Version of Record: https://www.sciencedirect.com/science/article/pii/S0093934X18300312
Manuscript_6df0f4156eb9f275eeacbe9981d0457d

# An fMRI-Adaptation Study of Phonological and Orthographic Selectivity to Written Words in Adults with Poor Reading Skills

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Short title: Phonological and orthographic selectivity in poor readers.

Keywords: reading, poor readers, dyslexia, fMRI, adaptation, phonology, orthography

Acknowledgements: This work was supported by the *Eunice Shriver* National Institute of Child Health and Human Development (HD067884 and HD056107) and the National Science Foundation (1026934). We thank the staff at the Center for Functional and Molecular Imaging (D040677) and our subjects for their participation.

## Abstract

Typical readers rely on two brain pathways for word processing in the left hemisphere: temporo-parietal cortex (TPC) and inferior frontal cortex (IFC), thought to subserve phonological decoding, and occipito-temporal cortex (OTC), including the "visual word form area" (VWFA), thought to subserve orthographic processing. How these regions are affected in developmental dyslexia has been a topic of intense research. We employed fMRI rapid adaptation (fMRI-RA) in adults with low reading skills to examine in independently-defined functional regions of interest (ROIs) phonological selectivity to written words in left TPC and IFC, and to orthographic selectivity to written words in OTC. Consistent with the phonological deficit hypothesis of dyslexia, we found responsivity but not selectivity to phonology, as accessed by written words, in the posterior superior temporal gyrus (pSTG) of the TPC. On the other hand, we found orthographic selectivity in the VWFA of the OTC. We also found selectivity to orthographic and not phonological processing in the IFG, a finding previously reported for typical readers. Together our results demonstrate that in adults with poor reading skills, selectivity to phonology is compromised in pSTG, while selectivity to orthography in the VWFA remains unaffected at this level of processing.

## 1 Introduction

Brain imaging studies have demonstrated that typical readers rely on left-hemisphere regions for word processing, including temporo-parietal (TPC), inferior frontal (IFC) and occipito-temporal (OTC), cortices (Church et al., 2008; Dehaene and Cohen, 2011; Martin et al., 2015; McCandliss et al., 2003; Pugh et al., 2001; Turkeltaub et al., 2003). A widely-accepted model of reading attributes phonological processing to the dorsal circuit, with TPC mediating phonological assembly and IFC phonological articulatory processes, while the ventral pathway, including the “visual word form area”, VWFA, is thought to be specialized for the fast recognition of single words and tuned to the orthography of words (Pugh et al., 2001). Further, during the early stages of development, reading is thought to be accomplished largely through phonological assembly (grapheme-phoneme-mapping) via the dorsal pathway, and as children advance, there is increasing use of the direct ventral orthographic route in the OTC (Pugh et al., 2001), with the VWFA playing an important role in word identification, especially for frequently encountered words. Specifically, it has been purported that the left TPC “guides and shapes” the OTC and that the development of word form recognition in the VWFA in the OTC therefore depends on well-functioning TPC. Recent evidence from Wise Younger et al. (2017) supports this theory, finding that functional connections between the dorsal and ventral streams are important during the initial stages of learning to read, while a reduction of dorsal stream engagement is associated with more advanced reading.

The process of learning to read falters in 5-12% of the population due to developmental dyslexia (Katusic et al., 2001). Dyslexia is a heritable reading disability unexpected in relation to other cognitive abilities and the provision of educational opportunities (Lyon et al., 2003). Most current theories posit a weakness in phonological processing/coding as the primary problem (Bruck, 1992; Morris et al., 1998; Stanovich and Siegel, 1994; Wagner and Torgesen, 1987) and imaging studies have revealed functional (Eden et al., 2004; Maisog et al., 2008; Richlan et al., 2009; Shaywitz et al., 1998) and anatomical (Eckert, 2004; Hoeft et al., 2006; Krafnick et al., 2014; Linkersdörfer et al., 2012; Richlan et al., 2013) differences in left hemisphere regions known to be involved in reading and phonological processing when comparing dyslexic and non-dyslexic readers (for a recent review see Eden et al., 2016). Consistent with the developmental model of reading acquisition described above, Pugh and colleagues (Pugh et al., 2001; Sandak et al., 2004) also posit that dyslexia arises from of a primary impairment in TPC, hampering phonological decoding of words. This deficit also hinders the dyslexic child's advancement to automatic sight word recognition of frequently encountered words in the VWFA, leading to the observed underactivity in this region of OTC. As such the OTC dysfunction is viewed as a consequence of (i.e., secondarily to) the TPC dysfunction. It has also been suggested that in response to these disruptions in posterior cortical regions, increased activity in the inferior frontal gyrus (IFG) in dyslexia serves as a compensatory mechanism involving articulatory processes (Pugh et al., 2001; Shaywitz et al., 1998). Others, however, have suggested that the OTC dysfunction may be more than just a consequence of TPC failure, but have a more central role (Kronbichler and Kronbichler, 2018; Richlan, 2012).

Therefore, both phonological and orthographic processing have been of critical interest for neurobiological models of reading and dyslexia, but their specific roles and relationship remain elusive. It is challenging to separate these processes, especially in brain imaging studies. Most reading tasks invoke both phonological and orthographic processing, even if only one of these is specifically targeted in the experimental design. It is difficult to engage one at the complete exclusion of the other. Therefore, a better assessment of the *specific* functional integrity of regions known to be involved in phonological and orthographic processing is needed. While functional magnetic resonance imaging (fMRI) technology has been instrumental in characterizing the reading brain, the information garnered is limited with regards to detail, as information is pooled over large neuronal populations within each voxel. Specifically, the density of selective neurons as well as the broadness of their tuning contribute to the average activity measured (Glezer et al., 2016). This makes it difficult to resolve if neurons in these regions are selective to phonological and/or orthographic representations of written words. In addition, because reading is a uniquely human skill, this information cannot be informed by other data, such as single unit recordings in animals, the way in which, for example, object recognition research has.

