

FUNCTIONAL AND STRUCTURAL NEURAL CONTRIBUTIONS
TO SKILLED WORD READING

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By

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ABSTRACT

Reading is an essential skill in our everyday lives and individuals are required to process, understand, and respond to textual information at an increasingly rapid rate in order to be active participants in society. The role of spatial attention in reading has recently been emphasized, whereby better spatial attentional skills are associated with stronger reading skills, and spatial attentional training has a large impact on improving reading ability. However, the neuroanatomical correlates of reading and attention have primarily been studied in isolation. Further, there has recently been a shift to understanding how underlying white matter connectivity networks contribute to cognitive processes. However, much of the research focusing on the intersection of reading and spatial attention, as well as underlying white matter connectivity, has focused primarily on individuals with reading impairments. This thesis will focus on unraveling the neural relationship between spatial attention and reading, and how structural connectivity accounts for functional activation in reading tasks. In Chapter 2, we examine the neural relationship between lexical and sublexical reading with voluntary and reflexive spatial attention. In Experiments 1 and 2, participants performed overt reading of both lexical exception word (EW; words with inconsistent spelling-to-sound correspondences, e.g., ‘pint’) and sublexical pseudohomophone (PH; non-words that when decoded phonetically sound like real words, e.g., ‘pynt’) reading tasks, as well as tasks involving either voluntary attention (Experiment 1) or reflexive attention (Experiment 2) during functional magnetic resonance imaging (fMRI). Experiment 3 used hybrid combined reading attention tasks during fMRI, whereby the spatial attentional cue preceded presentation of the EW or PH stimulus. Overall, the results from these experiments showed that sublexical reading was more strongly associated with brain regions involved in voluntary attention, whereas lexical reading was more strongly associated with brain regions involved in reflexive attention. Thus, Experiments 1, 2 and 3 lend support to the idea that lexical and sublexical reading strategies are differentially associated with these two types of attention. In Chapter 3, we examined the extent to which fine-grained underlying white matter connectivity is able to predict fMRI activation during both lexical reading and phonetic decoding in skilled readers. Experiment 4 employed EW and PH reading and a computational modeling technique to model the relationship between whole-brain structural DTI connectivity and task-based fMRI activation during lexical and sublexical reading. Results from this study showed that brain activation during both lexical and sublexical reading in skilled

readers can be accurately predicted using DTI connectivity, specifically in known reading and language areas, as well as important spatial attentional areas. Thus, this research suggests that there is a fine-grained relationship between skilled reading and extrinsic brain connectivity, showing that functional organization of reading and language can be determined (at least in part) by structural connectivity patterns. Together, the studies presented in this thesis provide valuable insight into functional and structural contributions to word reading that may serve as biomarkers of skilled reading, which in turn may have important implications for understanding and remediating reading impairments.

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LIST OF ABBREVIATIONS

AE	Absolute error
AF	Arcuate fasciculus
DTI	Diffusion tensor imaging
EEG	Electroencephalography
EPI	Echo-planar imaging
EW	Exception word
FEAT	FMRI Expert Analysis Tool
FEF	Frontal eye field
FLAME	FMRIB's Local Analysis of Mixed Effects
fMRI	Functional magnetic resonance imaging
FOV	Field of view
IFG	Inferior frontal gyrus
IFOF	Inferior fronto-occipital fasciculus
ILF	Inferior longitudinal fasciculus
IPL	Inferior parietal lobule
IPS	Intraparietal sulcus
LOC	Lateral occipital complex
LOOCV	Leave-one-out cross-validation
MAE	Mean absolute error
MNI	Montreal Neurological Institute
MPRAGE	Magnetization prepared rapid acquisition gradient echo
MTG	Middle temporal gyrus
PH	Pseudohomophone
RAN	Rapid automatized naming

ROI	Region of interest
SLF	Superior longitudinal fasciculus
SMA	Supplementary motor area
SPL	Superior parietal lobule
STG	Superior temporal gyrus
TPJ	Temporoparietal junction
UF	Uncinate fasciculus
vOT	Ventral occipitotemporal region
VWFA	Visual word form area

LIST OF APPENDICES

Appendix A: Stimuli from Experiments 1, 2, and 3

Appendix B: Stimuli from Experiment 4

Appendix C: Actual versus predicted activation for all participants

CHAPTER 1

AN INTRODUCTION TO READING AND ATTENTION

Portions of this chapter have been previously published or submitted for publication and redundant information has been removed. I was involved in every aspect of the research process for each project and made a substantial individual contribution to each of these works that merits their inclusion in this dissertation.

Ekstrand, C., Neudorf, J., Gould, L., Mickleborough, M., & Borowsky, R. (2019). Where words and space collide: The overlapping neural activation of lexical and sublexical reading with voluntary and reflexive spatial attention. *Brain Research*, 1706, 1-12. © 2018 Elsevier B.V. All rights reserved.

I contributed to this work in the following ways: Conceived the presented idea, developed the theory and hypotheses, programmed the experiment, carried out the experiments (including running the fMRI participants), analyzed the data, interpreted the results, drafted the manuscript and submitted it for publication, and performed any of the required revisions prior to publication.

Ekstrand, C., Neudorf, J., Kress, S., & Borowsky, R. (2019). How words and space collide: Lexical and sublexical reading are reliant on separable reflexive and voluntary attention regions in hybrid tasks. Under revision at *Cortex*.

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Reading is an essential skill in our everyday lives and individuals must be able to understand, process, and respond to textual information (e.g., books, magazines, digital media, navigational signage, etc.) at a rapid rate in order to be active participants in society. Previous research has indicated that the average person is exposed to 100 000 words (equivalent to 34 gigabytes of uncompressed textual information) every day, both in print and digitally (Bohn & Short, 2012). This statistic has undoubtedly increased, as it has recently been estimated that the average person spends over 11 hours a day interacting with the media, for example, through the use of smartphones, the internet, television, videogames, and print (The Nielsen Total Audience Report, 2018). Properly parsing textual information involves a complex process of visual scanning, decoding, attentional shifting, and inhibition of irrelevant stimuli (Facoetti et al., 2000), thus requiring many different cognitive processes to be effective, including spatial attention. However, the Canadian Council on Learning (2008) reported that approximately 48% of Canadian adults have inadequate reading skills (e.g., an inability to read a package label to determine the correct amount of medicine to give a child). Impaired reading is associated with several negative outcomes, including decreased employment, poorer health outcomes, lower civic participation and community engagement, and has also been linked to overall economic decline. Therefore, it is essential to understand the behavioural and biological cognitive mechanisms that potentiate and mediate skilled reading.

1.1 Behavioural Evidence for a Relationship between Spatial Attention and Reading

While the neural mechanisms of reading and attention have long been investigated in isolation, recent behavioral research suggests that they may interact during cognitive processing. Perhaps the strongest evidence for a role of visuospatial attention in word reading comes from studies examining dyslexia. In reading development, spatial attention is thought to be integral for establishing a functional reading system (Grainger, Dufau, & Ziegler, 2016), and early impairments to visuospatial attention can impair reading development. For example, some children with developmental dyslexia show deficits in low-level visual processing, including

visual crowding (i.e., increased difficulty identifying a stimulus when it is surrounded by other stimuli). Martelli, Filippo, Spinelli, and Zoccolotti (2009) examined the impact of stimulus contrast, letter spacing, and print size on reading in individuals with dyslexia and controls. Their results indicated that dyslexics had greater difficulty identifying long words at lower contrasts, required larger letter spacing to effectively parse stimuli, and needed larger text size to read than controls. These results suggest that individuals with dyslexia exhibit visual crowding deficits that are consistent with impairments in visuospatial attention (see also Pelli & Tillman, 2008, Whitney & Levi, 2011, and Gori & Facoetti, 2015 for reviews).

Further, there is evidence that individuals with dyslexia also show visual attentional shifting deficits. For example, Bosse and Valdois (2009) performed a cross-sectional study on a large cohort of children in grades 1, 3, and 5. The children performed reading tasks, as well as phoneme awareness (i.e., the ability to detect the sounds that make up words) and visual attention tasks. Their results indicated that spatial attention is essential to early word reading, particularly for irregular words (i.e., words that do not follow regular spelling-to-sound mappings), and that it may have a long-term influence on the acquisition of orthographic knowledge. Similarly, Franceschini, Gori, Ruffino, Pedrolli, and Facoetti (2012) performed a three-year longitudinal study examining attentional orienting ability of children prior to, and following, reading acquisition. Specifically, the children performed visual search and spatial cuing tasks at kindergarten age, grade 1, and grade 2, as well as tasks assessing reading development at grades 1 and 2. Results from this study indicated that subsequent poor readers showed deficits in serial search and spatial cuing at pre-reading age. Thus, early spatial attentional deficits were shown to be associated with impaired reading acquisition (see also Hari & Renvall, 2001; Valdois, Bosse, & Tainturier, 2004; Vidyasagar & Pammer, 2010, for reviews).

Further, research has suggested that visuospatial attentional training has a strong impact on reading ability. Franceschini et al. (2013) had Italian children with dyslexia play twelve hours of action videogames (games where the participant is required to navigate a complex, three-dimensional space) over a nine-day period. As action videogames have been shown to increase visuospatial attentional resources (e.g., Green & Bavelier, 2003), the researchers hypothesized that the increase in visuospatial attentional resources achieved from playing action videogames would improve reading ability. Their results showed that nine 80-minute sessions of videogame play led to improvements in the dyslexic childrens reading ability equivalent to one year of

spontaneous reading development at their current trajectory. However, unlike English, the Italian language has a shallow orthographic structure with highly consistent spelling to sound correspondence, and thus it was unclear whether this finding extends to languages with deep orthographies (in which the spelling to sound mappings are not consistent, e.g., English). Thus, Franceschini et al. (2017) performed a similar study with English speaking children. Results from this research showed that English-speaking children with dyslexia had improvements in word list reading and phonological decoding speed (i.e., pronounceable non-word list reading) following action videogame training, therefore supporting the conclusion that increasing spatial attentional skill enhances reading ability.

More contentiously, results from adults with reading disability have shown mixed evidence for a directional relationship between spatial attention and reading. For example, Collis, Kohnen, and Kinoshita (2013) illustrate cases of adults with reading impairment that also showed corresponding deficits in visuospatial attention. In addition, Moores, Cassim, and Talcott (2011) had adult participants with and without dyslexia identify the orientation of a target in a rapidly presented array of numbers. Results from this study indicated that the individuals with dyslexia showed a disproportionate amount of errors compared to controls: i) when the stimuli were in close proximity to one another, ii) when the number of stimuli increased, and iii) when external cues modulated attention. This suggests that, similar to children, adults with dyslexia are susceptible to visual crowding deficits, and that they use attentional cues less effectively than non-dyslexic readers. Further, evidence from Antzaka et al. (2017) extended the findings of Franceschini et al. (2013, 2017) to adult dyslexic readers by showing that action videogames are associated with improved reading ability. The researchers examined two groups of dyslexic adults (matched on age and text reading ability), one group with participants who were frequent action videogame players, and the other who were not. Their results indicated that the action videogame group had better spatial attentional skills and outperformed the non-action videogame group on a challenging reading task (i.e., reading briefly presented non-words). This research supports the conclusion that spatial attentional deficits play a role in reading impairments, even in adult readers.

In contrast, some research has found evidence for enhanced non-language visuospatial processing in adults with dyslexia. For example, Schneps, Brockmole, Sonnert, and Pomplun (2012) used a contextual cuing paradigm (whereby participants are required to search a visual

display for a hidden target, typically eliciting search benefits for previously presented scenes) to investigate spatial learning ability in dyslexic adults. Their results indicated that when scenes were not visually degraded, there were no reaction time differences between controls and individuals with dyslexia. However, when the displays were visually degraded (i.e., when a low-pass filter was applied) individuals with dyslexia showed *enhanced* processing ability compared to normal controls. The researchers suggest that this finding is due to compensatory mechanisms of parafoveal vision in dyslexic individuals due to their impairment in foveal vision (e.g., Silva-Pereyra et al., 2010). Further, Diehl et al. (2014) examined mental rotation (i.e., deciding whether two shapes are rotated versions of the same shape, or different) and identification of impossible figures (both measures of visuospatial abilities) in adolescents with and without dyslexia. Their results showed that dyslexic individuals have a processing advantage for these stimuli compared to controls, once again supporting the conclusion that some individuals with dyslexia show enhanced visuospatial processing. The discrepancy between impaired and enhanced visuospatial attentional abilities in adults with dyslexia highlights the importance of distinguishing levels of spatial attention (e.g., lower-level cuing paradigms versus higher-level mental rotation paradigms) when examining the relationship between reading ability and spatial attention, whereby low-level spatial attention processes appear to be impaired, with intact (or enhanced) higher-level spatial attentional processing.

Behavioural data from skilled readers has also found mixed evidence for a relationship between visuospatial attention and reading, depending on the task demands. For example, when using word frequency effects as a measure of word recognition processes, McCann, Folk, and Johnston (1992) concluded that reading and attentional processes operate independently of one another. Participants performed a modified lexical cuing task in which the stimuli were either high-frequency (i.e., words that occur frequently in written material), low-frequency (i.e., words that occur infrequently in written material), or non-words that were presented in either the expected spatial location (i.e., validly cued trials) or an unexpected spatial location (i.e., invalidly cued trials). Their results indicated that there was no interaction between word frequency and spatial attention. In contrast, using a similar task, Montani, Facoetti, and Zorzi (2014) examined processing of high-frequency, low-frequency, and non-words in a spatial attentional cuing task. Their results showed that processing of low-frequency words and non-words was impaired when attention was cued away from the orthographic target, and enhanced when attention was cued

towards the target. Conversely, high-frequency words showed processing enhancements when the spatial cue was invalid. This suggests that lexical reading of high-frequency words relies on a large scope of attention, whereas sublexical reading of non-words relies on controlled attention to the target. Further, when semantic relatedness (rather than word frequency) was used as the reading manipulation, Stolz and McCann (2000) did find evidence of an interaction between spatial attention and semantic relatedness. As semantic processes are thought to have an earlier effect than word frequency (e.g., Borowsky & Besner, 1993, 2006), the authors concluded that the interaction between spatial attention and reading occurs relatively early in processing.

Similarly, Ekstrand, Gould, Mickleborough, Lorentz, and Borowsky (2016) found evidence of an early interaction of reading and spatial attention, specifically at the level of lexical access. Participants performed an attentionally cued lexical decision task (whereby a ‘W’ or ‘N’ cue was presented on either the left or right of a central fixation cross) and were asked to expect a real word when a ‘W’ cue was presented and a non-word when an ‘N’ cue was presented. Following the cue, either an exception word (EW; words that cannot be decoded phonetically to be properly pronounced, e.g., ‘yacht’) or a pseudohomophone (PH; non-words that when decoded phonetically sound like real words, e.g., ‘yawt’) was presented on either the congruent or incongruent side to the cue. The results showed an interaction between lexical and spatial cuing, such that lexical cuing effects were larger when spatial location was validly cued. This research provides evidence of a behavioral interaction between reading and attention. While the above work suggests that there is a relationship between reading and spatial attention, the neural correlates of each have been primarily studied in isolation. However, both reading and attentional processes have been shown to bifurcate along the dorsal and ventral visual processing streams (Martin, Shurz, Kronbichler, & Richlan, 2015).

1.2 The Dorsal and Ventral Visual Processing Streams

Early primate research from Ungerleider and Mishkin (1982) established the existence of two cortical processing pathways, namely the dorsal and ventral streams, that have since been characterized in humans (e.g., Ungerleider & Haxby, 1994; Goodale & Milner, 1992; see Figure 1.1). The ventral visual stream extends from the primary visual cortex into the inferior temporal cortex and has been shown to be involved in object processing and recognition, and is often referred to as the “what” stream. Functional specialization of this stream includes colour processing, pattern recognition, object recognition, face and place processing, and, of particular

interest to the current work, word reading. Clinical case studies have supported early primate work and have shown that damage to the ventral stream leads to deficits in object, face, and colour processing (see Ungerleider & Haxby, 1994 for a review). Perhaps the most compelling evidence of the dorsal/ventral stream distinction comes from Goodale and Milner's (1992) patient, D.F..

Patient D.F. suffered carbon monoxide poisoning that damaged her ventral stream, particularly the middle occipital gyrus (an area strongly associated with object recognition). This damage led to the inability of D. F. to construct visual percepts of objects, a condition known as visual form agnosia. However, D. F. maintained the ability to use object size and orientation information to control visually guided grasping movements. Thus, although D. F. was essentially blind to the form of the objects, she was still able to interact with objects in the surrounding environment, providing evidence for a neural dissociation between visual processing for perception versus action. The ventral stream has also been shown to play an important role in speech and language, and is involved in decoding complex speech sounds and linking them to meaning (see Rauschecker, 2012 for a review). Saur et al. (2008) used functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) to identify language-processing pathways in humans. FMRI uses differences in the magnetic properties of oxygenated and deoxygenated blood to infer which regions of the brain are active during certain experimental conditions. DTI capitalizes on the diffusion properties of water in the brain, whereby water diffuses more isotropically (i.e., in any direction) in cerebrospinal fluid and grey matter, but more anisotropically (i.e., in a specific direction) parallel to large white matter tracts in the brain. Their results indicated that when participants listened to normal sentences compared to pseudoword sentences, there was greater activation in lexical-semantic processing areas (i.e., the middle and inferior temporal cortex, and ventrolateral prefrontal cortex), suggesting that the ventral stream is involved in higher-level sentence comprehension.

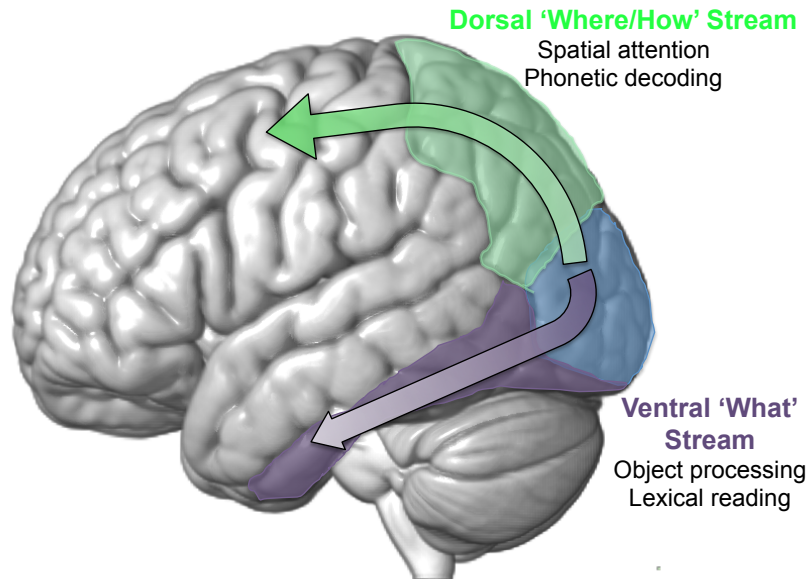


Figure 1.1: The dorsal and ventral stream distinction. The ventral ‘what’ stream (shown in purple) extends from the occipital lobe into the inferior temporal cortex and specializes in object processing, as well as lexical reading. The dorsal ‘where/how’ stream (shown in green) extends from the occipital lobe into the parietal and frontal cortices and specializes in spatial attention, object directed actions, as well as phonetic decoding. Adapted from Goodale and Milner (1995).

In contrast, the dorsal visual processing stream extends from the primary visual cortex into the posterior parietal cortex, and was originally implicated in spatial localization (Ungerleider & Mishkin, 1982), and thus is referred to as the “where” stream. Milner and Goodale (1995) extended this distinction to include the control of visually guided actions, thus referring to the dorsal stream as the “how” stream. This was based primarily on the findings from patient D. F., who showed no deficits in visually guided actions towards objects, despite the inability to identify the objects they were interacting with. Further, case studies where patients exhibit damage to their parietal lobe show deficits in visuomotor control and visually guided actions, with little or no impairments to visual perception (see Milner & Goodale, 1995). The dorsal stream has also been implicated in eye movements, particularly saccadic movements, which recruit the intraparietal sulcus (IPS) and superior parietal lobule (SPL), and is therefore critically involved in attentional processes (see Culham & Valyear, 2006 for a review). There is also evidence that the dorsal stream may be separated into two functional divisions, one that

extends from the occipital cortex into the superior parietal lobule thought to be involved in action control, and another that extends from the occipital cortex into the inferior parietal lobule that is thought to be involved in action understanding, as well as space perception (Rizzolatti & Matelli, 2003). The dorsal stream is also implicated in speech and language, and is thought to play a role in speech production and phoneme categorization during speech processing (see Rauschecker, 2012 for a review). In the combined fMRI and DTI study from Saur et al. (2008) discussed previously, listening to pseudowords compared to real words was shown to activate left temporal (i.e., the superior temporal gyrus, implicated in sublexical phonological processing during speech perception) and frontal areas (i.e., the prefrontal cortex and premotor areas, implicated in phonological processing related to speech preparation), highlighting the role of the dorsal stream in mapping sound to articulatory processes during language processing.

