that the higher levels of occipito-temporal connectivity in the poor readers reflect a delay or disruption in sensory processing, in that more experienced readers are already accessing linguistic information beyond simple pre-lexical orthography [45].

Frontal lobe connectivity changes have been shown to be a predictor of reading performance gains. Hoeft and colleagues [10] have shown that structural

connectivity linked to R.IFG is a predictor of performance gains in children with developmental dyslexia. In the present study, our functional and effective connectivity results did not clearly corroborate this account, since R.IFG showed distinct instances of increased connectivity both in PRE- and in POST-training sessions, as well as both positive and negative correlations to gains in assessment scores. Thus, it seems that structural connectivity alone is not enough – there must be functional and effective connectivity accompanying it for reading performance to be bettered.

Although we did not measure the TYP group's reading networks a second time, a meaningful comparison is still possible to address the question of whether the intervention (plus the intervening time period and other school activities) caused the post-FFW reading networks to more closely resemble the already substantially more skilled TYP reading networks. We found that indeed there was some closer resemblance in theta-band connectivity in the POST session, but only for the consonant strings. Even after six months of intervention, however, the FFW group's theta-band networks in the Pseudoword and Word conditions remained robustly distinct from the TYP group. These findings suggest that whereas some aspects of the reading network brain connectivity dynamics may have come to resemble more closely typical processing at early (i.e. pre-lexical) stages, the later and more complex stage processes still utilized alternative pathways. It remains unclear if this is because of a compensated efficiency in alternative pathways or because of poor coordination from typical regions (e.g. ectopias, that is, distorted cortical layering, disrupting processing in the left hemispheric language areas, [46]), or both.

In the gamma band, PRE- and POST-training session differences were somewhat less pronounced, but it is clear that the post-FFW network connectivity in the Pseudoword condition more closely resembles the TYP group after the training. The nature of the task is such that the Pseudoword condition is particularly taxing on phonological processing skills of the reader, forcing them to sound out the letter strings. In this regard, the improved performance of the post-FFW group in reading assessments may be related to their networks being more optimal (i.e. closer to the typical organization).

The underlying premise for this comparison between post-intervention FFW and TYP readers was to examine if a targeted reading intervention would shape the reading network connectivity dynamics in dyslexic children at the ms time scale to be more closely aligned to their typically-developing classmates, or if the training would instead optimize their existing “compensational” networks. These results suggest that for early orthographic processing, post-FFW readers' theta-band networks do seem to shift in such a way that orthographic processing follows pathways more similar to those of TYP readers. However, after this initial processing, as the orthographic information needs to be made available to the rest of the reading network (e.g. for phonological or semantic processing), post-FFW readers continue to use alternative bilateral pathways to achieve improved behavioral results.

This divergence in results between theta and gamma bands may be addressed by explanations proposing different functional properties of each frequency band [47], whereby theta-band PLVs represent long distance communication (e.g. occipito-frontal; [48]), whereas gamma-band oscillations work in conjunction with theta-band oscillations to aid in more localized computations. As for gamma-band connectivity, Lehongre and colleagues [14] showed a reduced ability for dyslexic individuals to synchronize their auditory processing at a gamma rate compared to controls. Goswami [15] went on to posit that this gamma synchrony deficit might account for phonological processing difficulties seen in dyslexic readers [16], as the average speed at which phonemes are read is at a gamma rate. This has the result that, when dyslexic readers attempt to string together speech sounds from text, they do so in an uncoordinated manner, resulting in poor reading performance.

What remains unclear is why phonological processing networks in the gamma band would shift toward a more typical organization, but the orthographic (consonant strings) or semantic processing (words) did not show so drastic a change. It is possible that more complex processing using higher language networks requires more time to remediate because plasticity across large-scale networks must be coordinated (see [16]).

Another perspective to consider is whether or not the presence of ectopias has altered the micro-structure of the reading-related brain regions to the point that pathways connected to these regions are under-utilized by the dyslexic reading networks in favor of alternative pathways (e.g. right hemisphere). An ectopia is a distortion of the cortex during development in which many neurons fail to migrate to their proper layer, ending up as clumps in layer I of cortex. Ectopias not only affect the operation of the cortical area in which they occur, but also they cause distorted processing in areas to which the affected area is connected [46]. In rats, ectopias cause difficulties in auditory processing specifically [46]. Ectopias are found in the brains of some dyslexic readers (post mortem) and are hypothesized to be at least one cause of the disorder [46]. If ectopias in the left hemisphere have disrupted the brain's ability to develop effective pathways and networks in the left hemisphere, then their coordination is also likely disrupted, and perhaps accounts for the challenges in phonological processing and compensation via expansion to the right hemisphere. These results suggest that, at least in the gamma band, enough coordination was shored up to the extent that the post-FFW networks statistically more closely resembled the TYP network, compared to the PRE training session. This and other conclusions would be strengthened by a similar experiment that would include a group of dyslexic students who did not receive training (perhaps because of unavailability; not done here due to ethical considerations), but who could then be compared to the trained dyslexic readers, thus characterizing in this population the effects of training plus classroom instruction and general development in contrast to the latter two alone.

5. Conclusion

EEG brain imaging indicated significant differences in local and largescale brain network connectivity dynamics between typical and dyslexic readers. Prior to FastForWord (FFW) training, a “bottleneck” in early orthographic decoding leads to greater posterior occipito-temporal connectivity with expansion into the right hemisphere in dyslexic readers compared to neurotypical readers.

After cognitive training, the “bottleneck” is relieved for consonant strings, while pseudowords and real words continue to utilize right- and cross-hemispheric networks rather than typical left-hemispheric networks, but involving more frontal areas overall. As dyslexic readers become more proficient, they are able to engage higher-level language areas faster and thus reduce posterior engagement. Brain-based cognitive training programs, such as FastForWord, further indicate significant potential for improving reading ability by accelerating reading network development in dyslexic children.

What are the implications of this study for treatment of dyslexia? It is clear that more research is needed to more precisely characterize both the brain network dynamics characterizing dyslexic reading, and also the effects of interventions such as FastForWord on these dynamics. We have mentioned several such possible studies earlier. In particular, however, a prospective study with more participants and an untreated control group is critical. More generally, however, it would be desirable to identify children at risk of dyslexia as early as possible in their reading

training, and engage them in a reading training program, so as to take advantage of brain plasticity in guiding the reading networks in the most efficient trajectory. Equally important, however, is the implication that such programs will not help all children equally. Even in our small sample we found a range of outcomes from the FastForWord program, from no improvement to significant improvement. How much will be gained from enrollment in such a program will depend on many factors, among them are the precise nature of the brain impairment causing the difficulty, and the amount of effort and motivation a student can bring to the program. Moreover, if the cause of the dyslexia is a brain abnormality, for example an ectopia in the left temporal lobe, then specific training likely will not result in a “normal” reading network because the ectopia cannot be “cured.” Nonetheless, improvement of the alternative, more right-hemisphere-oriented, network resulting from a training program can be expected in these cases.

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