One way to address these problems has been the use of fMRI rapid-adaptation techniques (fMRI-RA) to probe neuronal *selectivity* more directly. This allows for a better characterization of neuron-level processing and is critical for interpreting existing findings about hypo- and hyper-activity reported in various regions of the brain in prior studies of dyslexia. In fMRI-RA experiments, two stimuli are presented sequentially in each trial. If the two stimuli activate overlapping neuronal populations, neurons that are activated by both stimuli show adaptation on the second presentation (also referred to as repetition suppression), leading to an overall smaller blood oxygenation level dependent (BOLD)-contrast response following the second stimulus relative to the first (Dehaene et al., 2001, 2004; Grill-Spector et al., 2006). Specifically, the BOLD-contrast response to the *pair* is taken to reflect similarity of the neuronal activation patterns corresponding to the two individual stimuli, with the lowest response for two stimuli activating identical neuronal populations, and maximum signal if the two stimuli activate disjoint groups of neurons. In this way, adaptation has been used to infer if the BOLD signal is coming from a population of neurons selective for a specific attribute of the stimulus (Grill-Spector et al., 1999). Given that fMRI-RA provides a tool for characterizing the functional properties of neural populations (Grill-Spector and Malach, 2001) it has been applied to determine the specialization of brain areas involved in spelling (Purcell et al., 2017), face (Jiang et al., 2006) and word processing (Dehaene et al., 2001, 2004; Glezer et al., 2009), and for distinguishing orthography-selective regions from phonology-selective regions (Glezer et al., 2016).

In prior work (Glezer et al., 2009, 2015), this fMRI-RA approach was used in typical adult readers to show that the VWFA of the OTC contains neurons tightly tuned to visually presented real words, much like neurons in monkey IT that have been shown to be highly selective for specific objects after training the animals to identify novel, yet similar, objects (Logothetis and Pauls, 1995). In the case of reading, these results demonstrate that adults have developed orthographic “selective tuning” for specific words as a consequence of their reading experience and their constant need to discriminate them from other, visually similar words (such as “post” from “past”). This neuronal tuning to specific words creates neurons that show high selectivity to one word, but little response to other words, even if they are orthographically similar (e.g., differing only by one letter (Glezer et al., 2009)). Further, it is the experience with written words that results in such word-specific neuronal tuning: when typically reading adults underwent a training regimen to learn to recognize novel pseudowords, selectivity increased in the VWFA following the training to real word-like levels (Glezer et al., 2015), even within a single session (Riesenhuber and Glezer, 2016). This process is likely to be similar to the tuning process that occurs during normal reading acquisition in childhood.

Recently, fMRI adaptation was used to examine the selectivity to *phonological* as well as *orthographic* features of visually presented words in typical adults (Glezer et al., 2016). In this study there were three conditions of interest for the prime/target pairs: 1) the “same” word was presented as both the prime and target (same orthography and phonology), such as “hair” followed by “hair” (S), 2) the prime/target pair were “homophones” such as “hare” followed by “hair” (H), and 3) the prime was a “different” word from the target word (different phonology and different orthography, and also controlled for orthographic and phonological overlap of the H pairs), such as “hear” followed by “hair” (D). For regions tasked with phonological processing, the averaged response to a prime word followed by its homophone (H) target word would be equivalent to that observed for a target word that was primed with the exact same word (S, which is the condition that produces “maximal” adaptation), given the identical phonology of the two words in the pair in the H condition. That is, even though the two words in an H pair differ in orthography, a region selective for phonology should treat them identically, thereby leading to the same maximum adaptation as observed in the S condition (i.e., the two should be the same, S=H). Using fMRI-RA we demonstrated (in two groups of adults using slightly different experimental parameters for each group) that the pSTG of the TPC showed full adaptation to visually presented pairs of words that are homophones because this adaptation was (i) at the same level as identical (“same”) words *and* (ii) non-homophone written word pairs of analogous orthographic dissimilarity (D) showed no adaptation. These results (S=H<D) suggest that neurons in the pSTG of the TPC are exquisitely tuned to the phonology of written words. While one would expect the IFC to also show sensitivity to phonological features, the same study, surprisingly, showed that it did not.

For orthographic processing on the other hand, we found in the typically-reading adults that neurons in the VWFA are tightly tuned to the orthographic representations of words learned through prior experience. Specifically, under these conditions two similar but non-identical words in the D condition (e.g., “desk” and “disk”) have minimal neural overlap and therefore no adaptation occurs as already described above (D). However, this time (i) the responses to the H condition is identical to the D condition (H=D), given the orthographic difference of the word pairs (even though they sound the same) being treated like non-identical words, *and* (ii) both these conditions differ from the same condition (S<H=D), where the signal will be lowest as just described (two identical word repeatedly activate the same neural populations, causing maximum adaptation).

Notably, the study involved two groups of adult typical readers and for each group used two slightly different versions of the experiment with different tasks, yet the findings across the two studies converged, demonstrating they were robust. These findings in TPC and OTC are consistent with the original Pugh model (2001) and the idea of two pathways of reading (Coltheart et al., 2001; Levy et al., 2009); however the role of the IFC is less clear.

In the current study, we used the same approach as that used in Glezer et al., 2016 to characterize *phonological* and *orthographic* tuning in adults with poor reading skills. Since visually presented words are used for all of the experiment, it is important to note that “sensitivity to phonological information” throughout this paper refers to how phonological information is accessed for written words. Specifically, we examined the S, H, and D conditions in TPC, IFC and OTC using Experiment 1 from Glezer et al., 2016. For regions involved in phonology (e.g., TPC) prime words and target words with the same phonological representation, such as in “pain” and “pane” should cause maximal neural overlap for phonology and therefore adaptation, just as the same condition, and unlike the different condition (i.e., S=H<D, see Figure 1A). However, if neurons in the TPC are not tightly tuned to the phonological representation of words, as one would predict for poor readers, then there would be less adaptation and S would be significantly lower than H. For regions involved in orthography (i.e. the VWFA in the OTC) the responses to the H condition would be identical to the D condition and both should differ from the same condition (i.e., S<H=D, see Figure 1B). However, in poor readers, neurons in the VWFA may not be tightly tuned to the orthographic representations of words.