The dorsal and ventral streams have also been shown to interact at various stages of processing. In the visual object-processing domain, Mahon, Kumar, and Almeida (2013) used fMRI to examine tool-selective areas in the dorsal stream parietal cortex. Pictures of tools were presented at either high-spatial frequency (i.e., the components of an image with many changes across visual space, providing information about image detail; to preferentially activate the ventral stream), or low spatial frequency (i.e., the components of an image with few changes across visual space, providing gross information about the image; to preferentially activate the dorsal stream). Results from this study indicated that there was a portion of the inferior parietal cortex that was responsive to tools presented at high-spatial frequencies, suggesting that information from the ventral stream (which is sensitive to high-spatial frequencies) interacts with tool-processing areas in the dorsal stream. In the domain of word reading, Laycock et al. (2009) used transcranial magnetic stimulation (a technique where magnetic pulses are directed at the brain in order to stimulate nerve cells) of the occipitotemporal junction to examine the time course of interaction of the dorsal and ventral streams during word reading. Participants performed a masked target identification task, whereby a word stimulus was briefly presented prior to a visual white noise mask. Following the mask, the target and two distractor words were presented and the participant was required to identify (using a keyboard press) which stimulus was the target word. Results from this study found disruption of word reading (as indexed by a decreased ability to identify the target stimulus) at two distinct time points, one at a very early time course (4 ms post stimulus) and another at a later time course (99 ms post stimulus). This

research provides evidence for feedforward and feedback interactions between the dorsal and ventral streams during orthographic processing.

1.3 Neuroimaging of Reading

In line with the dorsal and ventral processing stream distinction, a prominent model of word reading processes, known as the Dual-Route Cascade Model (Coltheart & Rastle, 1994; Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Coltheart, 2006; see also Wingerak, Neudorf, Gould, & Borowsky, 2017; Owen & Borowsky, 2003; Borowsky & Besner, 2006), describes the existence of two distinct, yet interactive, pathways for processing orthographic stimuli. The lexical route is involved in fast, whole-word recognition processes and is generally thought to recruit the ventral visual processing stream. In contrast, sublexical processing is subserved by the dorsal visual processing stream and is involved in “sounding out” orthographic stimuli through the application of spelling-to-sound correspondence rules. Behavioural support for dual-route models of reading comes from evidence that real-words are read faster than non-words, with high-frequency words being read faster than low frequency words, suggesting that separable pathways subserve lexical versus sublexical processing (see Coltheart, 2005 for a review). Further, both developmental and acquired forms of phonological and surface dyslexia show behaviours that also support their separation (see Sprenger-Charolles, Siegel, Jimenez, & Ziegler, 2011 for a review).

This dorsal/ventral distinction of reading processes is supported by neuroimaging evidence, whereby lexical (i.e., whole-word) reading has consistently been shown to activate a left ventral occipito-temporal circuit, and is comprised of the left fusiform, inferior temporal, and lateral extrastriate regions that make up the ‘visual word form area’ (VWFA; however the specificity of this region to word stimuli has been debated throughout the literature; see Dehaene & Cohen, 2011 and Price & Devlin, 2004) and thus this area is thought to be involved in fast and automatic visual-orthographic whole-word recognition (e.g., Glezer et al., 2009; Dehaene & Cohen, 2011; Stevens, Kravitz, Peng, Tessler, & Martin, 2017) and word/non-word differentiation (Baeck, Kravitz, Baker, & Op de Beeck, 2015). A meta-analysis of 36 studies by Taylor, Rastle, and Davis (2013) also identified several regions that show greater activation to words than to pronounceable pseudowords that included the middle temporal gyrus (MTG), angular gyrus and supramarginal gyrus (collectively the temporoparietal junction, TPJ), parahippocampal and fusiform gyri, posterior cingulum and precuneus, medial orbitofrontal

cortex, and the gyrus rectus (see also Price, 2012 and Carreiras, Armstrong, Perea, & Frost, 2014 for a comprehensive review). Further, Richardson, Seghier, Leff, Thomas, and Price (2011) used dynamic causal modeling (a statistical technique that models the relationship between activation of different brain regions) to further characterize the ventral reading network. Participants performed four tasks during fMRI: silent reading, viewing false-fonts, listening to real words, and listening to reversed words. Their results indicated that there are three ventral pathways that subserve reading, one from the inferior occipital cortex to the posterior superior temporal sulcus and ventral occipitotemporal cortex, another from the inferior occipital and ventral occipitotemporal cortex to the posterior temporal sulcus, and the last from the ventral occipitotemporal cortex and posterior superior temporal sulcus to the anterior superior temporal sulcus. These results support models of reading that posit lexical reading is reliant on the ventral stream.

Lexical reading processes can be promoted through reliance on holistic-word knowledge, whereby EWs can be used to optimize an individual's reliance on the ventral stream (e.g., Cummine, Dai, Borowsky, Gould, Rollans, & Boliek, 2015; Cummine et al., 2012; Borowsky et al., 2006, 2007). EWs represent an interesting class of stimuli, as they must be read as whole-words in order to be properly parsed, thus relying solely on lexical word-recognition processes without the contribution of phonological decoding. Recently, strong evidence for the role of the ventral stream in processing EWs has shown that the anterior temporal lobe is necessary for lexical reading (Ueno, Meteyard, Hoffman, & Murayama, 2018). Ueno et al. (2018) used repetitive transcranial magnetic stimulation to disengage the anterior temporal lobe of participants while they read EWs. Their results indicated that when the anterior temporal lobe was stimulated, participants made significantly more regularization errors (i.e., erroneously relying on spelling-to-sound correspondence to parse a word; e.g., reading *pint* to rhyme with *mint*).

In contrast, phonetic decoding has been shown to rely on a more dorsal network of cortical regions, specifically a left dorsal temporo-parietal circuit, which is composed of the posterior superior temporal gyrus (STG), the angular gyrus, and the supramarginal gyrus. In their meta-analysis, Taylor et al. (2013) found activation greater for pseudowords than words in the left inferior frontal gyrus (IFG), precentral gyrus, superior temporal pole, posterior fusiform gyrus and occipitotemporal cortex, supplementary motor area (SMA), left insula, left parietal

cortex, and right inferior parietal cortex. Further, the dynamic causal modeling study of Richardson et al. (2011) that was previously discussed highlights the importance of the posterior temporal sulcus in pseudoword reading, thus implicating this region in orthographic processes. However, the pseudowords utilized in these studies have unfamiliar phonological outputs in comparison to real words, and thus lack the depth of representation associated with real words. One way to overcome this is to use PHs, which encourage reliance on phonological processes in skilled readers (who tend to more commonly engage in lexical reading strategies) and thus allow for examination of phonetic decoding in the absence of holistic reading processes.

Neuroimaging evidence supports the idea that PHs activate a more dorsal system of brain regions. FMRI evidence from Borowsky, Cummine, Owen, Friesen, Shih, and Sarty (2006) examined the neural correlates of phonetic decoding using PHs and results from this study indicated that PH reading lead to greater activation in the dorsal stream compared to EW reading, particularly in the angular gyrus, supramarginal gyrus, inferior parietal lobule (IPL) and SPL, and the motor cortex (see also Borowsky et al., 2007). Further, Braun et al. (2015) showed that, in skilled readers, PHs elicit greater activation in the left inferior/superior frontal and middle temporal gyri, left insula, and left superior parietal lobule than pseudowords (pronounceable non-words, e.g., grob), suggesting that, unlike pseudowords, PHs recruit lexical semantic information (similar to their real-word counterparts). Therefore, PHs may provide the ideal stimuli for directly comparing the neural relationship between lexical and sublexical reading based on their identical phonological output as well as their semantic representations.

Subcortical regions have also been implicated in reading processes. Of particular interest, the putamen has been suggested to be involved in reading at the level of speech production (e.g., Price et al., 1994, 1996; Dietz, Jone, Gareau, Zeffiro, & Eden, 2005; Borowsky et al., 2006; Hernandez & Fiebach, 2006). Seghier and Price (2010) used dynamic causal modeling to examine the role of the putamen in lexical and sublexical overt reading in comparison to object naming and articulation in the absence of word/non-word stimuli. Their results indicated that the left putamen was functionally associated with the anterior occipitotemporal cortex and precentral gyrus during familiar word reading, suggesting that the putamen is involved in transferring information from visual recognition areas to articulatory regions. Further, Oberhuber et al. (2013) examined fMRI activation for words and pseudowords relative to picture and color naming and found that both words and pseudowords led to significantly greater activation in the left putamen.

Words were found to more strongly activate the anterior putamen, whereas pseudowords more strongly activated the posterior putamen, suggesting differential putamen involvement depending on stimulus type. Gould, Mickleborough, Ekstrand, Lorentz, and Borowsky (2017) also found evidence of putamen activation for both EWs and PHs in a rhythm primed reading experiment, whereby activation was bilateral and occurred for both types of stimuli, which is consistent with the putamen's role in other forms of rhythmic processing (e.g., Grahn & Brett, 2007; Riecker, Wildgruber, Dogil, Grodd, & Ackermann, 2002).

In summary, both lexical and sublexical reading rely on widespread networks of brain regions that include both cortical and subcortical sites. In general, lexical reading relies more strongly on brain regions in the ventral visual processing stream, extending from the primary visual areas into the inferior temporal cortex. Specifically, lexical reading is primarily subserved by ventral visual stream areas, including the left ventral occipitotemporal region (vOT), MTG, angular gyrus, parahippocampal and fusiform gyri, posterior cingulum and precuneus, medial orbitofrontal cortex, the gyrus rectus, and the putamen. Conversely, sublexical reading relies more strongly on brain regions in the dorsal visual processing stream, extending from primary visual areas into the parietal and frontal cortices. Specifically, sublexical reading relies on dorsal visual stream areas that include the IFG (bilateral), precentral gyrus, superior temporal pole, posterior fusiform gyrus and occipitotemporal cortex, SMA, left insula, left parietal cortex, right IPL, and also the putamen. Further, an inferior frontal circuit of brain regions is thought to underlie phonological output for both lexical and sublexical reading processes, and includes the inferior frontal and precentral gyrus. It is suggested that both the dorsal and ventral streams converge at the left IFG when reading aloud, the dorsal stream via the superior longitudinal fasciculus (SLF) and the ventral stream via the inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFOF), and the uncinate fasciculus (UF), which we discuss in the upcoming section.

1.4 White matter tracts in reading

Skilled reading relies on adequate communication between the lexical, sublexical, and phonological regions discussed previously, as well as visual encoding and motor output regions via a network of white matter pathways, which can be reconstructed using DTI. DTI studies have identified several key white matter pathways involved in skilled reading and reading development. The primary ventral white matter tracts that are involved in reading are the left ILF,

left UF, and the left IFOF. The left ILF (which connects the occipital and anterior temporal lobes; Catani, Jones, & Ffytche, 2005; see Figure 1.2 for DTI reconstruction of these major left hemisphere white matter tracts) has been primarily implicated in reading accuracy and fluency (e.g., Odegard, Farris, Ring, McColl, & Black, 2009; Lebel et al., 2013). Further, several studies suggest that the IFOF (which connects the ventral occipital lobe to the orbitofrontal cortex; Catani & Thiebaut de Schotten, 2008) may support semantic and orthographic involvement during reading (see Vandermosten, Boets, Wouters, & Ghesquière, 2012 for a review). Recently, Rollans and Cummine (2018) showed that the left IFOF can be functionally subdivided into ventral and dorsal components, whereby the dorsal IFOF is more involved in word reading tasks that require visual attention and response selection (e.g., go/no-go tasks), whereas the ventral IFOF is associated more strongly with simpler naming tasks. The UF (which connects the anterior temporal lobe to the orbitofrontal cortex) has been implicated in single word comprehension (Vigneau et al., 2006; see also Cummine et al., 2015, who showed that EW naming reaction time accounts for significant unique variance in UF fractional anisotropy over and above regular word naming), and may also mediate the transfer of dorsal and ventral stream information necessary for reading and language (Feng, Chen, Zhu, He, & Wang, 2015).



Figure 1.2. Major left hemisphere white matter pathways implicated in reading. The AF is represented in blue, ILF in pink, IFOF in yellow, and UF in red. Fiber tracts were reconstructed

with DSI Studio (<http://dsi-studio.labsolver.org>) using the HCP-1021 template (Yeh & Tseng, 2011).

The major white matter tract associated with the dorsal phonological pathway is the left SLF (including the arcuate fasciculus, AF; see Figure 1.2), and has been implicated in reading development (e.g., Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012), language processing and word reading accuracy (e.g., Catani & Mesulam, 2008; Frye et al., 2010; Hoeft et al., 2011), and reading fluency and phonological decoding (e.g., Lebel et al., 2013; see also Arrington, Kulesz, Juranek, Cirino, & Fletcher, 2017). The AF connects the temporoparietal area to the IFG (i.e., Broca's area), and has connectivity to the VWFA (see Catani et al., 2005). Further, resection of the posterior aspect of the AF (that descends into the left inferior temporal gyrus) has been shown to lead to global reading impairments (Zemmoura, Herbet, Moritz-Gasser, & Duffau, 2015), thus underscoring the importance of the AF in reading. Right hemisphere tracts have also been implicated in reading. Horowitz-Kraus, Wang, Plante, and Holland (2015) found evidence that the right ILF is associated with word recognition. In addition, the right AF was associated with reading comprehension.

Further, the right AF has been shown to play a role in processing semantic and prosodic components of language (Catani & Mesulam, 2008), as well as visuospatial attention (Thiebaut de Schotten et al., 2011). The importance of spatial attention in reading has recently been emphasized (e.g., Ekstrand et al., 2016; Franceschini et al., 2012; Franceschini et al., 2013), which leads to the hypothesis that white matter pathways crucial for spatial attention may play a critical role in reading. Indeed, Carter et al. (2009) found evidence that children with dyslexia showed abnormalities in the right SLF compared to controls, a tract strongly implicated in spatial attention (see Thiebaut de Schotten et al., 2011). Thus, reading appears to be subserved by a complex network of structural connectivity that spans both brain hemispheres, and may include white matter tracts involved in not only word reading (i.e., the AF, UF, ILF, and IFOF), but also tracts integral to spatial attention, which will be discussed in the next section.

1.5 Neuroimaging of Attention

The neural mechanisms of attention have also been thoroughly examined. Early work from Friedrich, Rafal, and Beck (1998) examined attentional deficits in patients with either TPJ or SPL lesions. Results from this study indicated that TPJ lesions resulted in deficits in reflexive

attentional orienting, whereas SPL lesions resulted in deficits in voluntary attentional orienting. An influential review by Corbetta & Shulman (2002) highlights partially segregated networks of brain areas that perform differential attentional functions (see also Hopfinger, Buonocore, & Mangun, 2000; Kelley, Serences, Giesbrecht, & Yantis, 2007; see Figure 1.3). The dorsal system includes the intraparietal and superior frontal cortex, specifically the frontal eye field (FEF), SPL, and IPS, and is involved in goal-directed, top-down attention, particularly disengaging attention and voluntarily shifting it to a newly selected location (i.e., voluntary attention). The ventral system includes the TPJ (including the STG and IPS) and IFG and middle frontal gyrus (MFG; primarily in the right hemisphere) and is involved in the automatic detection of behaviorally relevant stimuli (i.e., reflexive attention). This system has been shown to modulate the dorsal system by reorienting attentional resources to salient events.

These findings have been further corroborated in a more recent review of the behavioral, neuropsychological, and neuroimaging studies of automatic and controlled attention by Chica, Bartolomeo, and Lupiáñez (2013), suggesting that spatial attention consists of two separable, but interacting, systems of reflexive and voluntary attentional processing. Specifically, in the ventral stream, the right TPJ has been implicated as a ‘circuit breaker’ of attention that automatically shifts the attentional spotlight to behaviorally relevant stimuli. For example, right TPJ activation is enhanced to targets presented in invalidly cued locations (as opposed to cued locations), regardless of response modality (Astafiev, Shulman, & Corbetta, 2006). In contrast, the right IFG is primarily involved in stimulus-driven reorienting when reorienting is unexpected, as well as during response suppression. In the dorsal stream, the FEF and IPS have been primarily implicated in indexing the locus of attention within the visual field and maintaining attention to a peripheral location, whereas the SPL is involved in voluntarily tracking the locus of spatial attention.

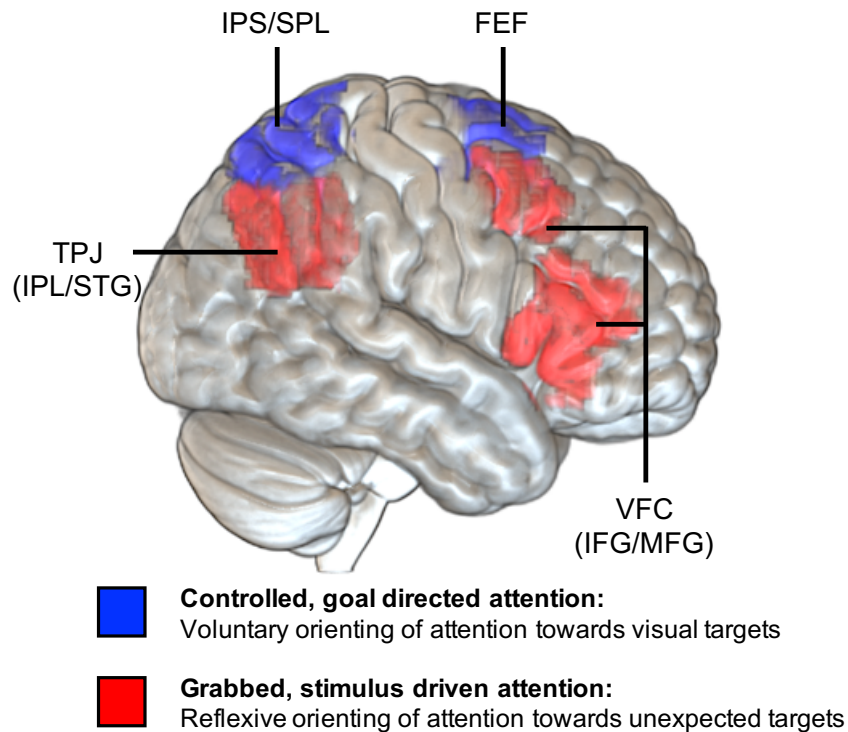


Figure 1.3. The dorsal and ventral streams of visuospatial attention. The ventral stream (shown in red) consists of the right TPJ (including the inferior parietal lobule (IPL) and superior temporal gyrus (STG)) and the right ventral frontal cortex (VFC; including the IFG and MFG) and is involved in voluntary shifts of visuospatial attention. The dorsal stream (shown in blue) consists of the right IPS/SPL and FEF, and is involved in reflexive shifts of spatial attention to unexpected stimuli. Adapted from Corbetta & Shulman (2002).

Recently, subcortical contributions to attentional orienting have also been described. For example, van Schouwenburg, den Ouden, and Cools (2013) used a spatial attentional switching paradigm in conjunction with functional neuroimaging and found evidence of a selective gating mechanism for attention that involves the basal ganglia. Specifically, their results suggested that basal ganglia structures are involved in inhibiting task-irrelevant representations via influence on top-down prefrontal processes. In line with this, Krauzlis, Bollimunta, Arcizet, and Wang (2014) propose a framework of attention that is reliant on basal ganglia circuits, particularly the striatum (i.e., putamen and caudate), whereby attention arises as a result of value-based decision-making processes. This framework is supported by evidence from clinical populations who have suffered damage to their striatum, which has been shown to lead to spatial attentional deficits (e.g.,

Karnath, Himmelbach, & Rorden, 2002; Murakami et al., 2014; Tommassi et al., 2015). It has been proposed that the basal ganglia is involved in modulating spatial attention, primarily by an influence on top-down attentional processing, that in turn modulates bottom-up processes (e.g., Saalman, Pinsk, Wang, Li, & Kastner, 2012).

1.6 White matter tracts in attention

DTI studies have identified several white matter pathways implicated in visuospatial attention. Thiebaut de Schotten et al. (2011) highlight the importance of three divisions of the SLF in mediating voluntary and reflexive attention (SLF I, SLF II, and SLF III). SLF I (the most superior projection of the SLF) is thought to overlap primarily with the dorsal spatial attentional network, projecting from the intraparietal cortex into the frontal cortex, and is thought to be involved in voluntary attention towards visual targets. SLF III is thought to overlap primarily with the parietal component of the ventral attentional network involved in reflexive attention to unexpected stimuli, and has been shown to be damaged in individuals with visuospatial neglect. SLF II has overlap with both the ventral and dorsal streams, spanning the parietal portion of the ventral attentional stream (i.e., the right TPJ) to the prefrontal component of the dorsal attentional stream (i.e., the right FEF). The SLF II is thought to mediate the communication between the dorsal and ventral spatial attentional streams during attentional orienting. This is corroborated by DTI research from Ge et al. (2013) who showed that spatial attentional orienting was primarily subserved by the SLF. In general, the tracts of this parieto-frontal network are larger on the right hemisphere than on the left (particularly the SLF II and SLF III), highlighting the neural asymmetry of attentional processing in the human brain.

1.7 Neuroimaging of reading and attention

Neuroimaging evidence has supported a relationship between reading and attention. For example, impaired reading development has been associated with deficits to the magnocellular-dorsal pathway involved in controlled attention (e.g., Boden & Giaschi, 2007; Gori & Facoetti, 2014; Vidyasagar & Pammer, 2010), suggesting that phonetic decoding processes may be disrupted by impairments in low-level visual processing in the dorsal stream. For example, in a postmortem study, Livingstone et al. (1991) found that individuals with dyslexia had fewer magnocellular neurons in their lateral geniculate nuclei (whereby magnocellular neurons project primarily into the dorsal visual stream) than individuals without dyslexia, suggesting that

dyslexia may be associated with aberrant dorsal stream processing (including visuospatial attention). This is corroborated by in vivo work from Giraldo-Chica, Hegarty, and Schneider (2015), who used high-resolution proton-density weighted MRI scans (a technique that allows for examination of the actual density of protons in the brain) to quantify the volume of the lateral geniculate nucleus in individuals with and without dyslexia. Their results indicated that the left lateral geniculate nucleus was significantly smaller in individuals with dyslexia, thus supporting the conclusion that dyslexia is associated with deficits to the magnocellular dorsal pathway. Further, Finn et al. (2013) used whole-brain connectivity analysis to examine the differences in functional connectivity between non-impaired and dyslexic readers. Their results showed that readers with dyslexia had differential connectivity between visual association areas and prefrontal attentional areas, such that there was decreased functional connectivity between the left IPS and bilateral prefrontal cortex. This suggests that dyslexic readers have impairments in focusing their attention on textual stimuli. As well, readers with dyslexia appeared to recruit more phonetic-decoding based reading circuits than non-impaired readers, suggesting a reduced ability to modulate their attention in order to integrate visual information. Thus, non-impaired readers may show better attentional modulation and integration of visual information that aids in word recognition processes, however attentional processes were not directly examined in this study.

Results from Facoetti et al. (2009) suggested that impaired readers show sluggish attentional shifting in a reflexive attention task that was associated with decreased right TPJ activation compared to controls, suggesting that impairments in skilled reading arise from a dysfunction of reflexive attentional orienting. However, little research has been done investigating the neural relationship between reading and attention in skilled readers. Cohen, Dehaene, Vinckier, Jobert, and Montavont (2008) showed that visually degrading real words led to increased activation in the bilateral SPL and bilateral occipito-temporal cortex (including the VWFA) as a function of degradation. Interestingly, and in contrast to the VWFA (which showed strong activation to normally displayed words, regardless of their position), the SPL showed no activation for words presented in their proper format, suggesting that the SPL is not strongly associated with lexical reading of familiar words in the absence of degradation.

Previous research has suggested that different reading strategies may be more strongly associated with one type of spatial attentional orienting than another. Specifically, phonetic decoding is thought to rely on focused, voluntary spatial attention processes, whereby units of

orthographic stimuli are assembled via a moving spotlight of attention (Vidyasagar & Pammer, 2010; see also Montani et al., 2014). In contrast, lexical processes are thought to be largely automatic, as indexed by the highly cited Stroop effect (see MacLeod, 1991 for a review and Lorentz et al., 2015 for thresholds of consciousness effects), suggesting contributions of reflexive attentional orienting. This conclusion is supported by event-related potential evidence from Strijkers, Bertrand, and Grainger (2015), who found that, when a participant had top-down intention to engage in a linguistic task, high-frequency written words elicited automatic recognition processes in the form of an earlier time course of electrophysiological response to these stimuli compared to the relatively delayed response to low-frequency words. Thus, lexical reading appears to be more strongly associated with reflexive spatial attention, whereas sublexical reading is more strongly associated with voluntary spatial attention, however this distinction has not been well characterized in skilled readers. Therefore, it is important to examine the neuroanatomical relationship between reading and attention in order to establish biomarkers of skilled reading.

CHAPTER 2

EXAMINING THE NEURAL RELATIONSHIP BETWEEN READING AND ATTENTION

Portions of this chapter have been previously published or submitted for publication. Redundant information has been removed:

Ekstrand, C., Neudorf, J., Gould, L., Mickleborough, M., & Borowsky, R. (2019). Where words and space collide: The overlapping neural activation of lexical and sublexical reading with voluntary and reflexive spatial attention. *Brain Research, 1706*, 1-12. © 2018 Elsevier B.V. All rights reserved.

Ekstrand, C., Neudorf, J., Kress, S., & Borowsky, R. (2019). Lexical and sublexical reading are reliant on separable reflexive and voluntary attention regions in hybrid tasks. Under revision at *Cortex*.

2.1 Introduction to the Neurocognitive Relationship between Reading and Attention

As discussed in Chapter 1, spatial attention appears to play an integral role in word recognition processes. However, much of the research examining the neural relationship between reading and attention has indirectly inferred the involvement of attentional processes. For example, several researchers have suggested that deficits to the magnocellular pathway that feeds into the dorsal visual processing stream are associated with impaired reading development (e.g., Boden & Giaschi, 2007; Gori & Facoetti, 2014; Vidyasagar & Pammer, 2010), without directly assessing dorsal stream processing. Further, Finn et al. (2013) suggested that impaired readers have a decreased ability to modulate spatial attention based on functional connectivity analyses that did not directly examine spatial attentional processes. In addition, the majority of studies evaluating attentional involvement in reading focus solely on reflexive attention, rather than voluntary attention (e.g., Cohen et al., 2008; Facoetti et al., 2009), and thus involvement of voluntary attentional mechanisms in word reading has remained relatively unexplored. As well, previous research has generally not made the distinction between lexical and sublexical reading when examining the influence of spatial attention on reading, instead using stimuli that can be

read both lexically and sublexically (i.e., ‘regular’ words, which have consistent spelling to sound correspondences), and non-words rather than PHs.

Perhaps most importantly for the current work, much of this research examining the neural relationship of reading and attention has focused on individuals with reading impairment (e.g., Facoetti et al., 2009; Finn et al., 2013), whereas skilled reading has been comparatively understudied. Understanding the behavioural and biological trademarks of skilled reading can have important implications for providing a baseline of healthy reading that in turn may guide diagnostics. While behavioural results provide evidence for a relationship between skilled reading and attention, such that phonetic decoding is more reliant on voluntary spatial attention (e.g., Vidyasagar & Pammer, 2010 and Montani et al., 2014) and lexical reading more reliant on reflexive attention (e.g., Strijkers et al., 2015), the neural basis of this relationship has remained relatively unexplored. Based on this, Chapter 2 focuses on systematically investigating the relationship between lexical and sublexical reading with both voluntary and reflexive attention. Experiment 1 focuses on an exploratory examination of the overlapping neural mechanisms of lexical and sublexical reading with voluntary attention. Experiment 2 investigates the relationship between lexical and sublexical reading with reflexive attention. These experiments will help us understand differential overlapping activation for lexical and sublexical reading, in order to examine whether neural regions involved in differential attentional strategies (i.e., voluntary vs. reflexive) may be more associated with one reading process over another. Experiment 3 combines reading and attentional processes into hybrid reading and attention tasks, which will allow us to examine relationships between the different factors. This work will help to identify the functional biomarkers that underlie skilled reading and the neural basis of how attention and reading processes may interact.

2.2 Experiment 1

In Experiment 1, we examine the overlapping neural activation of reading and voluntary spatial attention. We hypothesize that because reading of PHs requires stimuli to be phonetically decoded, this type of reading will show more overlapping activation with voluntary attentional orienting compared to lexical reading, particularly in dorsal attentional orienting areas including the SPL, IPS, and FEF. In addition, based on the work of Oberhuber et al. (2013) showing that both lexical and sublexical reading activate the putamen, and Krauzlis et al. (2014) showing the striatum is integral to spatial attentional processes, we also hypothesize that the putamen may have overlapping activation of reading and voluntary attention.

2.2.1 Materials and Methods

2.2.1.1 Participants

Fifteen participants (mean age 25.3, 4 males) performed voluntary attention, EW, and PH naming tasks, with the task order counterbalanced across participants. Because the same participants performed the voluntary attention task (Experiment 1), reflexive attention task (Experiment 2) and the lexical and sublexical reading tasks, the attention tasks were counterbalanced together, as were the reading tasks. All participants spoke English as their first language and reported normal or corrected-to-normal vision. Handedness was not assessed in this study. The participants gave written informed consent to participate in the study and all testing procedures were approved by the University of Saskatchewan Research Ethics Board and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

2.2.1.2 Stimuli and Procedure

Stimuli were presented using a PC running EPrime software (Psychology Software Tools, Inc., <http://www.pstnet.com>) via MRI compatible goggles (Cinemavision Inc., <http://www.cinemavision.biz>). Continuous perfect synchronization between the MRI and the experimental paradigm was maintained by detection of the leading edge of the fiber-optic signal emitted by the MRI by a Siemens fMRI trigger converter at the beginning of each acquisition volume that was then passed to the EPrime PC via the serial port. EWs for all experiments were chosen from Patterson and Hodges (1992) list of orthographic stimuli.

EW Reading Task

The EW and PH reading tasks were identical to those used in Gould et al. (2016). Participants were presented with 25 EWs in black Arial font on a white background in blocks of five (see Appendix A for EW stimuli), interspaced with blocks of relaxation (see Figure 2.1 for trial progression). Each stimulus remained on the screen for 1650 ms. EW and PH stimuli were matched on several of the characteristics available from the E-Lexicon Database (<http://elexicon.wustl.edu/>), specifically length ($t(48) = .436, p = .665$) and base word log frequency ($t(48) = -.176, p = .861$). Participants were required to read the presented EW aloud during the gap in acquisition directly following each stimulus presentation (1650 ms). During relaxation, a black central fixation cross (0.6° in height) was presented on the screen.

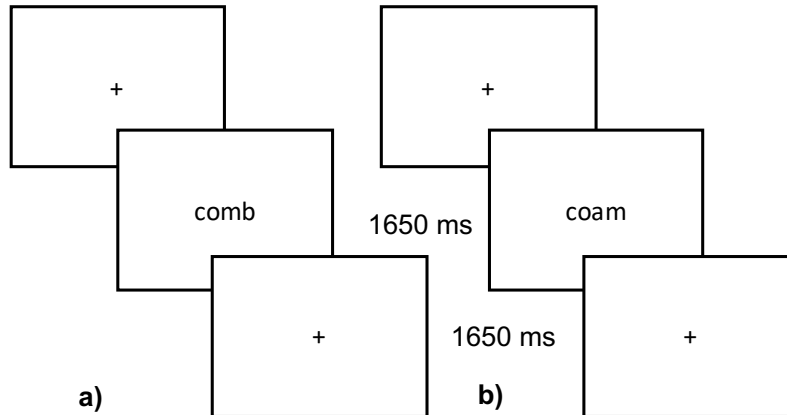


Figure 2.1. Trial progressions for the a) EW reading task and b) PH reading tasks.

PH Reading Task

The PH reading task was identical to the EW reading task, except the EWs were replaced with PHs (see Appendix A for PH stimuli). We chose to examine phonetic decoding of PHs rather than non-words in this experiment because PHs have identical phonological output to their word counterpart and the same meaning. Thus, differences in activation between PHs and EWs cannot be attributed to phonology or semantics and should directly reflect differences in decoding strategy (i.e., phonetic decoding versus whole-word reading). Therefore, PHs will offer the greatest experimental control for examining differences between lexical and sublexical reading.

Voluntary Attention Task

The voluntary attention task was identical to the task used in Mickleborough et al. (2016; see Figure 2.2 for the trial progression). A central fixation cross (0.6° in height) remained on the screen throughout the duration of the trials. Following initial fixation, a left or right arrow cue (1.3° in length) was presented for 200 ms 0.2° above fixation. Arrow cues have been shown to successfully activate the voluntary attention network differentially from purely reflexive cues (e.g., Ristic & Kingstone, 2006). Following a 700 ms interstimulus interval (i.e., a 900 ms stimulus onset asynchrony), an 'A' or 'H' target appeared on the screen 9.1° from fixation (50% probability; 0.9° in width and 0.8° in height) at either the cued or uncued (50% probability) location for 50 ms. Longer stimulus onset asynchronies (SOAs) have been argued to be the strongest factor for distinguishing voluntary from reflexive attentional allocation (e.g., Epstein, Conners, Erhardt, Marsh, & Swanson, 1997) and thus the longer SOA in this task compared to the reflexive task, as well as the central arrow cue, will lead to reliance on controlled attention mechanisms. Participants responded verbally as quickly and accurately as possible (e.g., Eriksen & Hoffman, 1972) whether they saw an 'A' or an 'H' and were asked to guess if they were unsure. Each participant performed six blocks with five trials per block.

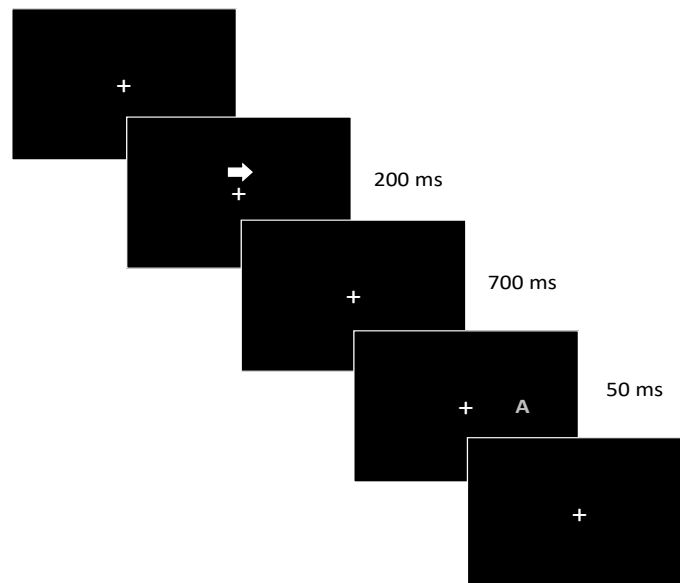


Figure 2.2. Trial progression for the voluntary attention task.

2.2.1.3 FMRI Protocol

All imaging was conducted using a 3 Tesla Siemens Skyra scanner. Whole-brain anatomical scans were acquired using a high resolution magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence consisting of 192 T1-weighted echo-planar imaging (EPI) slices of 1-mm thickness (no gap) with an in-plane resolution of 1×1 mm (field of view (FOV) = 256; TR = 1900 ms; TE = 2.08 ms).

For each of the functional tasks, T2*-weighted single shot gradient-echo EPI scans were acquired using an interleaved ascending EPI sequence, consisting of 65 volumes (for the attention task) and 55 volumes (for the reading tasks) of 25 axial slices of 4-mm thickness (1-mm gap) with an in-plane resolution of $2.65\text{-mm} \times 2.65\text{-mm}$ (FOV = 250) using a flip angle of 90° . The top two coil sets (16 channels) of a 20-channel Siemens head-coil were used, with the bottom set for neck imaging (four channels) turned off. Acquisition slices were positioned to prioritize complete coverage of the cortex. Additional foam padding was used to reduce head motion. In order to acquire verbal behavioral responses, we used a sparse-sampling (gap paradigm) fMRI method that allows the participant to respond during a gap in image acquisition (TR = 3300 ms, with a 1650 ms gap of no image acquisition; TE = 30 ms; flip angle = 90° ; e.g. Borowsky et al., 2007, 2012). Participants responded vocally during the regular, periodic 1650 ms gap in image acquisition that followed the offset of each volume of image acquisition, which allowed the participants to respond with no noise interference from the MRI.

2.2.1.4 FMRI Analyses

FMRI preprocessing and analysis was performed using FSL's FEAT (FMRI Expert Analysis Tool) protocol Version 6.0 (FMRIB, Oxford, UK, <http://www.fmrib.ox.ac.uk/fsl/>). Preprocessing included MCFLIRT linear slice-time/motion correction (Jenkinson, Bannister, Brady, & Smith, 2002), BET brain extraction (Smith, 2002), grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, high-pass temporal filtering (0.01 Hz; Gaussian-weighted least-squares straight line fitting, with $\sigma = 16.0$ s), and normalization to the Montreal Neurological Institute (MNI) 152 T1 2-mm template. For more accurate registration, the fMRI images were registered first to the high-resolution MPRAGE scan for each participant (6-df linear registration) before registration to the MNI 152 template (12-df linear registration). Functional images were then resampled using 2-mm isotropic voxels and smoothed with a Gaussian kernel of 5 mm full-width at half-maximum into standard space.

Lower-level analyses of the contrast between task versus rest for each condition were then performed (i.e., EWs, PHs, Voluntary attention) using a sinusoidal double-gamma hemodynamic response function convolution. Time-series statistical analysis was carried out using FILM with local autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001). Z (Gaussianized T/F) statistic images were thresholded using clusters determined by $Z > 3.1$ and a (corrected) cluster significance threshold of $p = .05$ (Worsley, 2001).

Conjunction analyses were performed outside of FEAT on the raw z-stat images for each condition obtained from the lower-level analyses using the `easythresh_conj` script in FSL (Nichols, 2007), with the whole brain as a mask and thresholds of $Z > 3.1$, cluster size $p = 0.05$.

2.2.1.5 Behavioral Analyses

In order to ensure that participants were adequately responding to the spatial cue, vocal responses were recorded using an Olympus LS11 digital recorder during both the voluntary and reflexive tasks. Reaction time (i.e., the time it took participants to correctly name the ‘A’ or ‘H’ target in milliseconds) was analyzed from the broadband spectrograms and waveforms using PRAAT software (Boersma & Weenick, 2009). Due to recorder malfunction, one participant’s vocal responses were unable to be analyzed, thus resulting in 14 participants in the final analysis.

2.2.2 Results

2.2.2.1 Behavioral Results

Paired samples t-tests found that reaction times in the voluntary task were significantly faster in the Valid ($M = 654.20$, $SD = 78.15$) versus the Invalid ($M = 673.23$, $SD = 84.98$) condition, $t(13) = -2.31$, $p = .038$. Thus, this task was effective at cuing spatial attention.

2.2.2.2 Task specific activation

Attention Task

The cluster statistics for the voluntary attention task are in Table 2.1. Significant clusters of activation were found in the right precentral gyrus, left putamen, bilateral lateral occipital complex (LOC), right MTG, left SPL, right precuneus, left fusiform gyrus, right lingual gyrus, and the right frontal pole. Results from this task closely replicate those from Mickleborough et al. (2016) and are consistent with the dorsal voluntary attention network highlighted in Corbetta and Shulman’s (2002) frontoparietal cortical network of attention.

Reading Tasks

The cluster statistics for the reading tasks are in Table 2.1. For the EW task, significant clusters of activation were found in the right MTG and STG, bilateral occipital pole, bilateral SPL, bilateral LOC, and left fusiform gyrus. For the PH task, significant clusters of activation were found in the left IFG, bilateral LOC, left inferior temporal gyrus, right occipital pole, left MTG and STG, bilateral cingulate gyrus, and left lingual gyrus. Though not identical, and with more stringent criteria for significance, our tasks identified many of the same regions as Borowsky et al. (2006), thus supporting the validity of our current findings.

Table 2.1. Task specific activation for the voluntary attention task, and the EW and PH reading tasks.

Task	Structure	Hemisphere	x	y	z	Z	Voxels
Voluntary Attention	Precentral Gyrus	R	44	-4	42	6.87	8044
	Putamen	L	-20	8	-2	5.98	2609
	Superior LOC/MTG	R	52	-62	0	6.85	1921
	Superior LOC/SPL	L	-20	-64	54	5.78	1227
	Precuneous	R	4	-54	56	4.63	714
	Fusiform Gyrus	L	-36	-64	-8	4.35	190
	Lingual Gyrus	R	18	-72	-8	4.4	173
	Frontal Pole	R	16	58	12	5.03	137
	Frontal Pole	R	38	38	28	3.86	131
	Frontal Pole	R	28	44	2	4.55	89
EW	MTG/STG	R	48	-32	-2	6.65	26971
	Occipital Pole/Inferior Temporal Lobe (including Fusiform gyrus)	L	-30	-96	-2	6.19	2181
	Occipital Pole/Inferior Temporal Lobe (including Fusiform Gyrus)	R	22	-92	-2	5.86	1571
	SPL	L	-24	-46	42	4.58	295
	Superior LOC	R	28	-64	36	4.71	156

PH	Superior LOC/SPL	L	-24	-62	44	4.67	133
	Cerebellum	L	-12	-68	-16	4.76	106
	IFG	L	-46	24	10	7.17	21019
	Inferior LOC/Inferior Temporal Lobe (including Fusiform Gyrus)	L	-44	-64	-14	7.06	5509
	Inferior LOC/Occipital Pole	R	40	-86	0	6.44	2690
	Superior LOC	R	28	-62	34	5.86	1974
	MTG/STG	L	-54	-30	-4	5.6	601
	Cingulate Gyrus	R/L	0	-22	30	3.93	118
	Lingual Gyrus	L	-14	-64	-16	4.47	91

Note. Coordinates represent the MNI coordinates of the voxel in the cluster with the greatest activation and Z is the z-score of that voxel.