## 2 Methods

The Georgetown University Institutional Review Board approved all experimental procedures, and written informed consent was obtained from each individual.

## 2.1 Subjects

Thirteen adults participated in this study. All participants were recruited through fliers posted on the university campus, including Georgetown University's Resource Center (which provides support for students with learning disabilities). All subjects were evaluated (see below) using standardized tests for assessing Intelligence Quotient (IQ), reading (timed single real word and pseudoword reading), and phonological processing skills (phonemic awareness, phonological retrieval and phonological working memory). All subjects had IQ scores within or above the normal range (> 85 standard score). Subjects were included if they scored at least one standard deviation below their performance IQ (i.e. > 15 points) on one or both measures of single word reading. This ensured the inclusion of participants who, despite most of them being university students, had persistent word naming and/or decoding difficulties. Six of the participants had a formal diagnosis of dyslexia. The fact that not all were given a formal diagnosis at some earlier time can be attributed to their reading being in the normal range, even though it was much lower than their performance IQ. Therefore, we use the term "poor readers" to describe a group of participants whose reading level was below that expected based on their strong cognitive abilities. Table 1 details the average scores and range of the group and reveals the relatively low reading skills (and weaknesses in skills that support reading) despite their high IQ.

## 2.2 Psycho-educational Measures

IQ was estimated using the Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler, 1999), measuring verbal (Vocabulary and Similarities), and non-verbal (Block Design and Matrix Reasoning) IQ. Real word reading was measured using the Sight Word Efficiency Test from the Test of Word Reading Efficiency (TOWRE; Torgesen, Wagner, & Rashotte, 1999). This assesses the number of printed single real words accurately read within 45 seconds, thereby offering a timed measure of real word reading accuracy. Pseudoword reading was assessed using the Phonemic Decoding Efficiency from the same instrument, assessing the number of pronounceable printed non-words that were accurately decoded in 45 seconds. Additionally, we measured skills in the domains of phonological processing: The Elision subtest from the Comprehensive Test of Phonological Processing (CTOPP (Wagner, R. K., Torgesen, J. K., & Rashotte, 1999)) was used to assess phonemic awareness, and the phonological retrieval subtest composite to measure rapid (automatized) naming. Digit Span from the Wechsler Adult Intelligence Scale-IV (WAIS, Wechsler, 2008) was used to measure phonological working memory. These three skills, broadly referred to as measures of phonological processing, are known to be predictive of reading success and impaired in people with dyslexia (Wagner et al., 1987).

## 2.3 fMRI Data Acquisition

MRI data were acquired at The Center for Functional and Molecular Imaging (CFMI), Georgetown University Medical Center on a 3T Siemens Trio scanner with a 12-channel head coil. For both the functional localizers and the fMRI-RA scans, 35 interleaved axial slices (4mm thick, no gap; 3.2x3.2mm$^2$ in-plane resolution) were acquired for fMRI data using an echo-planar sequence (flip angle=90°, TR=2.04s, TE=29ms, FOV=205$^o$, 64x64 matrix). Stimuli were presented using E-Prime (www.pstnet.com), back-projected on a screen located at the rear of the scanner, and viewed through a headcoil-mounted mirror.

## 2.4 fMRI Study Design

The study involved the acquisition of functional localizer scans for the identification of individual subjects' ROIs and these were then used to guide the analyses of the fMRI-RA data. Separate contrasts from the localizer were used for identifying ROIs, with one contrast used to identify areas involved in phonology (TPC and IFC) and another contrast used to identify the ROIs involved in orthography (VWFA of OTC), as described below and previously published for typical readers (Glezer et al., 2016).

### 2.4.1 *Functional Localizer Scans for Individual Subjects' ROI Identification (TPC, IFC and VWFA of OTC) for use in fMRI-RA analyses*

To allow us to focus on the regions known to be involved in the phonology (IFC and TPC) and orthography (OTC) of word processing, "functional localizer scans" were acquired for each subject with the goal of functionally defining those ROIs associated with orthography and phonology, respectively. An fMRI block design was used in which, following an initial 14.28s fixation period, ten pairs of words or ten pairs of visually scrambled words (using a scrambled size of 2x2 pixels) were presented to participants in blocks of 30.6s, separated by a 14.28s fixation block (Glezer et al., 2009, 2016). Within each block, each pair of images were displayed for 1500ms (one above and one below a fixation cross that was located at the center of screen), followed by a 1560ms blank screen. Each block began with a 2040ms cue, which instructed subjects to perform one of following tasks in the block: Word Matching – participants needed to decide whether the two simultaneously presented words were the same or different; Word Rhyming – participants needed to decide whether the two words in a pair rhymed with each other; Word Meaning – participants needed to decide whether the two words in a pair belonged to the same or different semantic category; Scrambled Words – participants needed to decide whether the two visual patterns (pixel-scrambled words) in a pair had the same or different contrast. This last condition served as a visual control.