2.2.2.3 Conjunction analyses

Voluntary attention and EWs

The results from the conjunction analysis between Voluntary Attention and EW reading can be found in Table 2.2. Significant areas of overlap were found in the bilateral putamen, bilateral SMA, left precentral gyrus, left MTG and STG and supramarginal gyrus, right SPL, bilateral superior LOC, right frontal pole, and left fusiform gyrus.

Table 2.2. Results for the conjunction analysis of voluntary spatial attention and EW reading.

Structure	Hemisphere	x	y	z	Z	Voxels
Putamen	R	18	8	4	5.67	2562
Putamen	L	-20	6	0	6.38	2243
SMA	R/L	-4	6	54	6.25	2036
Precentral Gyrus	L	-42	-6	32	4.91	1017
MTG/STG, Supramarginal Gyrus	R	48	-32	-6	4.91	734
SPL	L	-24	-44	42	4.93	157

Superior LOC	R	28	-66	34	4.86	117
Superior LOC	L	-24	-62	44	4.84	106
Frontal Pole	R	18	54	12	4.9	102
Fusiform Gyrus	L	-36	-64	-6	4.17	97

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

Voluntary attention and PHs

The results for the conjunction analysis between Voluntary Attention and PH reading can be found in Table 2.3. Significant areas of overlap were found in the bilateral putamen, bilateral SMA, left precentral gyrus, bilateral SPL, right MTG and STG and supramarginal gyrus, right superior LOC, left fusiform gyrus, and right frontal pole.

Table 2.3. Results for the conjunction analysis of voluntary spatial attention and PH reading.

Structure	Hemisphere	x	y	z	Z	Voxels
Putamen	R	18	8	4	5.67	2247
Putamen	L	-20	8	-2	6.37	1894
SMA	R/L	-4	6	56	6.24	1593
Precentral Gyrus	L	-42	-6	32	4.91	1085
SPL	L	-24	-44	42	4.93	707
MTG/STG, Supramarginal Gyrus	R	48	-32	-6	4.91	402
SPL	R	24	-52	44	4.16	237
Superior LOC	R	26	-66	38	4.86	201
Fusiform Gyrus	L	-36	-64	-6	4.17	99
Frontal Pole	R	18	54	12	4.9	99

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

Comparison of EW and PH conjunction analyses

Of particular interest to the current study are the areas in which one type of reading (i.e., lexical or sublexical) overlaps independently with voluntary attention, particularly in the attentional areas outlined by Corbetta and Shulman (2002).

EWs (shown in red) were shown to have unique overlap with voluntary attention in the right TPJ and right IFG (Figure 2.3a and b, respectively). PHs (shown in yellow) showed unique overlap in the bilateral SPL and IPS (Figure 2.3c and 2d, respectively). Orange regions represent overlap between both EWs and PHs with voluntary attention, whereby Figure 2.3e shows overlap between EWs and PHs with voluntary attention in the VWFA.

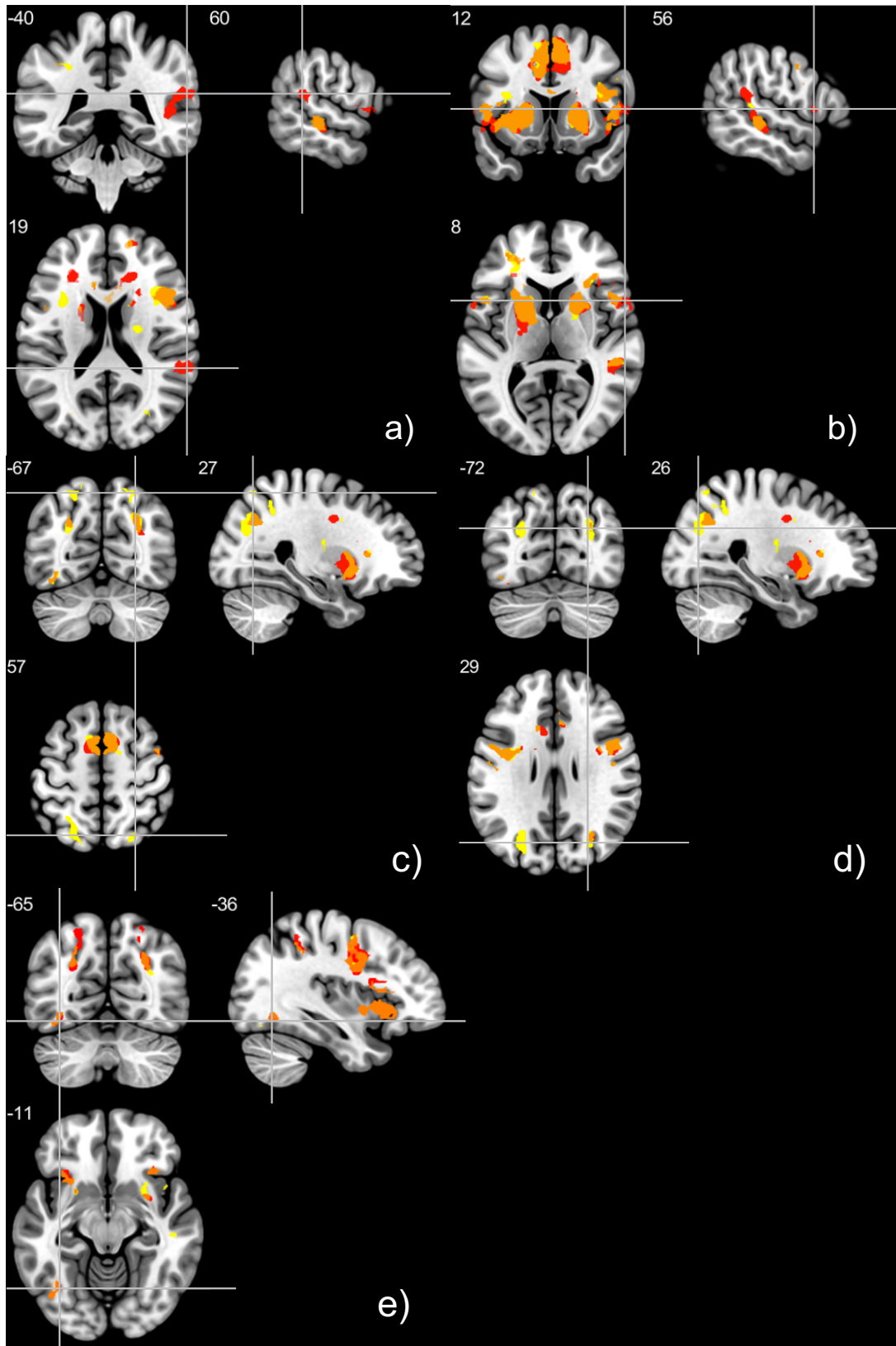


Figure 2.3. Unique conjunctive activation between EWs (red) and PHs (yellow) with voluntary attentional orienting. Crosshair locations depict unique activation in the a) right TPJ and b) right

IFG for the EWs, and the c) bilateral SPL and d) bilateral IPS for the PHs. Shared activation between the EWs, PHs, and voluntary attention (shown in orange) in the left fusiform gyrus is shown in panel e). Coordinates are in MNI space.

2.2.3 Discussion

This experiment sought to examine the overlapping neural correlates of lexical and sublexical reading strategies with voluntary attentional processes. We hypothesized that the PHs would show more unique activation overlap with the voluntary orienting task than EWs, particularly in dorsal spatial attentional areas, as these stimuli require phonetic decoding in order to be properly read. A summary of the main results is as follows.

There was a large amount of overlapping activation for the EWs and PHs with the voluntary attentional orienting task, specifically in the bilateral putamen, bilateral SMA, the left precentral gyrus, the left SPL, the right STG, supramarginal gyrus, MTG, the left and right superior LOC, and bilateral fusiform gyri. Of particular interest, both the EWs and PHs showed overlap with voluntary attention in the left fusiform gyrus (the putative VWFA). This is an interesting finding that merits further investigation, as it may suggest that voluntary attention is more strongly associated with reading processes in general. The PHs showed unique overlap with voluntary attention in the bilateral SPL and IPS, two areas associated with shifts in voluntary attention. This is particularly interesting, as these stimuli require phonetic decoding, which may be more reliant on scanning processes than reading of the EWs. Thus, this overlap may suggest that PH reading, and by extension phonetic decoding, relies on voluntary attentional resources in order to be properly processed. The EWs also showed unique overlap with voluntary attention in several areas, including the right insula, right TPJ, and right frontal operculum.

One limitation of this study was the use of the classic Posnerian voluntary attentional orienting paradigm (e.g., Posner, 1980; we return to this point in Chapter 4). Also referred to as ‘automated symbolic orienting’, arrow cues represent an overlearned stimulus that leads to automatic or near-automatic attentional orienting in the direction of the arrow (Hayward & Ristic, 2016; Ristic & Kingstone, 2006; Ristic, Landry, & Kingstone, 2012; Ristic & Kingstone, 2012). However, attentional orienting to arrow cues has been shown to result in an interaction of both reflexive and controlled attentional processes and is subserved by neural areas that span dorsal (e.g., SPL, IPS, FEF) and ventral (e.g., the angular gyrus, superior temporal sulcus attentional

areas) visual orienting streams. Therefore, the voluntary attention task used in this experiment may not optimally engage the voluntary attentional system and could partially contribute to the overall extent of overlapping activation between the EWs and PHs with this task. Thus, future research should also examine the overlap of reading and attention using other voluntary attentional orienting tasks to see if that may influence the amount of overlapping activation between lexical reading and voluntary attention. Such research should also manipulate cue validity in order to examine the impact of increasing the reliability of the cue on the neural relationship between reading and attention. We return to this point to Experiment 3.

Our findings also coincide with previous neuroimaging evidence showing that PHs activate dorsal stream regions (e.g., Borowsky et al., 2006; 2007). Further, PHs showed activation in this study that supports previous work, as they were shown to activate not only word reading areas such as the left angular and supramarginal gyrus, left IFG (e.g., Edwards, Pexman, Goodyear, & Chambers, 2005), and left fusiform gyrus, but also brain regions implicated in processing lexical semantic information, such as the middle temporal gyrus and angular and supramarginal gyri (e.g., Braun et al., 2015). In summary, results from Experiment 1 support our hypothesis that sublexical processing is more strongly associated with voluntary visuospatial attention. This is in concordance with theories of phonetic decoding that describe phonemic assembly via a moving spotlight of attention, that is reliant on focused, voluntary spatial attention processes (Vidyasagar & Pammer, 2010; see also Montani et al., 2014).

2.3 Experiment 2

While Experiment 1 examined the relationship between lexical and sublexical reading with voluntary attention, Experiment 2 will focus on investigating the neural overlap of these two reading processes with reflexive attention. We hypothesize that, based on the automaticity of lexical reading in skilled readers, lexical reading will show more overlap with reflexive attentional orienting compared to sublexical reading, particularly in attentional orienting areas such as the right TPJ and the left vOT.

2.3.1 Materials and Methods

The materials and methods for Experiment 2 were identical to those in Experiment 1, with the following exceptions. The same participants from Experiment 1 also performed Experiment 2.

2.3.1.1 Reflexive Attention Task

The methods for the reflexive attention task were the same as the voluntary attention task, with the following exceptions. Two 1.0° squares were presented (7.7° to the left and right of fixation) and remained on screen throughout the entire task (see Figure 2.4 for trial progression). The attention-directing cue consisted of either the left or right box flashing with a slight increase in brightness and slight increase in size for 50 ms. The ‘A’ or ‘H’ cue was then presented after a 100 ms interstimulus interval in either the cued or uncued square (50% probability). Task order for the attention and reading tasks was counterbalanced across participants.

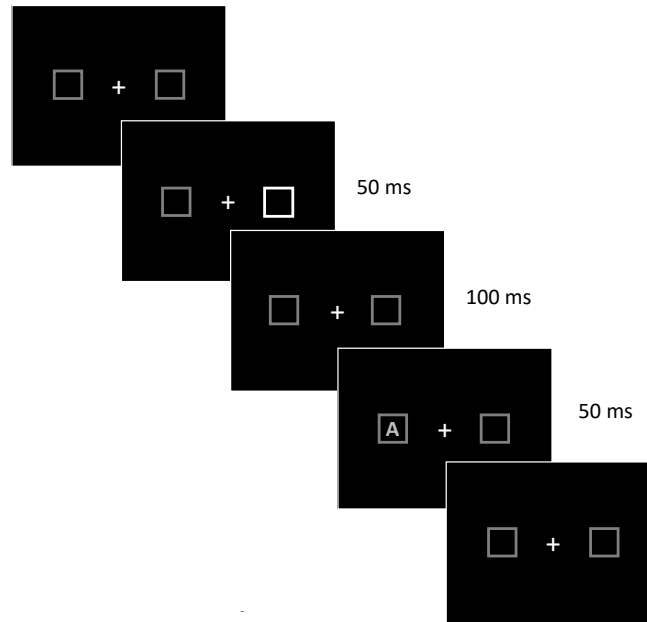


Figure 2.4. Trial progression for the reflexive attention task.

2.3.2 Results

2.3.2.1 Behavioural Results

Results from the paired-samples t-test showed that reaction times in the Valid condition ($M = 671.58$, $SD = 91.24$) were significantly faster than in the Invalid condition ($M = 685.79$, $SD = 92.82$), $t(13) = -2.31$, $p = .038$. Thus, this task was effective at cuing spatial attention.

2.3.2.2 Task-specific activation

For the Reflexive Task, significant clusters of activation were found in the right precentral gyrus, bilateral SMA, left putamen, bilateral MTG and STG, right frontal pole, right cerebellum, and the right superior LOC (see Table 2.4). Task specific activation for the EW and PH tasks was the same as Experiment 1.

Table 2.4. Task specific activation for the reflexive attention task.

Task	Structure	Hemisphere	x	y	z	Z	Voxels
Reflexive Attention	Precentral Gyrus	R	46	-2	44	5.62	3068
	SMA	R/L	-2	6	56	6.04	2565
	Putamen	L	-24	6	0	5.64	1799

MTG/STG	R	48	-32	-2	5.84	999
Frontal Pole	R	26	46	-8	5.17	199
Frontal Pole	R	18	56	16	4.43	172
Cerebellum	R	20	-62	-22	4.66	162
MTG/STG	L	-58	-24	-4	4.88	107
Superior LOC/MTG	R	50	-60	2	4.7	105

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

2.3.2.3 Conjunction Analyses

Reflexive attention and EWs

The results from the conjunction analysis between Reflexive Attention and EW reading can be found in Table 2.5. Significant areas of overlap were found in the bilateral putamen, right superior frontal gyrus, bilateral precentral gyri, right MTG and STG, right cerebellum, and two significant clusters in the right frontal pole.

Table 2.5. Results for the conjunction analysis of reflexive spatial attention and EW reading.

Structure	Hemisphere	x	y	z	Z	Voxels
Putamen	L	-22	6	0	6.02	1711
Putamen	R	18	8	4	5.39	1629
Superior Frontal Gyrus	R	6	12	60	5.95	1399
Precentral Gyrus	L	-46	-12	30	5.39	1072
Precentral Gyrus	R	36	-2	32	5.34	919
MTG/STG	R	48	-32	-4	6.00	773
Cerebellum	R	20	-62	-22	4.68	115
Frontal Pole	R	18	52	14	4.71	88
Frontal Pole	R	28	44	0	4.05	86

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

Reflexive attention and PHs

The results from the conjunction analysis between Reflexive Attention and PH reading can be found in Table 2.6. Significant areas of overlap were found in the bilateral putamen, right superior frontal gyrus, bilateral precentral gyri, right MTG/STG, and right cerebellum.

Table 2.6. Results for the conjunction analysis of reflexive spatial attention and PH reading.

Structure	Hemisphere	x	y	z	Z	Voxels
Putamen	L	-20	8	0	6.02	1369
Putamen	R	18	8	4	5.39	1185
Superior Frontal Gyrus	R	4	10	58	5.92	1158
Precentral Gyrus	L	-50	-9	30	5.31	887
Precentral Gyrus	R	46	-2	44	5.34	836
MTG/STG	R	48	-34	-2	5.99	394
Cerebellum	R	20	-62	-20	4.68	120

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

Reflexive attention

EWs showed unique overlap with reflexive attention in the right TPJ (Figure 2.5a), IFG (Figure 2.5a), and putamen (Figure 2.5b). There were no extensive areas of unique overlap for PHs and reflexive attention. PHs are shown in yellow and overlap between EWs and PHs is shown in orange.

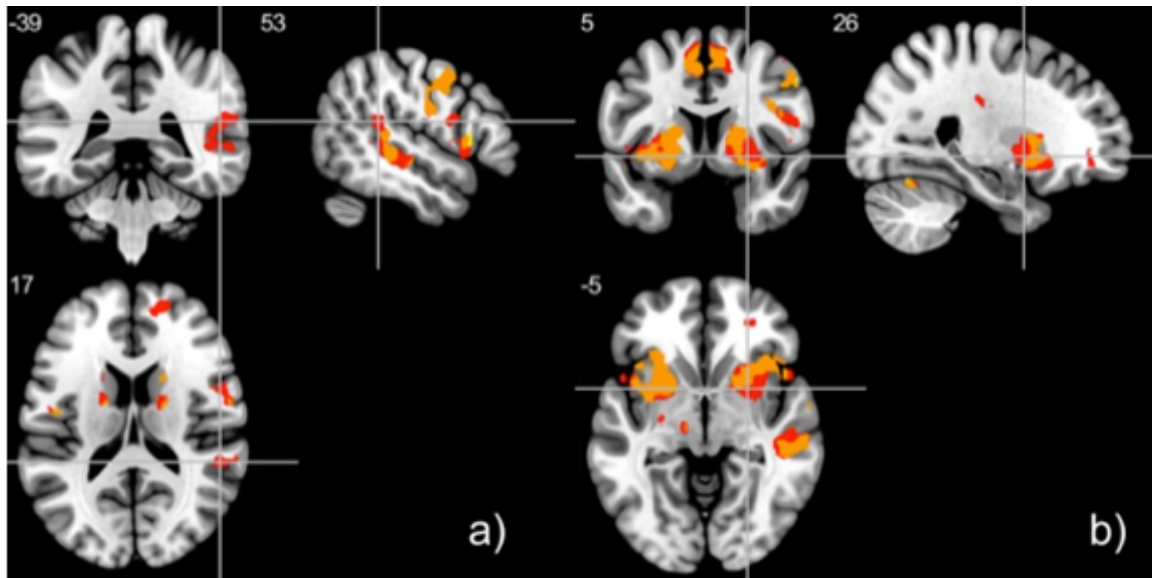


Figure 2.5. Unique conjunctive activation between EWs (red) and reflexive attentional orienting with crosshair locations in the a) right TPJ and b) putamen. Coordinates are in MNI space. PHs are shown in yellow and overlap between EWs and PHs is shown in orange.

2.3.3 Discussion

We hypothesized that, based on the automatic nature of lexical processing of familiar EWs, these stimuli would show more unique activation overlap with the reflexive attentional orienting task, particularly in ventral visuospatial attentional orienting areas. A summary of the main results is as follows. Both the EWs and PHs showed a large degree of overlap with reflexive attention throughout the brain, including the bilateral putamen, right superior frontal gyrus, bilateral precentral gyri, the right MTG/supramarginal gyrus, and the right vermis of the cerebellum. However, the EWs showed a greater amount of overlap with reflexive orienting in several areas, including two clusters the right frontal pole, and of particular interest: the putamen, the right TPJ, and the right IFG. The right TPJ and IFG have been implicated as important reflexive attentional orienting areas (e.g., Chica et al., 2013; Corbetta & Shulman, 2002) and thus these unique areas of overlap support our hypothesis that lexical reading should show greater overlap with areas in the ventral attentional orienting system. In contrast, there was very little activation in this comparison that appeared to be unique to PH reading and reflexive attention.

2.4 Comparison of Experiments 1 and 2

Experiments 1 and 2 showed that there was unique overlapping activation of EWs and PHs as a function of attention type, however it is also possible to examine whether there is unique overlapping activation of reflexive and voluntary attention as a function of reading strategy (i.e., lexical versus sublexical). Thus, in order to examine differences in overlap with attention type within stimulus type, we also performed a comparison of Experiments 1 and 2. Specifically, we examined the unique overlapping activation of EWs with voluntary attention, as well as reflexive attention, which allows us to determine how the different reading strategies overlap with the different attention types. We also examined the unique overlapping activation of PHs with voluntary attention and reflexive attention. This analysis will allow us to ensure that the reflexive and voluntary tasks used in these experiments were adequate at recruiting separable attentional systems. Further, this comparison may provide support for our conclusion that the voluntary arrow cue may be recruiting both reflexive and voluntary attentional networks, based on overlapping activation for both attention tasks with EWs in the right TPJ.

2.4.1 Results

2.4.1.1 Comparison of EWs with voluntary and reflexive attention

EWs were shown to overlap with both the reflexive (shown in red) and voluntary (shown in yellow) attention tasks in the right TPJ (Figure 2.6a; overlap shown in orange). Unique activation was found in the right IFG for the conjunction between EWs and reflexive attention (Figure 2.6b), and in the bilateral IPS for the conjunction between EWs and voluntary attention (Figure 2.6c).

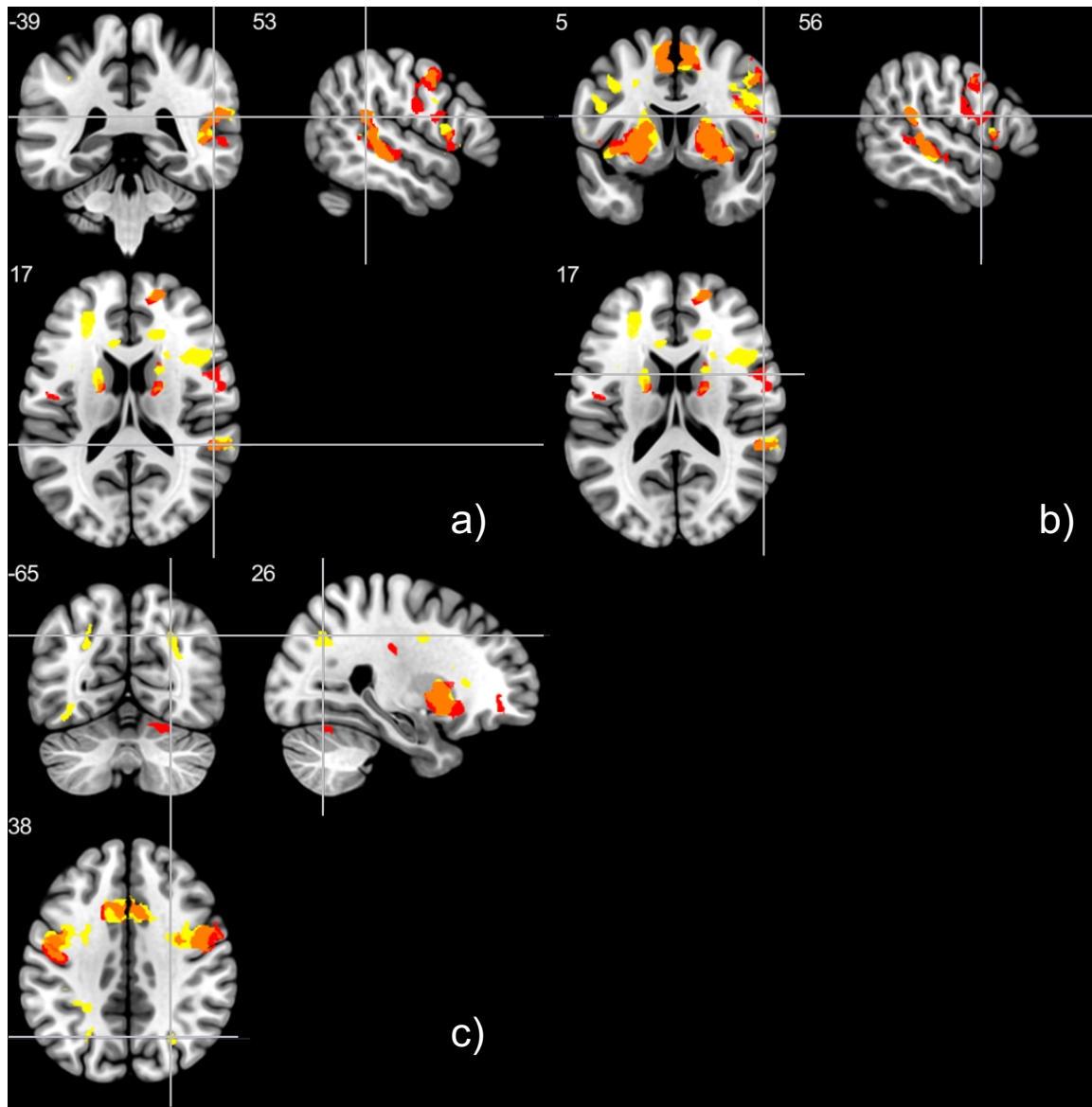


Figure 2.6. Conjunctive activation between reflexive (red) and voluntary (yellow) attention with the EWs (overlap is shown in orange). Crosshair locations depict a) overlapping activation in the right TPJ for EWs in both the reflexive and voluntary tasks, b) unique activation in the right IFG for the conjunction between EWs and reflexive attention, and c) unique activation in the IPS for the conjunction between EWs and voluntary attention.

2.4.1.2 Comparison of PHs with voluntary and reflexive attention

PHs were shown to have unique overlapping activation with voluntary attention (shown in yellow) in the bilateral IPS/SPL (Figure 2.7a) and left fusiform gyrus (Figure 2.7b). Unique

overlapping activation between PHs and reflexive attention (shown in red) was found in the bilateral primary motor cortices (Figure 2.7c). Overlap between reflexive and voluntary attention with PHs is shown in orange.

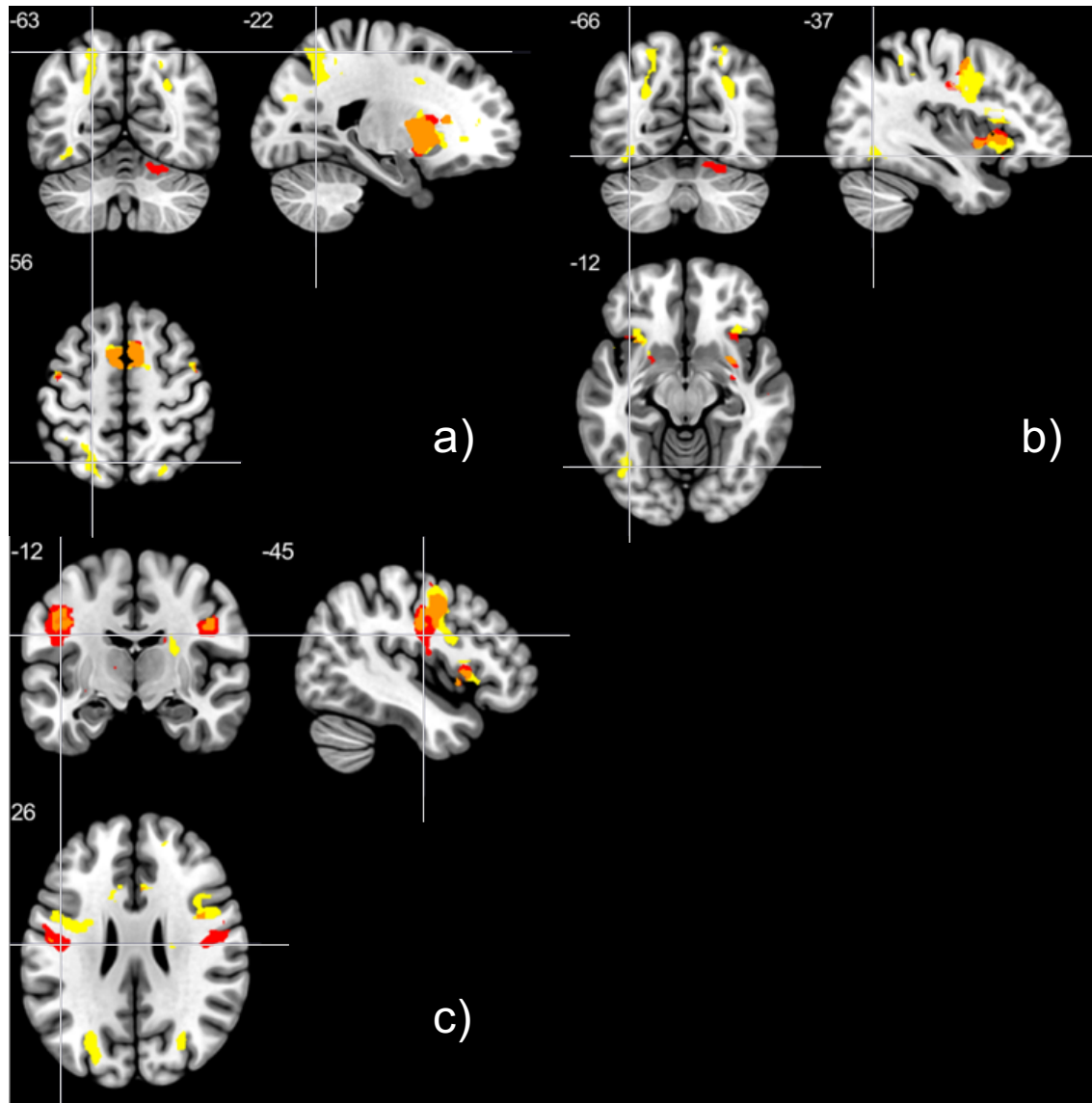


Figure 2.7. Conjunctive activation between reflexive (red) and voluntary (yellow) attention with PHs (overlap is shown in orange). Crosshair locations depict a) unique overlapping activation in the bilateral SPL/IPS for PHs in the voluntary task, b) unique activation in the left fusiform gyrus for the conjunction between PHs and voluntary attention, and c) unique activation in the bilateral primary motor cortices for the conjunction between PHs and reflexive attention.

2.4.2 Discussion

When comparing the conjunction analyses for EWs in both the voluntary and reflexive attention conditions, we found unique overlapping activation between the EWs and reflexive attention in the right IFG, a ventral attentional orienting area. Further, unique overlapping activation was also found in the bilateral IPS (but not SPL) for EWs and voluntary attention, suggesting some involvement of dorsal stream voluntary attentional processing in lexical reading. We also found support for our conclusion that the arrow cue may have been recruiting both voluntary and reflexive attentional systems based on the overlapping activation in the right TPJ for EWs in the reflexive and voluntary tasks. This suggests that the arrow cue may not fully isolate voluntary attentional processes. When comparing the conjunction analyses for PHs in both the voluntary and reflexive conditions, we found unique overlapping activation with voluntary attention in the bilateral IPS/SPL and the left fusiform gyrus (i.e., the VWFA), suggesting that the voluntary cue did successfully recruit voluntary attentional orienting regions. Unique overlapping activation of PHs with the reflexive task was found in the bilateral primary motor cortices. Overall, results from this comparison of Experiments 1 and 2 suggest that, although the voluntary arrow cue may recruit both voluntary and reflexive attentional mechanisms, our cues were still effective at tapping into separable voluntary and reflexive attentional networks.

This work provides, to our knowledge, the first empirical investigation of the neural overlap between voluntary and reflexive attention with lexical and sublexical reading, particularly with EW and PH stimuli. The tasks used in these experiments have been previously validated (e.g., identical reading tasks used in Borowsky et al., 2006; 2007 and attention tasks used in Mickleborough et al., 2016), and this preliminary investigation of the question of the neural overlap of reading and attention with empirically validated tasks provides a valuable first step into understanding the neural relationship between these critical and intertwined cognitive processes. The conjunction of reading and attention is an important and novel comparison that had not been previously evaluated. Further, our use of PHs rather than non-words allows for the full engagement of phonological and semantic systems in phonetic decoding, thus more accurately reflecting the actual reading process, and allowing for a fairer comparison of reading strategy (i.e., lexical and sublexical) to attentional processing. Based on this, we can ensure that the conjunctive overlap found in this study did not arise from confounds based on the tasks used.

Importantly, this work is an important first step towards unravelling the complex relationship between reading and attention.

2.5 Experiment 3

Experiments 1 and 2 focused solely on uncovering overlapping activation between the reading and attention tasks that may serve as an impetus for future research to uncover their interaction, however a factorial design is necessary to uncover how these processes may be differentially associated with one another. Experiment 3 seeks to further develop our understanding of how reading and attention processes are shared by examining the neuroanatomical relationship between reading and attention using hybrid combined reading attention tasks during fMRI rather than reading tasks presented separately from attention tasks. These hybrid reading and attention tasks will provide an important extension to the task conjunction analysis used in Experiments 1 and 2. Specifically, it will allow us to investigate the relationship between the different types of reading (i.e., lexical and sublexical) and attention (i.e., voluntary and reflexive), while participants engage in both reading and attention within the same task. We hypothesize that, in line with Experiments 1 and 2, lexical reading should be more associated with reflexive attentional orienting regions (specifically the right TPJ and right IFG). Similarly, sublexical reading should be more associated with voluntary attentional orienting regions (specifically the right SPL and right IPS). Further, based on the work of Laycock et al. (2009) showing that the left occipitotemporal junction is critically involved in mediating interactions between the dorsal and ventral streams during word reading, and Levy et al. (2009) showing differential functional connectivity between the left occipitotemporal junction and the middle occipital gyrus for word versus pseudoword reading, we hypothesized that spatial attention and reading may interact in early occipital areas.

2.5.1 Methods and Materials

2.5.1.1 Participants

Thirty participants (mean age 27.2, 16 males) performed voluntary-cued-EW, voluntary-cued-PH, reflexive-cued-EW, and reflexive-cued-PH reading conditions. All participants spoke English as their first language and reported normal or corrected-to-normal vision. The participants gave written informed consent to participate in the study and all testing procedures were approved by the University of Saskatchewan Research Ethics Board and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

2.5.1.2 Stimuli and Procedure

Stimuli were presented using the same apparatus and acquisition parameters as Experiment 1 and the list of EW and PH stimuli can be found in Appendix A. The order of the cued reading conditions was counterbalanced between participants.

Voluntary cued EW reading condition

The trial progression was as follows (see Figure 2.8a). Participants were presented with 30 cued reading trials in blocks of five, interspaced with blocks of relaxation. A black central fixation cross (0.6° in height) on a white background was presented. During the trial blocks, the black fixation cross changed to either pink or blue for 300 ms. Prior to participation, participants were instructed to covertly shift (i.e., without eye movements) their attention to the right if the fixation cross changed to pink, and the left if the fixation cross changed to blue (50% probability). The EW target was presented for 1000 ms on either the congruent (i.e., cued) or incongruent (i.e., uncued) location (75% validity, spatially predictive). These validity proportions have been shown to optimize reliance on voluntary versus reflexive attention (see Chica et al., 2014 for a review). Participants were asked to read the EW aloud as quickly and accurately as possible during the gap in acquisition when the stimulus was presented (1650 ms). EW stimuli were matched on several characteristics available from the E-Lexicon Database (<http://elexicon.wustl.edu/>), specifically length, word frequency, and orthographic neighborhood. During relaxation, a central fixation cross was presented on the screen.

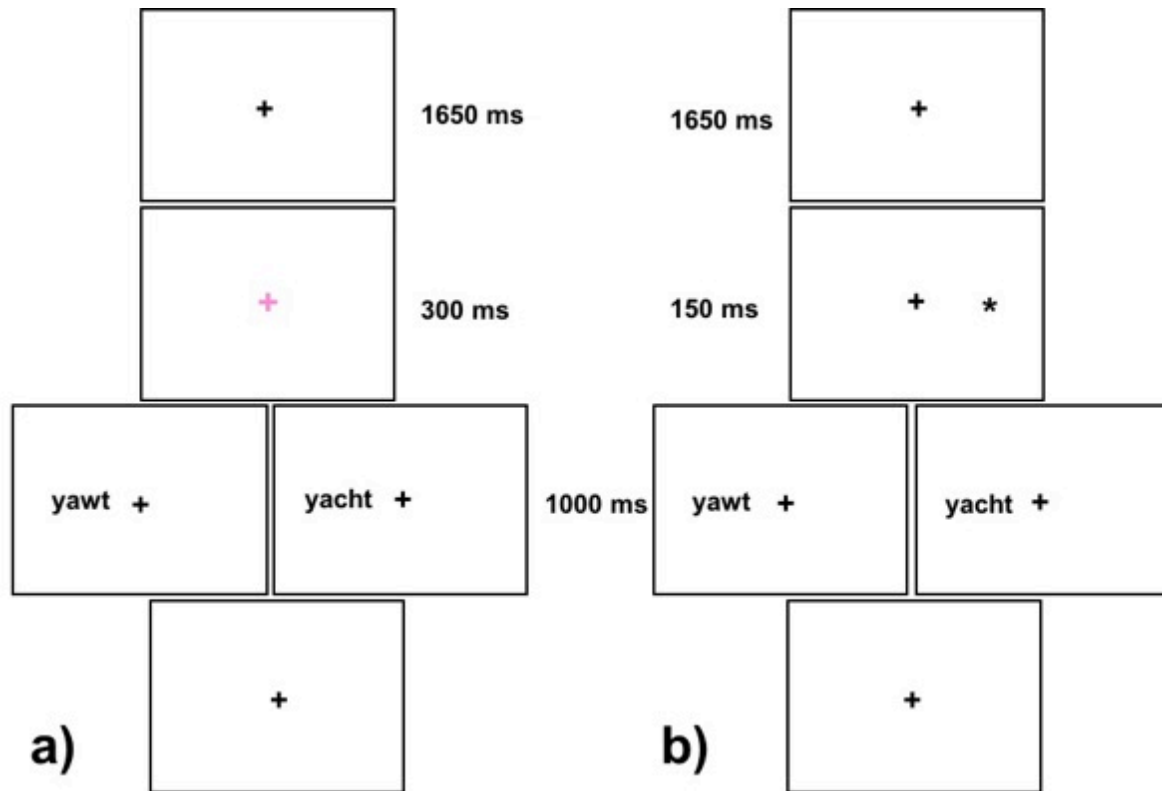


Figure 2.8. Trial progressions for the cued reading tasks. a) Voluntary attention task: the cue was either pink (shown, expect target on the right) or blue (expect target on the left; 50% probability). The target was either an EW or PH presented on either the invalid (shown) or valid side (75% validity). b) Reflexive attention task: the cue was an asterisk presented on either the right (shown) or left (50% probability). The target was either an EW or a PH presented on either the invalid (shown) or valid side (50% validity).

Voluntary cued PH reading condition

The voluntary cued PH reading task was identical to the voluntary cued EW reading task, with the exception that the EWs were replaced with PHs. In line with Experiments 1 and 2, we chose to examine phonetic decoding of PHs rather than pseudowords in this experiment because PHs have identical phonological output to their EW counterpart and the same meaning. Thus, differences in activation between PHs and EWs cannot be attributed to phonology or semantics and should directly reflect differences in decoding strategy (i.e., sublexical phonetic decoding

versus lexical whole-word). Therefore, PHs will offer the greatest experimental control for examining differences between lexical and sublexical reading.

Reflexive cued EW reading condition

The trial progression for the reflexive cued reading tasks can be found in Figure 2.8b. Participants were presented with the central fixation cross. Following this, an asterisk was presented either to the left or right of fixation (50% probability) for 150 ms. The EW target (identical to those used in the voluntary cued EW task) was then presented for 1000 ms in either the congruent or incongruent location (50% validity; spatially non-predictive, see Chica et al., 2014 for a review). Participants were asked to read the EW aloud as quickly and accurately as possible during the gap in acquisition when the stimulus was presented (1650 ms). During relaxation, a central fixation cross was presented on the screen.

Reflexive cued PH reading condition

The reflexive cued PH reading task was identical to the reflexive cued EW reading task, with the exception that the EW targets were replaced with PHs (identical to those used in the voluntary cued PH task).

2.5.1.3 FMRI Protocol

The fMRI protocol was similar to Experiments 1 and 2, with the following exceptions. For each of the functional tasks, T2*-weighted single shot gradient-echo EPI scans were acquired using an interleaved ascending EPI sequence, consisting of 55 volumes of 25 axial slices of 4-mm thickness (1-mm gap) with an in-plane resolution of 2.65-mm \times 2.65-mm (FOV = 250) using a flip angle of 90°.