Stimuli were as follows: For the Word Matching task, sixty 3-6 letter high and low frequency words were used and there were two conditions – 1) same (two words were the same, e.g., desk-desk), and 2) different (two words differing by one letter, e.g., desk-disk); For the Word Rhyming task, eighty 3-6 letter, low and high frequency words were used, and there were four conditions – 1) words with the same orthography that rhymed (e.g. cave-save), 2) words with different orthography that rhymed (e.g. bows-toes), 3) words with the same orthography that did not rhyme (hose-lose), and 4) words with different orthography that do not rhyme (plow-fear). For the Word Meaning task, forty high frequency animate and forty high frequency inanimate words were used, and there were two conditions – both words in a pair belonged to 1) the same category (Animate vs Inanimate) (e.g., lion-fish, or shoe-book), or 2) different category (e.g., lion-book). Finally, for the Scrambled Words task, pixel-wise scrambled images from sixty words were used, and there were two conditions – the two scrambled images were 1) the same image with the same contrast, or 2) different images with additional 30% difference in luminance. There were two runs and during each run each condition was repeated twice in a pseudorandomized order with new stimuli. Each run lasted for 389.64s, and participants were asked to perform the tasks according to the cues, while keeping their fixation at the center of the screen. The order of conditions was counterbalanced between the two runs.

The phonological ROIs (TPC and IFC) were identified using the contrast of Word Rhyming > Fixation masked by Word Rhyming > Word Matching (Glezer et al., 2016). We used this contrast with the masking to help constrain selective regions to peak clusters of a reasonable size (see below). The orthographic ROI (VWFA in OTC) was identified using the contrast of Word Matching, Word Rhyming and Word Meaning combined (referred to as “Word Processing”) versus Fixation, masked by the contrast of Word Matching, Word Rhyming and Word Meaning combined (i.e., “Word Processing”) versus Visual Pattern (scrambled words) (Glezer et al., 2016).

### *2.4.2 Event-related fMRI-RA Experiment*

As in Experiment 1 Glezer et al., 2016, fMRI images from four event-related scans were collected for each subject. Each run lasted 579.36s and had two 30.6s fixation periods, one at the beginning and the other at the end. Between the two fixation periods, a total of 127 trials were presented to participants at a rate of one every 4.08s. During each trial, following a 1000ms fixation, two visually-presented words were displayed sequentially (400ms each with a 200ms blank screen in-between), and followed by a 2080ms blank screen. For each run, there were 25-26 trials each condition.

There were three conditions of interest of varying intra-pair stimulus similarity: 1) the *same*, such as hair-hair (S), 2) a *homophone* pair, such as hare-hair (H), and 3) a the prime was a *different* word from the target, such as hear-hair (D). The different word (D) stimuli always contained the same number of overlapping and repeated letters as the H stimuli. To create these triplets, first the homophone pairs were selected. Then a word was created for the D condition that matched the word in the H condition in length, number of letters/phonemes changed from the S condition, frequency and part-of-speech (POS). All the words in the triplet were one syllable and had the same number of phonemes. All lists were matched for POS which was based on the English Lexicon Project (Balota et al., 2007), and frequency and orthographic neighborhood were based on MCWord (Medler and Binder, 2005). For the POS matching, all words occurred as nouns, verbs or adjectives or a combination. Word lists were matched based on the most frequently occurring POS for each word. Trial order was randomized and counterbalanced using M-sequences (Buračas and Boynton, 2002) and the number of presentations was equalized for all stimuli.

To engage subjects' attention, yet avoid potential task-related confounds of the BOLD-contrast response to the conditions of interest (Grady et al., 1996; Sunaert et al., 2000), there was an "oddball" task (orthogonal task). Throughout the experiment subjects were asked to perform an "oddball" detection task (Glezer et al., 2009, 2015, 2016). Specifically, as in Experiment 1 of the 2016 study, subjects were asked to press a button with their right hand every time they saw a two-syllable word. These two-syllable words were generated in addition to the other word stimuli that were all one-syllable words (there were no differences in word length between oddball and experimental words). Appearance of the two-syllable “oddball” stimulus occurred approximately 20% of the trials (either the first or the second one of the pair of words, with the other word being one of the items for the adaptation experiment). Importantly, while these trials ensured that subjects were constantly engaged during the experiment, the trials containing the pairs with a two-syllable word were not used for the fMRI-RA analysis.

## 2.5 fMRI Data Processing and Analysis

### 2.5.1 General fMRI Data Preprocessing and Analyses

For both the functional localizers and the fMRI-RA scans, all preprocessing and most statistical analyses were done using the SPM2 software package (http://www.fil.ion.ucl.ac.uk/spm/software/spm2/), consistent with our prior work (Glezer et al., 2009, 2015, 2016). After discarding the first five acquisitions of each run, the EPI images were temporally corrected to the middle slice (for event-related scans only), spatially realigned, resliced to 2 x 2 x 2 $mm^3$ and normalized to a standard MNI reference brain in Talairach space. Images were then smoothed with an isotropic 6mm Gaussian kernel. After removing low frequency temporal noise from the EPI runs with a high pass filter (1/128Hz), fMRI responses were modeled with a design matrix comprising the onset of trial types and movement parameters as regressors using a standard canonical hemodynamic response function (HRF).

### *2.5.2 Individual Subjects' ROI Identification (TPC, IFC and VWFA of OTC) using Functional Localizer Scan Data (for application to fMRI-RA analyses)*

The TPC and IFC ROIs were identified for each subject individually (see the Results section for the specific locations) using the contrast of Word Rhyming > Fixation ($p<0.00001$, uncorrected) masked by Word Rhyming > Word Matching ($p<0.05$, uncorrected). In order to select ROIs that were of approximately equivalent size (Goh et al., 2010; Park et al., 2004), the thresholds were adjusted beyond this point in order to obtain a cluster that was between 10 and 100 voxels. The VWFA region in the OTC was also identified for each individual subject with the data from the localizer scans, this time using the contrast of Word Processing (Word Matching, Word Rhyming and Word Meaning combined) versus Fixation ($p<0.00001$, uncorrected) masked by the contrast of Word Processing (data acquired during Word Matching, Word Rhyming and Word Meaning combined) versus Scrambled Words ($p<0.05$, uncorrected). This contrast typically resulted in only 1-2 foci per subject in the left ventral occipitotemporal cortex ($p<0.05$, corrected at the cluster level). ROIs were selected by identifying in each subject the most anterior cluster that was significant at the corrected cluster-level of at least $p<0.05$ in the ventral occipitotemporal cortex (specifically, the occipitotemporal sulcus/fusiform gyrus region) in a location closest to the published location of the VWFA, approximate Talairach coordinates -43 -54 -12 ±5 (Cohen and Dehaene, 2004). Thresholds were adjusted in order to obtain a cluster that was between 10-50 voxels (Glezer et al., 2015, 2016).