2.5.1.4 FMRI Analyses

FMRI analyses were identical to Experiment 1, with the following exceptions. Lower-level analyses of the contrast between task versus rest for each condition were performed using a sinusoidal double-gamma hemodynamic response function convolution. Time-series statistical analysis was carried out using FILM with local autocorrelation correction (Woolrich et al., 2001). Z (Gaussianized T/F) statistic images were thresholded using clusters determined by $Z > 3.1$ and a (corrected) cluster significance threshold of $p = .05$ (Worsley, 2001). Higher-level group analyses were performed using FSL's FLAME 1 (FMRIB's Local Analysis of Mixed Effects).

Our primary analysis was a 2 (Reading; lexical, sublexical) x 2 (Attention; voluntary, reflexive) repeated measures ANOVA. Post-hoc analyses were performed using paired-sample t-tests. Results from the whole-head analyses were thresholded by $Z > 3.1$ and a corrected cluster significance threshold of $p < 0.05$ (Worsley, 2001).

Using the occipital lobe as a Region of Interest (ROI)

Based on our hypothesis that voluntary and reflexive attention and lexical and sublexical reading may be interacting in early occipital areas, we also performed a ROI analysis for the entire occipital lobe. The fMRI analyses were identical to the whole-brain analysis described previously, however prior to post-statistical thresholding, a binary mask of the occipital lobe (from the MNI structural atlas included with the software package) was applied, in order to constrain post-statistical processing to this region.

2.5.1.5 Behavioral Analyses

In order to ensure that our attention tasks used during fMRI can adequately cue spatial attention to orthographic stimuli, we performed a behavioral experiment outside of the scanner. The tasks were identical to those used in the scanner, with the following exceptions.

Participants

26 participants performed the voluntary-cued-EW, voluntary-cued-PH, reflexive-cued-EW, and reflexive-cued-PH reading tasks. Two participants were excluded from the final analysis due to mean reaction times greater than three standard deviations away from the mean, resulting in 24 participants (mean age 22.2, 6 males) in the final analysis.

Apparatus

The experiment was completed on a PC with Windows OS and E-Prime 2.0 software was used to program and run the experiment (Psychology Software Tools, Inc., <http://www.pstnet.com>). Participants were seated approximately 100 cm from a 15-inch Compaq 7500 CRT monitor, on which the trials were presented. A LabTec AM-22 microphone interfaced with the E-Prime serial response box was triggered upon the participant's vocal response in order to obtain their RT for each trial.

Procedure

Participants were required to fixate on a central fixation cross until the researcher initiated each trial. They then made a vocal response to the target stimulus, which consisted of 120 EWs and 120 PHs and were the same as those used in Ekstrand et al. (2016). The researcher then coded ‘1’ for a correct response, ‘2’ for an incorrect response, and ‘3’ for a spoil (if the microphone was triggered prematurely or failed to be triggered upon initial response). There was no time limit on how long the participant had to respond and the object disappeared from the screen when the microphone voice key was triggered.

Analysis

We performed two 2 (Reading; EW, PH) x 2 (Validity; Valid, Invalid) repeated measures ANOVAs on mean vocal response reaction times, one for the voluntary condition and the other for the reflexive condition in order to assess whether our conditions produce typical attentional reaction time cuing effects with orthographic targets.

2.5.2 Results

2.5.2.1 Whole-brain repeated measures ANOVA

The cluster statistics for the repeated measures ANOVA can be found in Table 2.7. Results from our 2 (Reading; lexical, sublexical) x 2 (Attention; reflexive, voluntary) repeated measures ANOVA found a significant main effect of Reading (averaging over the levels of attention type), such that EWs showed greater activation in the right supramarginal and angular gyri coinciding with the right TPJ, and right inferior parietal lobule (IPL; Figure 2.9a). PHs showed significantly greater activation than EWs in the bilateral SPL/IPS (Figure 2.10a), left precentral gyrus/IFG, right cerebellum, left IFG (i.e., Broca’s area; Figure 2.10c), and the bilateral LOC (extending into the fusiform gyrus of the temporal lobe, including the left VWFA; Figure 2.10d). The main effect of Attention identified no significant differences in activation between the two attention types, averaging over the levels of Reading. In this whole brain analysis, there were no regions that showed a significant Reading x Attention interaction.

Table 2.7. Results from the whole-brain repeated measures ANOVA.

Contrast	Structure	Hemisphere	x	y	z	Z	Voxels
EW > PH	Supramarginal/Angular Gyrus	R	58	-46	44	4.6	302

	Angular Gyrus	L	-44	-70	48	4.3	108
PH > EW	Inferior LOC/Fusiform	L	-36	-84	2	6.5	2141
	Inferior LOC/Fusiform	R	44	-82	4	5.3	1186
	Precentral Gyrus/IFG	L	-44	26	26	4.8	600
	SPL/IPS	L	-26	-58	54	5.1	289
	Cerebellum	R	30	-66	-22	5.4	278
	IFG	L	-48	30	2	4.0	115
	LOC/IPS	R	26	-68	44	4.2	93

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

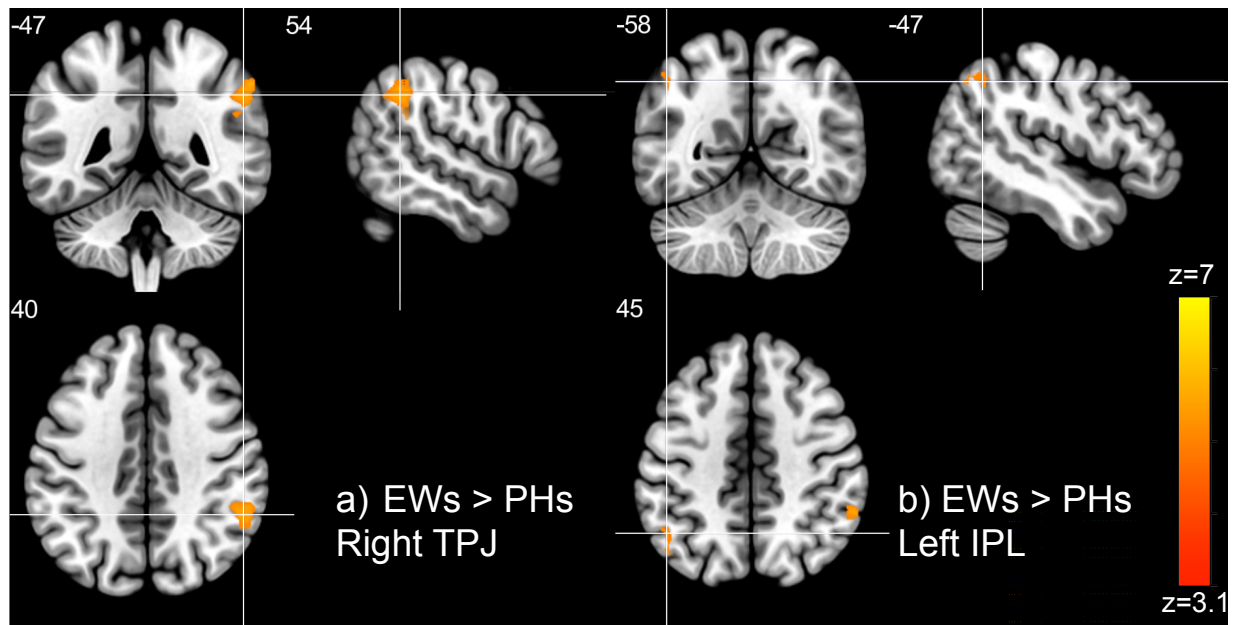


Figure 2.9. Results of the whole-brain repeated measures ANOVA EW > PH. Significant activation for the main effect of Reading EWs > PHs in the a) right TPJ b) left inferior parietal lobule (IPL), averaging over the levels of Attention type. Coordinates are in MNI space.

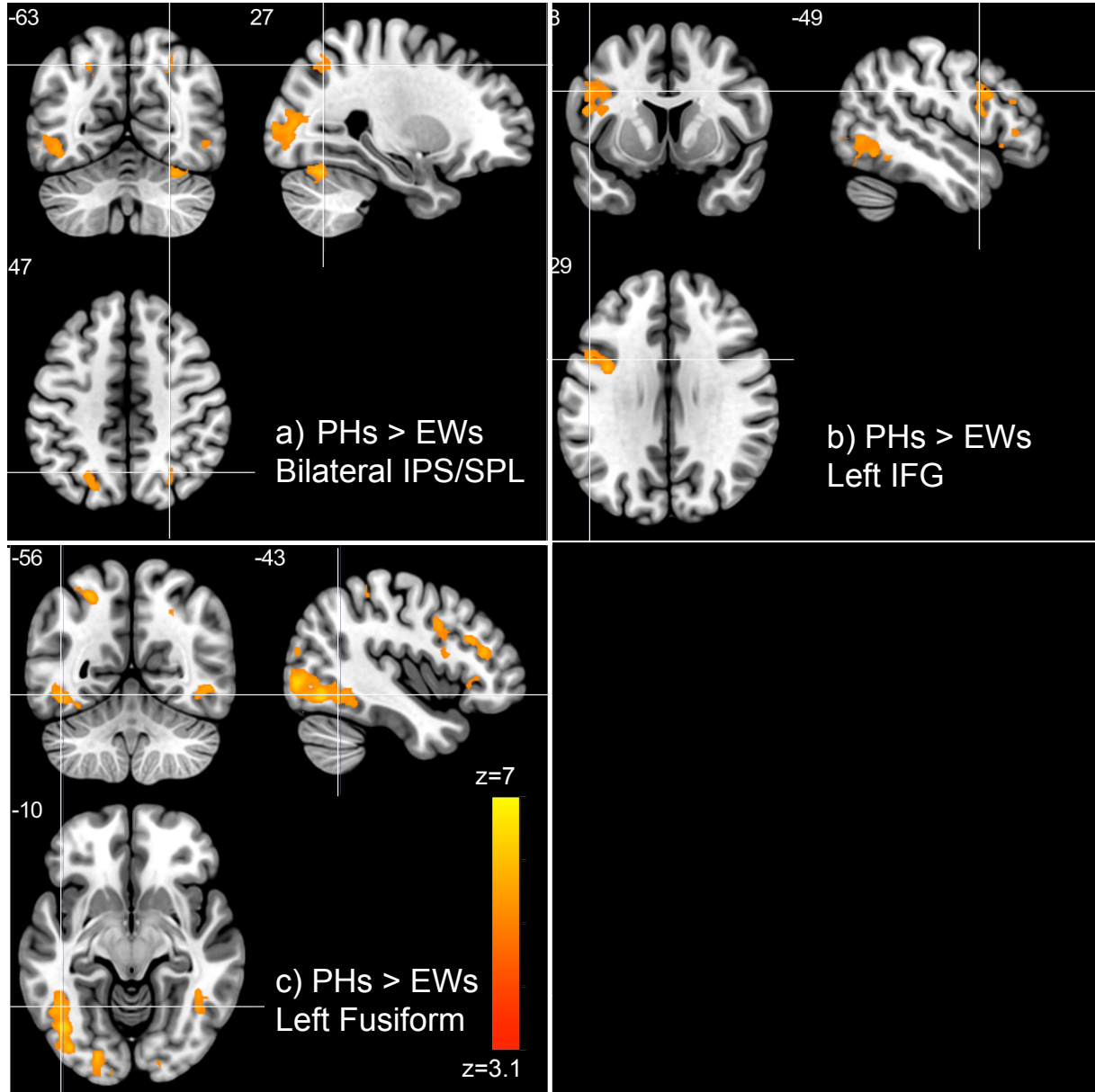


Figure 2.10. Results of the whole-brain repeated measures ANOVA PH > EW. Significant activation for the main effect of Reading PHs > EWs in the a) bilateral SPL/IPS, b) left IFG (i.e., Broca's area), and c) left fusiform gyrus (including the VWFA), averaging over the levels of Attention type. Coordinates are in MNI space.

2.5.2.2 Occipital ROI repeated measures ANOVA

The cluster statistics for the occipital ROI repeated measures ANOVA can be found in Table 2.8. Results from this analysis found a significant main effect of Reading averaging over

the levels of attention type, such that PHs showed greater activation in the bilateral inferior LOC and fusiform gyrus (refer to Figure 2.10c). Further, we also found a main effect of Attention, whereby voluntary attention showed greater activation than reflexive attention in the right middle occipital gyrus. Importantly, we also found a significant Reading x Attention interaction in the left middle occipital gyrus (Figure 2.11).

Table 2.8. Results from the occipital ROI repeated measures ANOVA.

Contrast	Structure	Hemisphere	x	y	z	Z	Voxels
Voluntary > Reflexive	Middle Occipital Gyrus	R	32	-92	2	4.04	45
PH > EW	Inferior LOC/Fusiform	L	-36	-84	2	6.39	1032
	Inferior LOC/Fusiform	R	44	-82	4	4.75	193
Attention x Word	Middle Occipital Gyrus	L	-30	-92	2	4.14	54

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

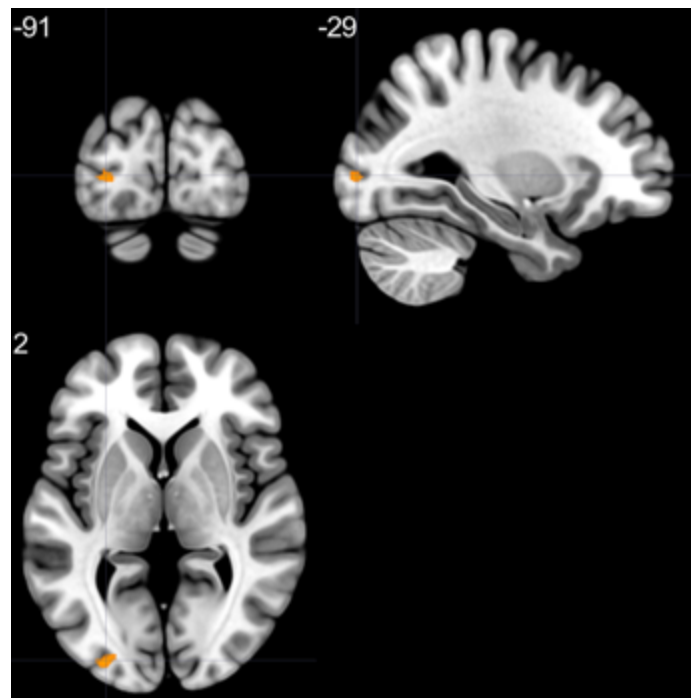


Figure 2.11. Results of the occipital ROI repeated measures ANOVA. Significant activation for the Attention (Voluntary, Reflexive) x Reading (Lexical, Sublexical) in the left middle occipital gyrus. Coordinates are in MNI space.

2.5.2.3 Paired sample t-tests based on attentional condition

To further disentangle the main effect of Reading, we performed two paired samples t-tests as a function of Attention type. For the Voluntary Attention condition, we found significant activation in the right TPJ for EW > PH (Figure 2.12a) and no significant activation for PH > EW. For the Reflexive Attention condition, we found significant activation for PH > EW in the right IPS/SPL (Figure 2.12b), left IFG (Figure 2.12c), and left fusiform gyrus (corresponding with the VWFA; Figure 2.12d), but no significant activation for EW > PH. The cluster statistics for the paired-samples t-tests are in Table 2.9.

Table 2.9. Results for the paired-sample t-tests as a function of attentional cuing task.

Task	Contrast	Structure	Hemisphere	x	y	z	Z	Voxels
Voluntary	EW > PH	Supramarginal/ Angular Gyrus	R	56	-46	42	3.84	180
Reflexive	PH > EW	LOC/Inferior Temporal Gyrus	L	-36	-86	-2	5.16	1402
		LOC	R	36	-82	2	4.58	579
		IFG	L	-46	22	26	4.73	291
		Inferior Temporal Gyrus/Fusiform	R	42	-60	-12	4.30	131
		Cerebellum	R	22	-70	-16	4.72	129
		IPS/SPL	R	26	-60	44	4.22	114
		IPS/SPL	L	-24	-64	46	4.02	99
		Postcentral Gyrus	L	-42	-42	54	4.20	90

Note. R = right, L = left, Z = maximum Z score of the voxel in the cluster. Coordinates are in MNI space.

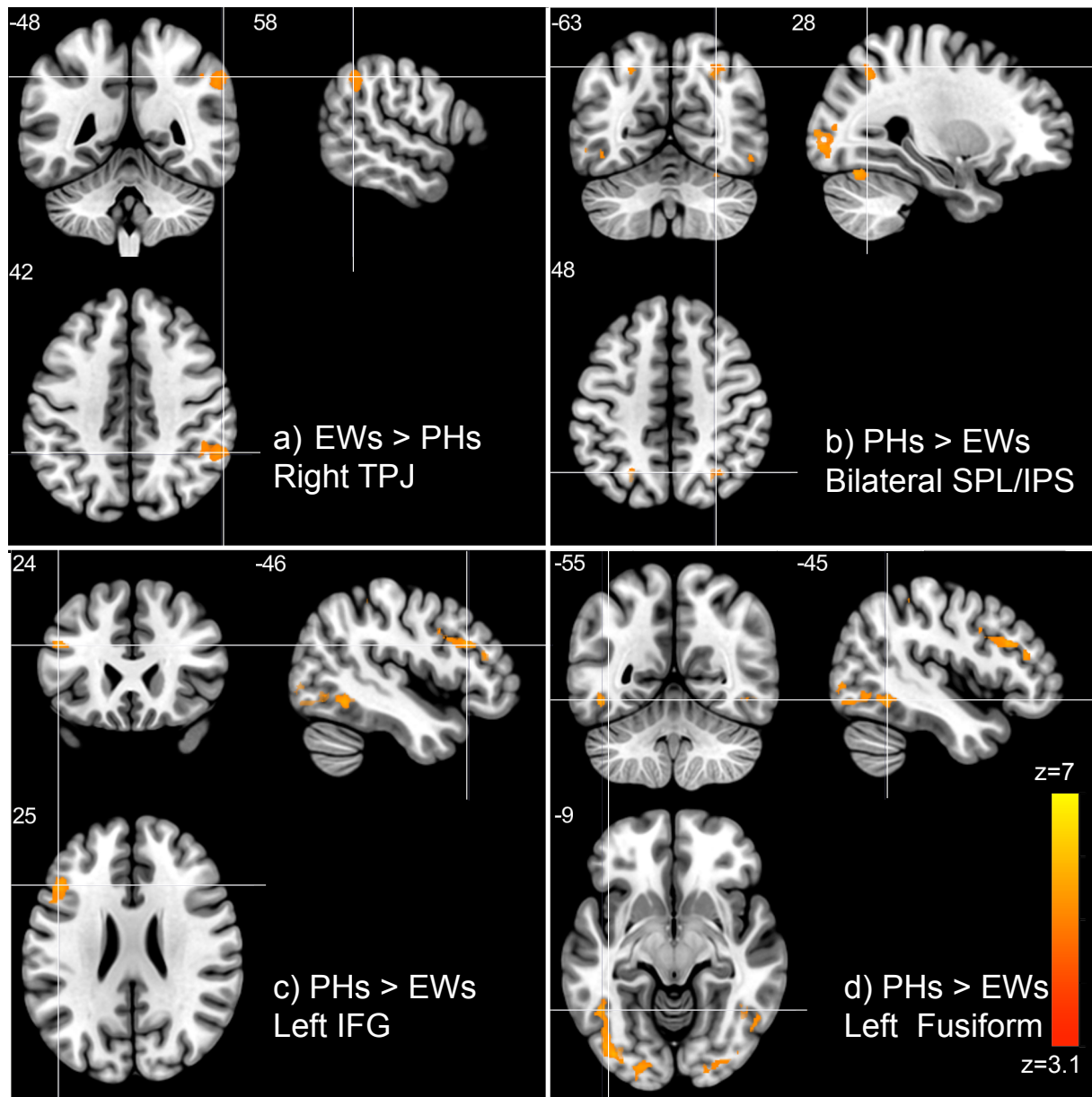


Figure 2.12. Results of the paired-samples t-tests for each attention type (i.e., voluntary versus reflexive). Crosshairs localize significantly greater activation a) in the voluntary attention task than the reflexive attention task for EWs versus PHs in the right TPJ, and significantly greater activation in the reflexive orienting task than the voluntary attention task for PHs versus EWs in the b) bilateral SPL/IPS, c) left IFG (i.e., Broca's area), and d) left fusiform gyrus (including the VWFA), averaging over the levels of Attention type. Coordinates are in MNI space.