### *2.5.3 fMRI-RA analysis*

Following preprocessing and the general analysis described above we then extracted the mean percent signal change of the three ROIs for each subject with the MarsBar toolbox (Brett et al., 2002), and conducted one-way repeated measures ANOVAs (applying Greenhouse Geisser correction when Mauchley's Test of Sphericity was violated). We also conducted post-hoc pairwise comparisons using Bonferroni correction on the percent signal change.

## 3 Results

### 3.1 Individual Subjects' ROI Identification (TPC, IFC and VWFA of OTC) using Functional Localizer Scan Data (for application to fMRI-RA analyses)

ROIs were identified in all subjects for all three regions: TPC and IFC identified with the phonological functional localizer data, and VWFA in the OTC identified with the orthographic functional localizer. The MNI coordinates of the average maxima location (and standard deviation) are provided here. In the TPC, pSTG (BA 22/39): -54±5, -48±8, 15±8; in the IFC, pars *opercularis* (BA 44): -56±6, 7±4, 8±6, and in the OTC, the VWFA (BA 37): -47±7, -56±7, -15±6. Each subject's ROIs were used to extract the fMRI-RA signal as described above and the results are presented in the next section.

### 3.2 Event-related fMRI-RA Experiment

We expected that in all ROIs (OTC, TPC and IFC) the signal would be lowest in the same (S) condition (see Figure 1), as the two word stimuli were identical and would therefore repeatedly activate the same neural populations, causing maximum adaptation. We also expected the least amount of adaptation for the different (D) condition, because the two word stimuli differ completely (both in phonology and orthography) and the second stimulus would therefore be most likely to activate a different subpopulation of neurons. We found both to be the case. The key condition of interest that tests for *phonological representation* is the homophone (H) condition (Figure 1A) where phonological processing of visually presented words would be revealed by S=H<D. On the other hand, orthographic representation would be revealed by S<H=D (Figure 1 B).

In the pSTG of the TPC, our group of adults with poor reading skills did not show full adaptation for the phonological condition, because we did not find S=H<D. While H was less than D, H did not equal S (Figure 2), demonstrating some responsivity to phonology but at the time no strong selectivity. Specifically, a one-way repeated-measures ANOVA revealed that there was a significant main effect of condition on the amount of adaptation ($F(2, 24) = 20.658$, $p < .0001$, $\eta_{p^2}=.633$ ). Post-hoc pairwise comparisons revealed that while H was significantly lower than D ($p= 0.016$), adaptation was not complete since H was significantly higher than S ($p=0.033$). There was a significant difference between S and D ($p< 0.0001$). Selective phonological tuning would have been demonstrated if S and H had not been significantly different from each other, as demonstrated in previous work with typical readers (Glezer et al., 2016). This suggests that adults with unexpectedly poor reading skills do not have finely tuned neuronal representations for phonology in response to visually-presented words in the TPC, although responsivity to phonological information was not entirely absent.

For the *pars opercularis* of the IFC, even though defined by a phonological localizer, the group did not show phonological sensitivity. Instead we found S<H=D, which indicates sensitivity to orthographic processing. Specifically, one-way repeated-measures ANOVA (with Greenhouse-Geisser correction applied) revealed that there was a significant main effect of condition on the amount of adaptation ($F(1.228, 13.504) = 9.283$, $p = .007$, $\eta_{p^2}=.45$. Post-hoc pairwise comparisons revealed that H was not significantly lower than D ($p= 0.078$), and H was significantly higher than S ($p= 0.034$), and there was a significant difference between S and D ($p= 0.024$).

In the VWFA of the OTC, our group showed the pattern illustrative of orthographic tuning, S<H=D. Specifically, a one-way repeated-measures ANOVA revealed that there was a significant main effect of condition on the amount of adaptation ($F(2, 24) = 23.328$, $p < .0001$, $\eta_{p^2}=.660$ ). Post hoc pairwise comparisons showed that S was significantly lower than H and DIFF (p<0.0001) but H and DIFF were not significantly different (p= 1.0, see Figure 2). These results reveal full orthographic selectivity in our adult poor readers in the VWFA.

Together these results show that adults with unexpectedly poor reading skills the pSTG in TPC does not show full adaptation, suggesting weak phonological selectivity in this region. On the other hand, the VWFA in OTC, and the IFC showed selectivity to orthography.

## 4 Discussion

The goal of this study was to examine the phonological and orthographic selectivity in key areas that subserve reading – left TPC, IFC and OTC– in adults with unexpectedly poor reading skills. We employed fMRI-RA to examine the tuning of (i) left TPC and IFC to phonological and (ii) left OTC to orthographic properties of visually presented words. We found that there was not full adaptation in the pSTG of the TPC to phonological features of written words: while there was responsivity (H<D) it failed to show selectively (S did not equal H). The *pars opercularis* of the IFC showed no tuning to phonology and, instead, showed selectivity to orthographic processing (as previously shown in adult typical readers). There was also strong selectivity in the VWFA of the OTC to orthographic properties. We conclude that in adult poor readers tuning in pSTG is atypical, while tuning in the VWFA follows normal conventions for orthographic processing, much as the phonological deficit hypothesis and the brain-based model of reading and reading disability by Pugh and colleagues (2001) would have predicted.

### 4.1 Temporo-Parietal Cortex (TPC)

The neural bases of reading have been widely documented (Jobard et al., 2003; Martin et al., 2015; Turkeltaub et al., 2002) and studies have also examined the constituent components of reading, such as phonology, orthography and semantics (Pugh et al., 1996). Specifically, phonological tasks in response to visually presented words engage pSTG (Wernicke's area) as well as angular gyrus (AG) and supramarginal gyrus (SMG) in the inferior parietal lobule, often referred to collectively as the TPC in the dorsal stream (Binder, 2017; Price, 2012). There has also been a long-held view that dyslexia is due to dysfunction of TPC in the left hemisphere (Pugh et al., 2001). TPC, has been shown to be underactivated in several studies of dyslexia as best illustrated by recent meta-analyses (Linkersdörfer et al.; Maisog et al., 2008; Richlan et al., 2009). It is thought that this underactivity is related to dyslexics' poor phonological processing, impeding their ability to apply sound-correspondence-rules for decoding of words, eventually hampering with the process of building a sight word vocabulary in the VWFA, that in normal readers ultimately facilitates fluent reading (Pugh et al., 2001).

While the TPC dysfunction is currently the most influential model, there are several other theories that suggest a phonological deficit and the TPC are not necessarily at the core of the reading problems. Recently, a paper by Richlan (Richlan, 2012) has advanced a model where the OTC and not the TPC is the primary cause of reading deficits in dyslexia and TPC dysfunction follows (see also Kronbichler and Kronbichler, 2018). Boets and colleagues (Boets et al., 2013) also argued that phonetic representations in TPC are not affected *per se* in adults with dyslexia, but instead, they assert that there are abnormal connections between superior temporal and frontal areas (via the arcuate fasciculus), revisiting the idea of a "disconnection syndrome" in dyslexia between parietal and frontal regions (Paulesu et al., 1996). While our findings may seem at odds with Boets et al., (2013), there are several potential reasons for the apparent conflicting results. Firstly, their study used speech stimuli, while ours used visually-presented words. Secondly, the STG region Boets et al. examined was anterior to the region reported here. Because of this, it is difficult to directly compare the results as they represent different modalities and different brain areas. At the same time, when taken together, the results may indicate that there is intact neural representations to speech sounds in an anterior region of the STG in dyslexia, yet at the same time, there is coarser neural tuning to the phonology of written words in a posterior STG region. Further, for phonological information to be extracted from written words, the word has to be decoded and then its pronunciation retrieved. It is possible that this is less efficient in dyslexia. Future studies will need to examine this posterior STG region in dyslexia using auditorily-presented phonological information.

Several other studies have focused more directly on examining cross-modal integration of information in dyslexia. Work by Booth and colleagues has shown that posterior superior temporal sulcus (STS) is involved in cross-modal integration (Gullick and Booth, 2014), and, together with the fusiform gyrus (FG), differs in dyslexia. Specifically, there is a relationship between cross-modal integration in the FG and ability to perform a phonological awareness task in controls but not dyslexics (McNorgan et al., 2013). Similarly the work by Blau (Blau et al., 2009) has emphasized the importance of the integration or conversion of orthography to phonology in typical readers and its failure in dyslexia. While this idea aligns with some aspects of the Pugh model, which attributes “mapping the visual percepts of print onto the phonological structures of language,” the Pugh model assigns this function to the TPC (Pugh et al., 2001), as have others (Benson, 1994; Black & Behrmann, 1994; Geschwind, 1965). In this context the question arises whether this particular area of the TPC shows any involvement in orthographic processing? We do know from our prior study (Glezer et al., 2016) that typical readers show strong phonological tuning in TPC with no sensitivity to orthography. In our group of poor readers, however, we did not find strong tuning to either phonology or orthography in TPC.

In accordance with the Pugh model, our results suggest the mapping of phonological information in people with poor reading is imprecise: written homophones are mapped onto similar but not identical phonological representations in the TPC, causing partial rather than full adaptation. This confirms the hypothesis that poor readers show weak selectivity for phonological coding and fits well with prior work demonstrating differences in left pSTG in dyslexic adults (Richlan et al., 2011; Shaywitz et al., 1998) and the overall theory of a phonological deficit and dorsal pathway impairment in dyslexia (Pugh et al., 2001). Yet, here we are able to demonstrate directly that there is a deficit specific to phonology of written words without concern for contamination by orthographic aspects of the stimulus.

The pSTG has specifically been of prior interest in adults with dyslexia (Richlan et al., 2011; Shaywitz et al., 1998). Notably, the left pSTG ROI discussed in the current study is the same region shown through meta-analytical studies to be underactivated in adults with dyslexia (Richlan et al., 2011) and to contain less gray mater volume in dyslexia (Richlan et al., 2013). The nature of these differences in dyslexia has been debated, as they could be causal in nature (Pugh et al., 2001), secondary to a primary OTC dysfunction (Richlan, 2012), or the consequence of not learning to read (Krafnick et al., 2014). The present study does not entirely disambiguate a primary deficit from the consequence of not learning to read. This could be addressed more definitively in future studies employing a reading level-match or longitudinal designs in children. Nevertheless, our finding of compromised STG is consistent with the Pugh model.

## 4.2 Inferior Frontal Cortex (IFC)

The IFC has long been described as having a role in phonological assembly as well as articulation of phonological representation (Démonet et al., 1992; Poldrack et al., 1999; Tan et al., 2005). Specifically, in studies of typical readers this region has been noted for being relatively more activated during low-frequency words and pseudowords than high-frequency words (Fiez and Petersen, 1998). In addition, it has been indicated in articulatory recoding of print (Sandak et al., 2004). Our participants showed no sensitivity to the phonological features of the word in the IFC, but rather to orthographic features. It should be noted however, that in our prior study, typical adult readers did not show sensitivity here to phonological processing either, and also showed orthographic tuning here instead (Glezer et al., 2016).