2.5.2.4 Investigation of the occipital ROI interaction

In order to further understand the nature of the interaction in the middle occipital gyrus identified in the occipital ROI repeated measures ANOVA, we performed an investigation using the activation cluster as an ROI using FSLs Featquery GUI. Featquery takes an ROI mask in MNI space and transforms it into each participant's native space for each contrast (i.e., voluntary-cued-EW, voluntary-cued-PH, reflexive-cued-EW, and reflexive-cued-PH) and calculates statistics of the image. In particular, we were interested in the percent signal change in the middle occipital gyrus ROI for each participant, which converts the contrast of parameter estimate (COPE) values into percent signal change by scaling the COPE image by the height of the regressor (i.e., the maximum range of the explanatory variables in the model, in this case, height = 1) and dividing this value by the mean functional value over time across the original functional image. We then ran a repeated measures ANOVA across participants on the percent signal change data. Results from this analysis found a main effect of Attention, $F(1, 29) = 9.31$, $MSE = .091$, $p = .007$, such that means in the voluntary task were significantly higher than the reflexive task ($M = .6156$, $SD = .5152$ and $M = .4565$, $SD = .5240$, respectively). We also found a main effect of Reading, $F(1, 29) = 8.62$, $MSE = .182$, $p = .006$, such that signal change was higher for PHs than EWs ($M = .6504$, $SD = .5748$ and $M = .4218$, $SD = .4644$, respectively). There was also a significant Attention x Reading interaction, $F(1, 29) = 21.06$, $MSE = .076$, $p < .001$. Post-hoc paired sample t-tests (significance assessed at a Bonferroni corrected significance for four comparisons of $p < 0.0125$) indicated that the interaction in the middle occipital gyrus appears to be primarily due to lower percent signal change in the reflexive-EW condition compared to the three other conditions (see Figure 2.13 for means and 95% confidence intervals according to the Loftus & Masson, 1994 method). The t-test results for each comparison were: Voluntary-cued-EW to Voluntary-cued-PH, $t(29) = .026$, $p = .979$, Voluntary-cued-EW to Reflexive-cued-EW, $t(29) = 4.34$, $p < .001$, Voluntary-cued-PH to Reflexive-cued-PH, $t(29) = -1.29$, $p = .208$, and Reflexive-cued-EW to Reflexive-PH, $t(29) = -4.27$, $p < .001$.

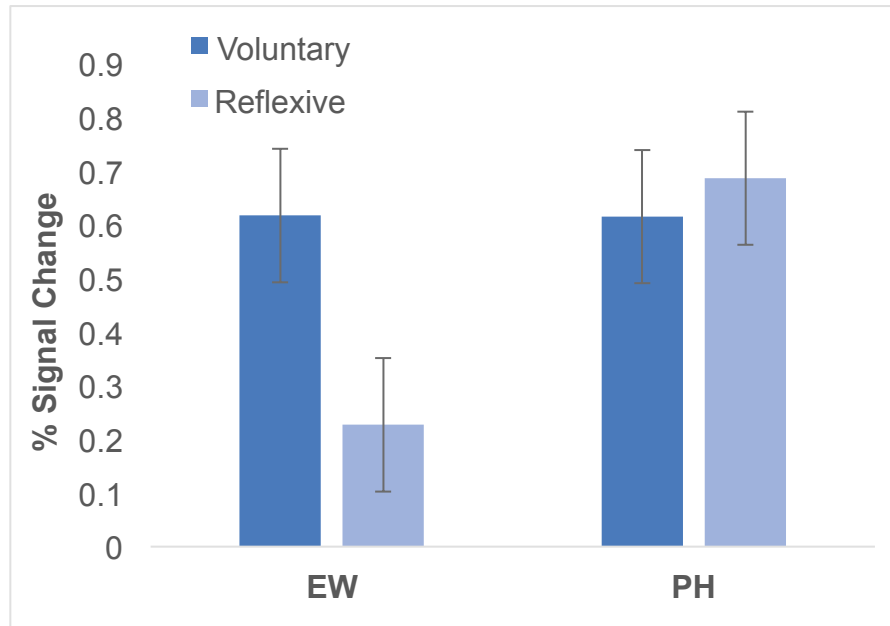


Figure 2.13. Percent signal change in the middle occipital gyrus interaction ROI for EWs and PHs as a function of attention type. Error bars represent 95% confidence intervals according to the Loftus & Masson (1994) method.

2.5.2.5 Behavioral Results

Results from the 2 (Reading; EW, PH) x 2 (Validity; Valid, Invalid) repeated measures ANOVA for the voluntary attention condition showed main effects of Reading, $F(1, 23) = 14.91$, $MSE = 5901.60$, $p = .001$, such that EWs were read significantly faster than PHs ($M = 653.42$, $SD = 96.49$ and $M = 713.97$, $SD = 107.17$, respectively), and Validity, $F(1, 23) = 5.539$, $MSE = 403.267$, $p = .028$, such that Valid trials were significantly faster than Invalid trials ($M = 678.87$, $SD = 99.32$, and $M = 688.52$, $SD = 104.34$, respectively). The Reading x Validity interaction was not significant, $F(1, 23) = .126$, $MSE = 541.63$, $p = .725$. The mean and standard deviation for each condition were as follows: Valid EW: $M = 649.45$, $SD = 94.99$, Invalid EW: $M = 657.40$, $SD = 97.99$, Valid PH: $M = 708.30$, $SD = 103.65$, Invalid PH: $M = 719.64$, $SD = 110.69$. Thus, our voluntary cue was effective and led to significant behavioral spatial cuing effects for EW and PH reading.

Results from the 2 (Reading; EW, PH) x 2 (Validity; Valid, Invalid) repeated measures ANOVA for the reflexive attention condition showed main effects of Reading Type, $F(1, 23) =$

14.92, $MSE = 5780.42$, $p = .001$ (such that EWs were significantly faster than PHs, $M = 647.74$, $SD = 87.18$ and $M = 707.69$, $SD = 101.10$, respectively), and Validity, $F(1, 23) = 130.29$, $MSE = 1033.10$, $p < .001$ (such that Valid trials were significantly faster than Invalid trials, $M = 640.27$, $SD = 96.16$, and $M = 715.16$, $SD = 92.12$, respectively). The Reading x Validity interaction was not significant, $F(1, 23) = .911$, $MSE = 559.26$, $p = .350$. The mean and standard deviation for each condition were as follows: Valid EW: $M = 607.99$, $SD = 86.45$, Invalid EW: $M = 687.49$, $SD = 87.92$, Valid PH: $M = 672.54$, $SD = 105.87$, Invalid PH: $M = 742.83$, $SD = 96.32$. Thus, our reflexive cue was effective and led to significant behavioral spatial cuing effects for EW and PH reading.

2.5.3 Discussion

This experiment sought to disentangle the contributions of dorsal and ventral attentional regions to lexical and sublexical reading using hybrid tasks and included an analysis using a factorial design. We hypothesized that, in line with Experiments 1 and 2, lexical reading would show reliance on reflexive attentional orienting regions, whereas sublexical reading would show reliance on voluntary attentional orienting regions. In support of these predictions, results from this study show that involvement of attentional regions during reading processes is dependent on the type of reading strategy employed. Specifically, results from the whole-brain repeated measures ANOVA indicated that when averaging over attentional orienting strategy, EWs showed greater activation than PHs in the right TPJ, as well as the left IPL. Further, based on the results of the paired sample t-tests, this main effect appears to be driven by greater activation for EWs than PHs in the right TPJ in the voluntary, rather than reflexive, orienting condition. This suggests that lexical reading relies on reflexive attentional mechanisms even in circumstances where it is not required by the task demands (i.e., in the voluntary attention condition). These results support the findings of Experiment 2 that found activation overlap between lexical reading and reflexive attention in the right TPJ and right IFG, and extend them by isolating the locus of the overlap between lexical reading and reflexive attentional orienting to the right TPJ in this factorial design, and not the right IFG when separate tasks for attention and reading are used.

In contrast, based on the whole-brain repeated measures ANOVA, PHs showed greater activation than EWs in several areas including the bilateral LOC (extending into the fusiform gyrus of the temporal lobe, including the left VWFA), left IFG, left precentral gyrus, right cerebellum, and, of particular interest, the bilateral SPL/IPS. Based on the paired sample t-tests,

this effect appears to be driven by greater activation for PHs than EWs in the reflexive attention condition, whereby there was significantly greater activation in the right IPS/SPL, left IFG, and left fusiform gyrus (i.e., the VWFA) for PHs than EWs, whereas PHs showed no activation greater than EWs in the voluntary attention condition. This suggests that sublexical reading relies on voluntary attentional mechanisms in the dorsal stream even in the reflexive attention condition. These results also support Experiment 1's findings that sublexical reading showed greater overlap with attention in dorsal attentional regions (including the right IPS/SPL). In summary, this study lends support for an integral role of the right TPJ in lexical processing, after controlling for contributions from semantics and phonological output (through the use of PHs) and voluntary attentional processes in reading using a factorial design. Similarly, there is evidence of an important role of the right IPS/SPL to sublexical reading, after controlling for semantics, phonology, and reflexive attentional mechanisms. Further, results from the repeated measures ANOVA in the occipital ROI provides evidence of an interaction between reading and spatial attention in the left middle occipital gyrus, an area implicated in skilled reading (see Martin et al., 2015 for a review) and comprehension (Ryherd et al., 2018). Based on our investigation of this ROI, it appears that the nature of the interaction is due to lower percent activation change in the Reflexive-cued-EW task than all other tasks. This is a particularly interesting finding, as it may suggest that EWs bypass this region in the reflexive attention task, perhaps relying more strongly on the ventral processing stream.

One limitation of the current study is the inability of fMRI to adequately capture fast and brief cerebral events, including attentional orienting, which may have contributed to the lack of an attention main effect found in this study. Thus, we propose that future research should utilize the current paradigm during electroencephalography (EEG) to examine the temporal relationship between lexical and sublexical reading and reflexive and voluntary visuospatial attention. In line with this, future work should also examine how different cue-to-target stimulus onset asynchronies and types of reflexive and voluntary cues impact the neural relationship between reading and attention. Future research should also explore pseudowords (as well as PHs), as pseudowords do not have corresponding semantic and phonological representations and therefore prevent post-access comparison of the target to their real-word counterpart, which may differentially recruit neural resources. We return to this point in Chapter 4. As well, investigation of the anatomical connectivity between reflexive and voluntary attentional orienting regions

(specifically, the right TPJ and SPL/IPS, respectively) and lexical and sublexical processing regions (including the VWFA) would be highly beneficial in order to identify the structural network that underlies the relationship between reading and attention.

In summary, this study provides the most direct evidence to date that lexical and sublexical reading recruit differential attentional orienting regions during single-word reading in skilled readers. Specifically, the right TPJ (a reflexive orienting area) appears to be associated with lexical processing, whereas the SPL/IPS appears to be associated with sublexical processing. Further, we show that reading and attention interact in the left middle occipital gyrus, suggesting that attention may have an influence on reading at a relatively early stage of processing. These results have interesting implications for broadening our understanding of skilled reading as well as how attention may play an integral role in reading development depending on the reading strategy employed. Our results also provide interesting insight into how attentional impairments may be associated with specific reading impairments and raise the potential for the use of targeted attentional training programs based on the nature of an individual's reading impairment (e.g., the deficit in sublexical phonetic decoding seen in phonological dyslexia may benefit from training in controlled attention, whereas the deficit in lexical whole-word reading seen in surface dyslexia may benefit from training in reflexive attention). We return to this discussion in Chapter 4.

2.6 Interim Discussion: Chapter 2

Together, results from Experiments 1, 2, and 3 provide important insight for expanding our understanding of word reading. First, results from Experiments 1 and 3 corroborate the idea that phonetic decoding of PHs has greater overlap in processing with voluntary attentional orienting in areas such as the right SPL and IPS. This is congruent with the findings of Montani et al. (2014) and Vidyasagar and Pammer (2010) discussed in Chapter 1, who showed that phonetically decoding non-words relies on controlled attentional processing. Also, our findings suggest that lexical reading processes engage attention regions that are largely automatic, as lexical reading was shown to have greater overlap with reflexive attentional orienting areas than PHs in Experiments 2 and 3. Therefore, our results are consistent with theories that posit that reading proficiency develops from a shift in conscious, attentionally demanding phonetic decoding strategies to more reflexive, holistic processing (e.g., Stuart & Coltheart, 1988). Thus, automaticity in word reading may be associated with reliance on reflexive attentional resources more so than voluntary attentional resources. Further, in Experiment 3, we identified an area in the middle occipital gyrus that showed sensitivity to voluntary attention and sublexical reading, but not to lexical reading in the reflexive attention task.

These results may have interesting implications for understanding dyslexia and how different types of dyslexia may be associated with different attentional impairments. It has previously been shown that some dyslexias may arise as a function of spatial attentional impairments (Franceschini et al., 2012, 2013; Gabrieli & Norton, 2012; Vidyasagar & Pammer, 2009), however our results are consistent with the conclusion that specific reading impairments may be associated with different types of attentional deficits. The PHs showed unique overlap primarily in voluntary attentional areas (i.e., the SPL and IPS), which may suggest that these stimuli require greater allocation of voluntary attention in order to be successfully decoded. This is in concordance with dyslexias that are characterized by visual search deficits, whereby proper allocation of the attentional spotlight along the word or sentence is impaired (e.g., Vidyasagar & Pammer, 1999; Facoetti, Paganoni, Turatto, Marzola, & Mascetti, 2000; Bosse, Tainturier, Valdois, 2007). Further, the EWs were shown to have unique overlap with attention primarily in reflexive attentional areas (i.e., the right TPJ and IFG), which suggests that deficits in lexical reading (as with surface dyslexia) may arise from disruptions to the reflexive attentional orienting system. Results from Franceschini et al. (2012) support these conclusions, as children who went

on to develop reading impairments showed deficits in both visual search (voluntary attention) and reflexive attentional orienting.

Our results are also consistent with previous research examining attentional impairments in dyslexia. For example, Peyrin et al. (2012) reported on two participants with dyslexia, L.L., who showed slowed speech production (i.e., phonological dyslexia resulting in impaired phonological output) in the absence of impaired pseudoword reading, and F.G., who showed deficits in both lexical and sublexical reading. Interestingly, L.L. showed comparable activation in the right SPL to controls and a normal visual attention span, suggesting intact spatial attentional abilities (particularly voluntary). This is in line with our conclusion that the right SPL is involved in phonetic decoding. In contrast, F.G. showed significantly decreased right SPL activation compared to both L.L. and controls, as well as a decreased visual attention span. Thus, impairments to lexical and sublexical processing may be associated with attentional impairments, particularly voluntary attention (see also Facoetti et al., 2007 for evidence of an association between non-word reading impairments and abnormal reflexive visuospatial attention impacting voluntary attentional processes).

In line with this, our results may also provide an interesting perspective on how the developmental trajectory of attention and reading may lead to specific reading impairments (see McDougall, Borowsky, MacKinnon & Hymel, 2005 for a discussion of developmental surface and phonological dyslexias and an approach for dissociating the lexical and sublexical processes that are respectively impaired, and Habib 2000 for a review of the neurological basis of developmental dyslexia). Based on the associations revealed by our current findings, a prediction that follows is that early deficits in reflexive attention may be associated with selective impairments in the development of lexical reading skills, whereas deficits in voluntary attention may co-occur with phonetic decoding processes. This hypothesis is supported by research examining rapid automatized naming (RAN; i.e., the ability to rapidly vocalize presented letters or digits) and phonological awareness (i.e., the sub-lexical ability to identify and manipulate the sound units of language) ability over the lifespan. Phonological awareness has been shown to be important in early reading skill acquisition (i.e., during phonetic decoding), whereas RAN scores are associated with a shift from phonology to lexical reading after children reach a ceiling in their decoding accuracy (see Norton & Wolf, 2012 for a review, and Wile & Borowsky, 2004, for variants of the RAN task that require either holistic letter/digit names to be produced that

uniquely account for variance in EW naming, or decoded letter-sounds to be produced that uniquely account for variance in PH naming). Thus, the relationship between reading ability and typical letter/digit RAN may be based on reliance on reflexive attention, whereas phonological awareness draws upon voluntary attentional mechanisms to successfully parse visual stimuli. As such, deficits to reflexive attention may impair the shift from phonetic decoding to lexical reading, whereas deficits to voluntary attention may impair phonetic decoding.

It would also be interesting to extend the current research to individuals with reading impairments, who may show differential overlap between reading and attention compared to unaffected populations based on the nature of their impairment. Further, it would be interesting to examine the overlap of attention with phonetic decoding of non-words, which would eliminate any PH activation of corresponding semantic and phonological representations and any potential post-access comparison of the PHs with their real word counterparts that may be reflected in the current activation patterns. As well, based on the overlap between reading and reflexive attention in the vermis of the cerebellum found in Experiment 2 and the critical role of the cerebellum in cognitive processing (see Pleger & Timman, 2018 and Striemer, Cantelmi, Cusimano, Danckert, & Schweizer, 2015 for cerebellar contributions to reading and covert reflexive attention, respectively), future research should also further examine the relationship between reading and attention in the cerebellum. Finally, extending this work to the level of sentence processing may provide valuable insight into how reading and spatial attention are related in an extended, ecologically valid paradigm, possibly through the use of a combined fMRI/eye-tracking experiment. Such an experiment would allow for accurate examination of attentional shifts during both single word and sentence level processing that can be analyzed as a behavioral measure and correlated with neuroimaging data.

In conclusion, this research provides a novel exploration into the overlapping neural activation of reading and spatial attention. Our results provide evidence of differential overlap between reading and spatial attention based on reading strategy (i.e., lexical vs. sublexical) and attentional orienting strategy (i.e., voluntary vs. reflexive). As EWs were shown to be more strongly associated with reflexive orienting areas compared to PHs based on conjunctions with both voluntary and reflexive attention in Experiments 1 and 2, as well as in the voluntary cued attention task in Experiment 3, there is evidence that lexical reading may employ more automatic attentional mechanisms in comparison to phonetic decoding. In contrast, PHs were shown to be

more strongly associated with voluntary attention compared to EWs in the conjunction with voluntary attention in the SPL and IPS in Experiment 1, as well as in the reflexive cued attention task in Experiment 3. This provides evidence that PHs may rely more heavily on voluntary attention in order to be effectively processed. Further, we suggest that one locus of interaction between lexical and sublexical reading and reflexive and voluntary attention is in the middle occipital gyrus, which has been shown to be an interface between the dorsal and ventral visual processing streams (e.g., Laycock et al., 2009). Our research may have interesting implications for studying the diverse nature of dyslexias, whereby different dyslexias may be characterized by unique deficits in attentional orienting as a function of reading strategy. Further, these findings broaden our understanding of the potential cortical neural overlap that underlies the relationship between reading and spatial attention, and extends our knowledge of how reading strategy and spatial attentional orienting strategy may be associated with one another. We hope this research will serve as an impetus for further investigation of the relationship between spatial attention and reading processes, including how underlying white matter structural connectivity patterns may potentiate this relationship.

CHAPTER 3

PREDICTING ACTIVATION IN READING TASKS FROM STRUCTURAL CONNECTIVITY

Portions of this chapter have been previously submitted for publication. Redundant information has been removed:

Ekstrand, C., Neudorf, J., Kress, S., & Borowsky, R. (2019). Structural connectivity predicts cortical activation during lexical and sublexical reading. Submitted to *NeuroImage*.

3.1 White-matter tracts and reading ability

As discussed in Chapter 1, underlying white matter connectivity has been shown to be integral to reading development. Saygin et al. (2013) examined the relationship between different facets of reading ability (i.e., phonological awareness, rapid naming of objects, colors, and letters, and letter knowledge) and white matter tract integrity in the left AF, ILF, and parietal portion of the SLF in kindergarten students with little or no reading instruction. Their results indicated that phonological awareness scores were positively correlated with left AF volume (i.e., total tract area), thus showing that early (i.e., pre-reading) deficits in white matter connectivity may be associated with poorer reading outcomes. Similarly, Wang et al. (2016) examined white-matter pathways of children either at familial risk for developing dyslexia or healthy controls, from pre-reading to fluent reading stages. Their results indicated that children with familial risk for dyslexia had lower fractional anisotropy (a measure of tract integrity) in the left AF, SLF, and ILF compared to controls after reading instruction. Further, subsequent good readers (regardless of group) showed faster white matter development in the left AF and ILF than subsequent poor readers.

Vanderauwera et al. (2018) examined the development of major ventral orthographic white matter tracts in pre-readers and readers after two years of reading acquisition, specifically the IFOF, ILF, and UF. Behavioural measures of pre-reading, phonological and orthographic ability were obtained. Their results found a relationship between pre-reading skill and tract integrity in the left IFOF and ILF. After two years of reading acquisition, tract integrity in the left

IFOF significantly predicted early orthographic ability. None of these ventral tracts were shown to predict phonological ability. These results suggest that orthographic knowledge may be reliant on the left IFOF during reading development. Together, these findings provide strong evidence that underlying anatomical connectivity plays an important role in reading development and proficiency.