Studies of the role of the IFC in dyslexia have been conflicting, with some studies reporting hypoactivation in dyslexics relative to controls (Eden et al., 2004) and others hyperactivation (Shaywitz et al., 1998) or no differences (Paulesu, 2001; Paulesu et al., 1996). Recent meta-analyses of functional brain imaging studies in dyslexia have noted the inconsistency of the IFC (Linkersdörfer et al., 2012; Maisog et al., 2008; Richlan et al., 2011). Notably, Richlan and colleagues performed separate meta-analyses of dyslexic children and adults and found left IFC hypoactivation in adults but not in children, suggesting that group differences here occur as a function of age/experience.

## 4.3 Occipito-Temporal Cortex

The strong focus on phonological skills in behavioral research has engendered tremendous interest in the function of dorsal regions of the left hemisphere around the TPC in typical readers and those with dyslexia. However, more recently, regions within the OTC ventral stream have emerged with surprising consistency in studies of dyslexia and have received increasing attention, specifically the

VWFA (Pugh et al., 2000, 2001; Sandak et al., 2004; Shaywitz et al., 2002, 1998; van der Mark et al., 2009), which is altered in dyslexia independent of age (Richlan et al., 2011), socioeconomic status (Monzalvo et al., 2012) and language (Paulesu, 2001). Our results show that poor readers demonstrate normal selectivity in the VWFA for real word stimuli. It seems that as in normal readers (Glezer et al., 2009), the VWFA is highly sensitive to orthographic information and functions as an orthographic lexicon following experience with words that have shaped the tuning of this region.

Our participants were high functioning adults with full IQ scores on average in the 90th percentile and reading on average in the 24th percentile. Future studies will need to examine if these findings generalize to those adults with cognitive performance in the lower range and more severe reading difficulties. It is unlikely, however, that the normal tuning to orthography in the VWFA can be explained by anything having to do with our specific sample. Our group had deficits in several domains, including real and pseudoword reading as well as poor phonological decoding skills, and these dovetail with the poor phonological tuning observed in the TPC. Taken together, our findings suggest that in dyslexia phonological tuning in TPC is adversely affected while orthographic tuning in the OTC appears to be preserved.

## 5 Conclusion

In the current study, we used fMRI-RA in adults with unexpectedly poor reading skills to examine selectivity of phonological (as accessed by written word reading) and orthographic representations in TPC, IFC and OTC. We tested the hypothesis that the weaknesses in phonological coding exhibited in people with reading difficulties are attributed to dysfunction of TPC and IFC, specifically to weak selectivity for phonological information for visually-presented (written) words. At the same time, we asked whether poor reading is associated with poor representation of written word forms in the OTC (i.e., weak selectivity to orthographic representation of words). Our findings show disrupted tuning to phonological features as accessed from written words in the pSTG of the TPC, but normal tuning to orthographic features of visually-presented words in the VWFA of the OTC. The IFG did not show tuning to phonology, rather it showed tuning to orthography, consistent with typically reading adults in similar fMRI adaptation experiments. Our results support the idea that phonological processing during written word reading and the underlying brain region that performs this task (pSTG), is compromised in poor readers.

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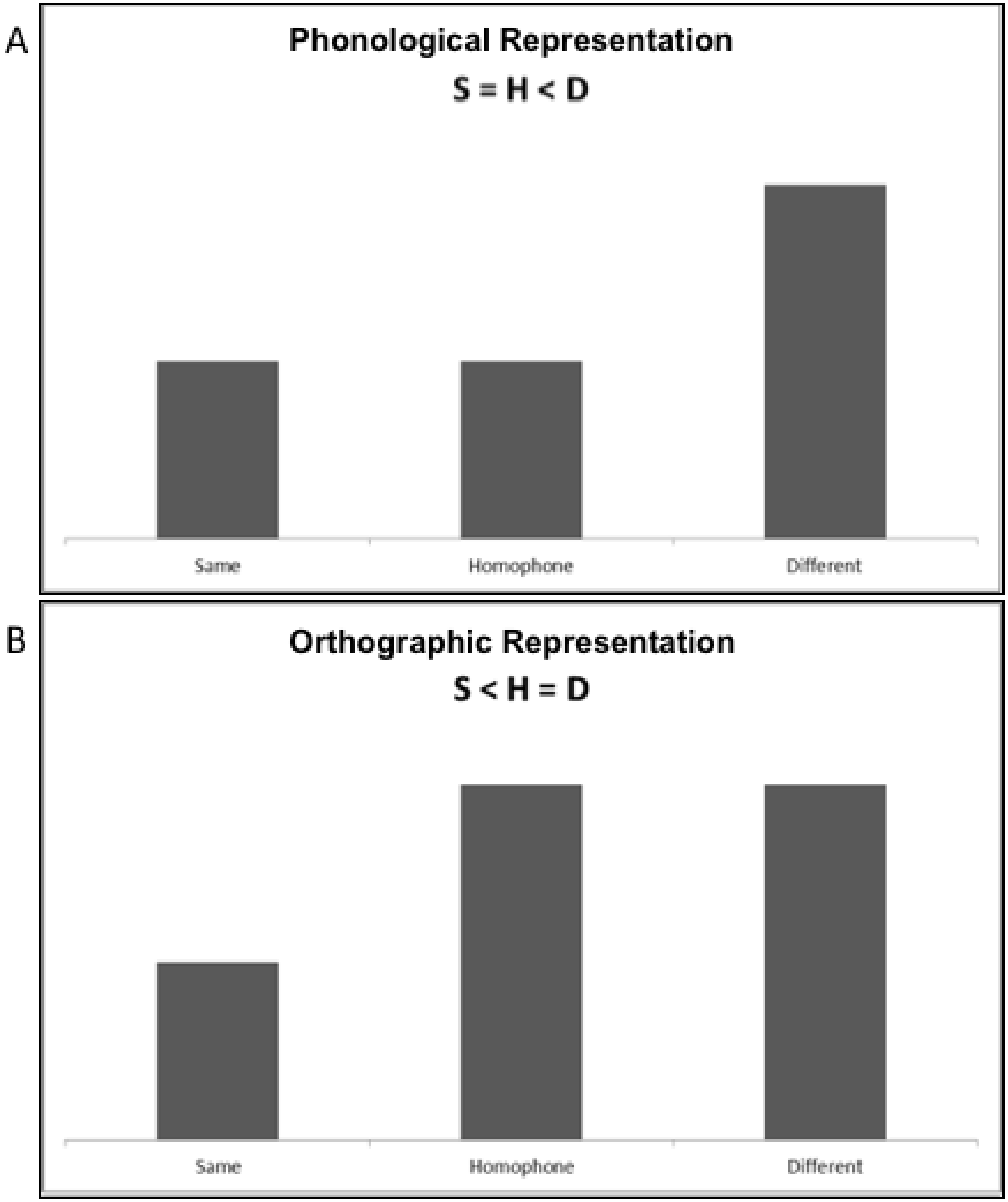
## Figure Legends

**Figure 1**. Predictions for fMRI-RA response to the different conditions for (A) phonological and (B) orthographic representations.

**Figure 2**. Percent signal change in the individually-defined TPC, and IFC and VWFA ROIs. Error bars represent within-subject SEM. *$p < 0.05$, ***$p < 0.0001$.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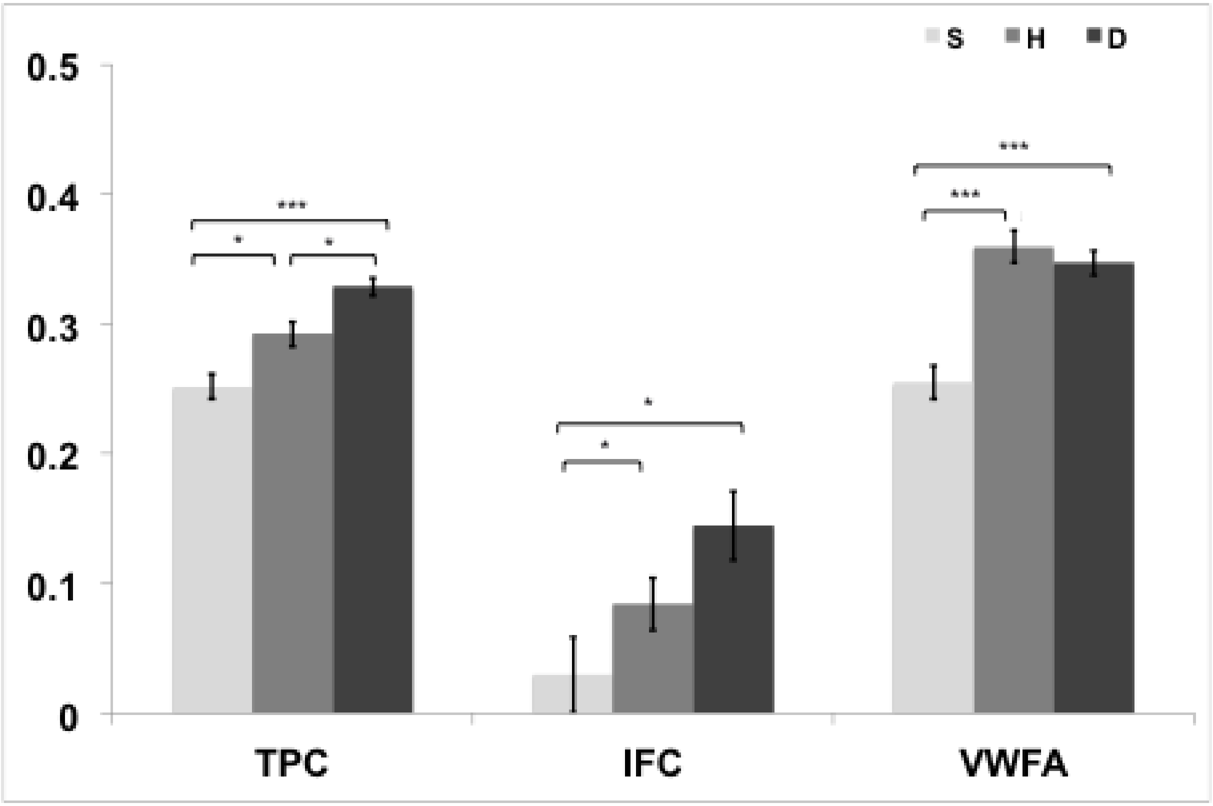

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TPC
IFC
VWFA

|  | *n=13 (7M, 6 F)* |  |  |
|---|---|---|---|
|  | Mean | SD | Range |
| **Age (yrs.)** | 23.8 | 4.5 | 18-32 |
| **Intelligence Quotient** |  |  |  |
| Full IQ | 119.3 | 10.3 | 100-136 |
| Verbal IQ | 116.5 | 12.9 | 93-139 |
| Performance IQ | 118.1 | 8.2 | 106-128 |
| **Single Word Reading** |  |  |  |
| Real Words | 89.9 | 12.4 | 71-113 |
| Pseudowords | 89.8 | 12.0 | 70-115 |
| **Phonological Processing** |  |  |  |
| Sound Elision | 95.4 | 13.1 | 70-110 |
| Rapid Naming | 86.4 | 11.3 | 67-106 |
| Digit Span | 97.3 | 14.8 | 75-115 |

***Table 1.*** *Behavioral scores. All are standardized scores, with 100 representing the average and 15 points representing one standard deviation.*