Beyond examining individual fiber tracts, previous research has shown that fine grained anatomical connectivity can be used to predict fMRI activation for several cognitive processes, including face, object, scene, and body processing. Seminal work by Saygin et al. (2012) examined the ability of voxel-wise DTI connectivity to predict face selectivity in the right fusiform gyrus. Results from this study were robust and suggested that fMRI activation to faces could be accurately predicted from DTI connectivity alone. DTI connectivity also predicted fMRI activation better than group fMRI average models, suggesting increased sensitivity of this technique to identify individual differences in task-based fMRI activation. Osher, Saxe, Koldwyn, Gabrieli, Kanwisher, and Saygin (2016) extended these findings to four visual categories (faces, objects, scenes, and bodies) across the entire brain (rather than just the fusiform gyrus). Their results indicated that models built solely from DTI connectivity outperformed group fMRI average models (whereby the researchers argue that group average data is currently the only alternative means of predicting voxelwise neural responses in a new participant) and were able to successfully predict functional responses across the four visual processing categories. This suggests that individual DTI connectivity can be used to predict brain responses to cognitive functions.

Of particular interest to the current study, previous research has suggested that fine-grained anatomical connectivity is strongly associated with reading ability, particularly during reading development. Saygin et al. (2016) examined white matter connectivity to the VWFA in children pre-literacy (age 5) and after reading acquisition (age 8) to see if early VWFA connectivity could predict subsequent reading acquisition. To achieve this, the researchers identified the location of the VWFA at age 8, and created a model that utilized the DTI connectivity of the child at age 5 to predict activation in the VWFA at age 8. Their results showed that even prior to when there is functional selectivity in the VWFA for words (i.e., at pre-literacy), there is a distinctive pattern of structural connectivity that is able to predict subsequent reading regions. This suggests that reading ability can be characterized by distinct patterns of

individual structural connectivity. However, the relationship between fine-grained anatomical connectivity and skilled reading ability has yet to be explored. Examination of the relationship between structure and function of skilled reading will be essential for identifying biomarkers of skilled reading, which in turn may inform the assessment of literacy skills and interventions.

3.2 Experiment 4

The current study seeks to examine the extent to which fine-grained underlying white matter connectivity (measured via DTI tractography) is able to predict fMRI activation during both lexical reading and phonetic decoding in skilled readers. To do this, we will use a similar technique to Osher et al. (2016) that models the relationship between whole-brain structural DTI connectivity and task-based fMRI activation during both lexical and sublexical reading. In line with Saygin et al. (2016), we hypothesize that there will be a strong relationship between structural connectivity profiles and brain function that will be sensitive to lexical and sublexical reading ability in skilled readers. Therefore, using computational modeling techniques, individual structural connectivity should predict fMRI activation in reading tasks, particularly in areas such as the left fusiform gyrus (including the VWFA), IFG (i.e., Broca's area), and supramarginal and angular gyri, as well as attentional areas that may contribute to reading ability, including the right TPJ, SPL/IPS, IFG, and FEF.

3.2.1 Materials and Methods

3.2.1.1 Participants

Thirty participants (mean age 27.1, 15 males) performed DTI scans, and EW and PH reading tasks during fMRI. All participants spoke English as their first language and reported normal or corrected-to-normal vision. The order of the EW and PH tasks was counterbalanced between participants. The participants gave written informed consent to participate in the study and all testing procedures were approved by the University of Saskatchewan Research Ethics Board and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

3.2.1.2 Diffusion Tensor Imaging Acquisition Parameters and Tractography

All imaging was conducted using a 3 Tesla Siemens Skyra scanner. Whole-brain anatomical scans were acquired using a high resolution MPRAGE sequence consisting of 192 T1-weighted EPI slices of 1-mm thickness (no gap) with an in-plane resolution of 1×1 mm (FOV = 256; TR = 1900 ms; TE = 2.08 ms).

DTI data were acquired using 195 EPI slices of 4-mm thickness (no gap) with an in-plane resolution of 1.72×1.72 , (FOV = 220; TR = 3700 ms; TE = 95 ms; diffusion weighting isotropically distributed along 60 directions; b-value 1000 s mm^{-2} , with a b_0 volume interspersed

every 10 diffusion directions). The top two coil sets (16 channels) of a 20-channel Siemens head-coil were used, with the bottom set for neck imaging (four channels) turned off. Preprocessing included alignment to the b_0 images using FSLs eddy-correct tool (<http://fmrib.ox.ac.uk/fsl>) to correct for head motion and eddy current distortions, removal of non-brain tissue using the Brain Extraction Tool (BET) from FSL (Smith, 2002), and registration to the high resolution anatomical (T1-weighted structural) scans using FSLs *flirt* (Jenkinson & Smith, 2001; Jenkinson et al., 2002). Next, the GPU version of FSLs *bedpostx* (Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques; Hernandez et al., 2013), ran on a NVIDIA GTX 1070 GPU with 8 GB of RAM, was used to build sampling distributions of the diffusion parameters at each voxel necessary for probabilistic tractography.

Tractography proceeded as follows. First, each of the 268 regions from the Shen, Tokoglu, Papademetris, and Constable (2013) atlas were transformed into diffusion space using FSLs *flirt* and were checked and corrected for registration errors (if necessary). The DTI-registered parcels were then used as seed and target regions for fiber tracking. Fiber tracking was performed using the GPU version of FSLs *probtrackx* tool (Hernandez-Fernandez et al., 2016), which uses probabilistic tractography to create a connectivity distribution at each voxel in the seed region (5000 streamline samples per voxel) to each of the target regions, with the distance correction option. This procedure results in a vector of connection probabilities from each voxel in the seed region to all other brain regions.

3.2.1.3 FMRI Protocol

FMRI acquisition was identical to Experiments 1 and 2, with the following exceptions. For each of the functional tasks, T2*-weighted single shot gradient-echo EPI scans were acquired using an interleaved ascending EPI sequence, consisting of 65 volumes of 25 axial slices of 4-mm thickness (1-mm gap) with an in-plane resolution of 2.65-mm \times 2.65-mm (FOV = 250) using a flip angle of 90°.

3.2.1.4 Stimuli and Procedure

Stimuli were presented using a PC running EPrime software (Psychology Software Tools, Inc., <http://www.pstnet.com>) via MRI compatible goggles (Cinemavision Inc., <http://www.cinemavision.biz>). The EW and PH stimuli can be found in Appendix B. Continuous synchronization between the MRI and the experimental paradigm was maintained by detection of

the leading edge of the fiber-optic signal emitted by the MRI by a Siemens fMRI trigger converter at the beginning of each acquisition volume that was then passed to the EPrime PC via the serial port. The order of the EW and PH reading conditions was counterbalanced between participants.

Reading tasks

The trial progression for each of the reading tasks was as follows. Participants were presented with 30 target stimuli (either EWs or PHs depending on the task) in blocks of five, interspaced with 5 blocks of relaxation. These stimuli were the same as were used in Experiment 3. A black central fixation cross (0.6° in height) on a white background was presented. Following this, a jitter of 100, 200, 300, 400, or 500 ms (presented randomly) occurred before presentation of the EW or PH stimulus. This jitter was included to provide more accurate estimates of activation across conditions by staggering the temporal relationships between trial types, thus sampling different components of the hemodynamic response function (Amaro Jr. & Barker, 2006). Participants were asked to read the stimulus aloud as quickly and accurately as possible during the gap in acquisition when the stimulus was presented (1650 ms). EW stimuli were matched on several of the characteristics available from the E-Lexicon Database (<http://elexicon.wustl.edu/>). In line with Experiments 1, 2, and 3, phonetic decoding of PHs was used to examine sublexical reading as opposed to pseudowords based on PHs identical phonological output to their word counterpart and identical meaning. Thus, PHs offer the greatest experimental control for examining differences between lexical and sublexical reading by ensuring that differences in activation are due solely to differences in decoding strategy, not phonology or semantics. EW and PH stimuli were matched on several of the characteristics available from the E-Lexicon Database (<http://elexicon.wustl.edu/>), specifically length ($t(58) = .197, p = .844$) and base word log frequency ($t(58) = -.159, p = .874$). During relaxation, a central fixation cross was presented on the screen.

3.2.1.5 FMRI Analyses

Lower level fMRI analyses were identical to Experiments 1 and 2, with the following exceptions. Prior to analysis, the functional scans for the EW and PH reading tasks were merged across time to create a single functional volume. Individual subject level comparisons of EW and PH reading, as well as EW greater than PH and PH greater than EW contrasts were performed for

each participant, thus resulting in four t -statistic images. The t -statistic images were standardized using the same technique as Osher et al. (2016). Specifically, we subtracted the mean functional value of the whole brain activation from the functional response at each voxel and divided it by the standard deviation of the whole brain activation. All modeling was then performed on these standardized t -statistic images. We then transformed the whole-brain standardized t -statistic images into DTI space using FSLs *flirt* by first registering the original functional images to the DTI image and then applying this transformation matrix to the t -statistic images (Jenkinson & Smith, 2001; Jenkinson et al., 2002). Next, the standardized t -statistic images were masked with the same Shen et al. region masks into 268 anatomical parcels that were the same size as the DTI connectivity images.

3.2.1.6 Modeling Methods

Our modeling approach was comparable to the approach used by Osher et al. (2016) and was implemented using in-house Python code. Participants were divided into two groups whereby modeling for Group 1 ($N = 15$) was validated using leave-one-out cross-validation (LOOCV) and modeling for Group 2 ($N = 15$) was performed by applying the final model from all of the participants in Group 1 to each of the participants in Group 2 to evaluate how well the model can generalize to new data. Each participant's anatomical brain was divided into 268 cortical regions using the Shen et al. (2013) atlas in their native space, allowing for individual anatomical variations during modeling.

Group 1

For Group 1, to predict function from connectivity, we employed the LOOCV approach, whereby the connectivity and functional data of a single participant was excluded and a model was trained on the remaining participants before being applied to the left-out subject. We repeated the LOOCV for all participants to create independent predictions for each subject. The modeling proceeded as follows (see Figure 3.1): each of the 268 regions from the Shen parcellation for each subject was used as a seed parcel, whereby every voxel of the seed parcel had a functional response to the fMRI contrast (a $1 \times N$ (number of voxels in the seed regions) vector), as well as DTI connectivity to 267 target parcels ($267 \times N$ matrix, where rows are voxels and columns are connectivity to each of the target regions). Neural responses and DTI connectivity were concatenated (i.e., combined into one matrix, where rows represent voxels

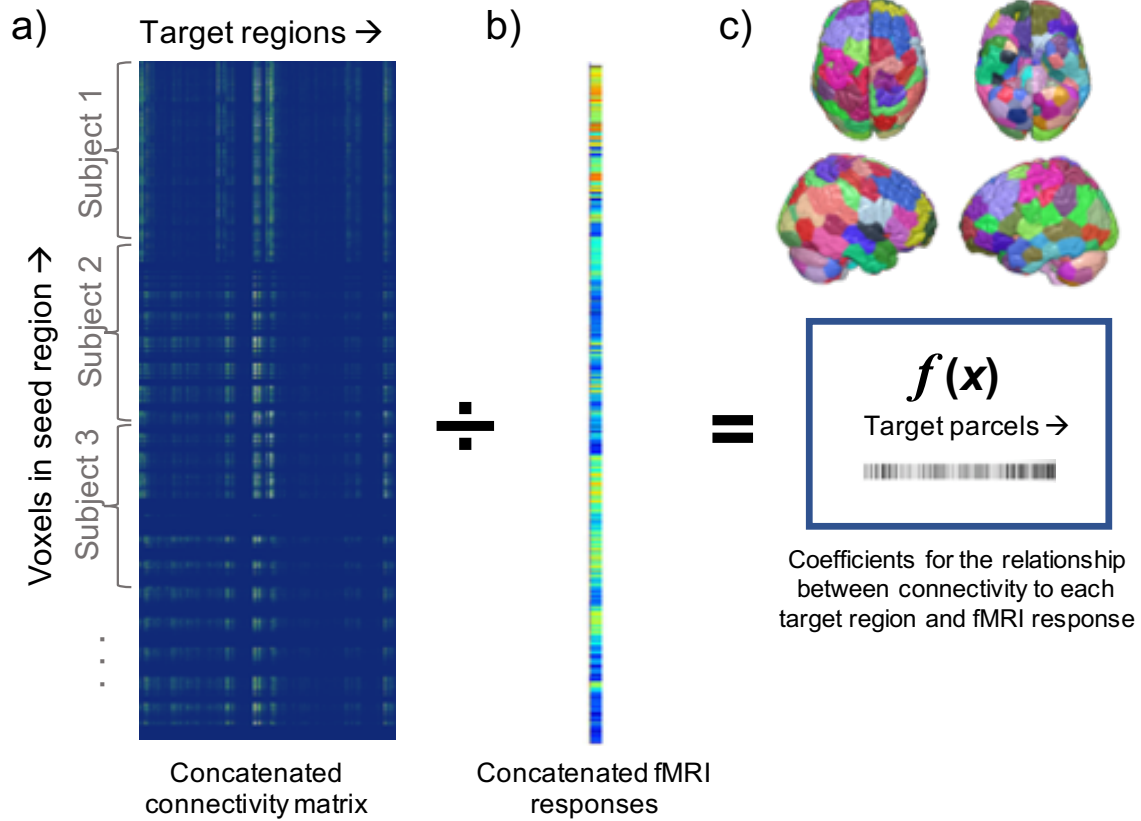
across all participants and columns represent connectivity of the voxel to target regions) for all but the left-out participant. Next, the relationship between the fMRI response of a voxel and its DTI connectivity was modeled using a linear regression implemented by the scikit-learn linear regression library of the Python language (Pedregosa et al., 2011). This resulted in a 1×267 vector of coefficients relating the relevance of the DTI connectivity from the seed parcel to each of the target parcels for predicting the fMRI response in the seed parcel. We then applied these coefficients to the $N \times 267$ DTI connectivity of the left-out subject, resulting in a predicted fMRI value for each voxel of the left-out participant's seed parcel.

This procedure was repeated for each of the 268 seed regions of the Shen et al. (2013) atlas and concatenated in order to produce predictions for the entire brain of the left-out participant. We then compared the activation predicted by the model to the participant's actual fMRI activation images for each contrast and calculated the absolute error (AE; i.e., the absolute value of actual minus predicted activation) for each voxel. Finally, we created a model using all fifteen participants from Group 1's DTI connectivity and fMRI data that we then applied to the other 15 independent participants in Group 2.

Group 2

The overall model coefficients from all fifteen participants in Group 1 were then applied to an independent group of subjects' ($N = 15$) individual DTI connectivity data to produce predicted fMRI maps in a similar way to Group 1. We then calculated prediction accuracies by examining the AEs between actual and predicted activation (in the same way as Group 1).

Training



Testing on independent data

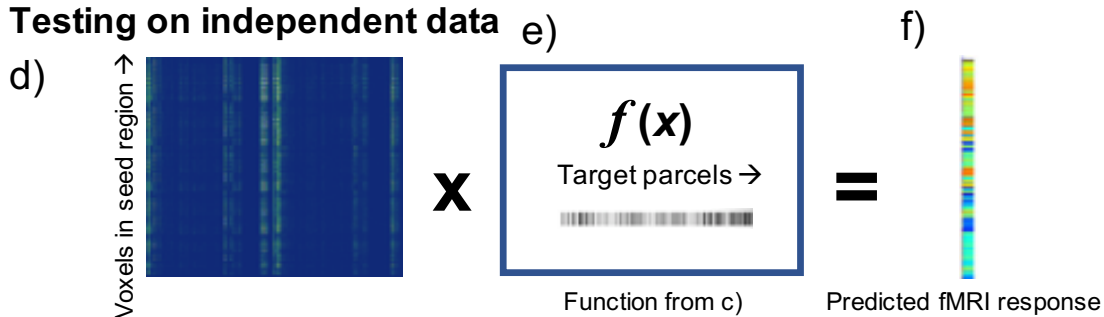


Figure 3.1. Overview of the modeling procedure. Each participant's brain was first divided into 268 regions from the Shen et al. (2013) atlas, as shown by the colored brain in c). Each region was then modeled separately using the following procedure: a) Voxel-wise DTI connectivity from the modeled region to the remaining 267 regions was concatenated for all but one participant (i.e., the left-out participant). b) fMRI t-statistic values corresponding to each of the voxels in a) are concatenated for all but the left-out participant. c) A linear regression (represented by \div) models the relationship between DTI connectivity in a) and fMRI activity in b). This results in a vector of coefficients (depicted as a greyscale vector) of length 267 (i.e., the number of columns in a) representing each target region) reflecting the contribution of each target

region to predicting the fMRI response. d) The left-out participant also has a DTI connectivity matrix with 267 columns that e) the function, $f(x)$, from c) is applied to each voxel in the left-out participants connectivity matrix resulting in f) a vector of predicted fMRI activation for each voxel. Predicted responses are then compared with the actual fMRI responses for each voxel. This procedure is then repeated for each of the other 267 seed regions in c) for each participant, with every participant in Group 1 left out iteratively in order to generate independent predictions for each participant. To predict fMRI activation for Group 2, a final model, $f(x)$, is generated from all of Group 1's voxelwise connectivity and fMRI data, which is then applied to each participant in Group 2. This entire procedure is repeated for each contrast (i.e., EW, PH, EW > PH, PH > EW).

3.2.1.7 Model Validation

In order to assess the validity of our generated models, we compared the performance of our connectivity models to group activation models both across the cortex as well as in specific ROIs. The SciPy (Jones et al., 2001, <http://www.scipy.org>) Stats module was used to compare mean AEs (MAEs; i.e., the average of all AEs across the brain) between the connectivity and group activation models, as discussed below.

Comparison to Group Activation Models

Group activation models were also created using LOOCV using a similar technique to Osher et al. (2016). First, each participant's functional data was transformed into standardized MNI space using FSL's *flirt*. All participants except the left-out participant's fMRI images in standardized space were then superimposed to create composite maps (i.e., the predicted activation for the left-out participant was the average activation from all other participants in the group). We then used this group averaged fMRI image as the input to FSLs FEAT using the same contrasts as those used on the individual subject data. This resulted in t -statistic images for each of the contrasts (i.e., EW, PH, EW > PH, PH > EW). This predicted image was then transformed back into the left out participant's native space and AEs and the MAE was calculated. This was repeated for each of the participants in Group 1 to create 15 independent predictive models based on group activation.

For Group 2, the group activation model was created from the average activation for all of the subjects in Group 1, and the resulting model was transformed to each participant's native space in a similar way as for Group 1.

Regions of Interest

Each participant's whole-brain AE images were then transformed to the MNI 152 T1 2-mm template using FSLs *flirt* to ensure all ROIs were comparable across participants. Regions of interest were derived from parcels in the Shen et al. (2013) 268-region parcellation in the participant's native space and corresponded to the left VWFA (four regions: Shen 198, 199, 200, 201), IFG (two regions: Shen 151, 156), and temporoparietal regions (two regions: Shen 182, 183). Further, based on the proposed integral role of spatial attention in reading and the importance of right hemisphere white matter tracts in skilled reading, we also examined the ability of our model to predict activation in primary spatial attentional regions. Specifically, in the ventral stream we examined the right IFG (two regions: Shen 16, 19) and TPJ (two regions: Shen 47, 48), and in the dorsal stream the right FEF (Shen 32) and SPL/IPS (Shen 43), thus resulting in a total of 14 ROIs.

AEs for each region were calculated in a similar way to the whole-brain connectivity versus group average fMRI comparison. A voxel-wise paired-sample t-test was performed per participant across all gray-matter voxels in each ROI. A Bonferroni-corrected threshold of $p < 0.05/(\text{total number of subjects in both groups times the number of ROIs}) = 1.19 \times 10^{-4}$ was used to determine the number of participants whose activation pattern was better predicted by the connectivity than the group average activation model. We also calculated MAEs over all of the voxels in each ROI (i.e., the average activation in each ROI) for each participant and performed a paired-sample t-test with all of the participants in each group using a Bonferroni-corrected threshold of $p < 0.05/(14 \text{ ROIs}) = 3.57 \times 10^{-3}$. We then used a sign test to determine whether a significant number of participants showed better prediction accuracy for the connectivity model than the group average model for each region and contrast, whereby significance in a region occurs if 12 of the 15 participants (80%) in each group show better connectivity for the DTI model than group average model ($\chi^2 = \sum((O_i - E_i)^2 / E_i) = (((12 - 7.5)^2) + ((3 - 7.5)^2)) / 7.5 = 5.4, 5.4 > \chi^2_{\text{crit}}(1) = 3.84$).

3.2.2 Results

3.2.2.1 Predicted neural responses from DTI modeling across all grey-matter voxels

First, we concatenated the 268 predicted region images from the DTI connectivity based model for each participant, which represented whole-brain predictions from each of the models. Then, AEs were calculated by finding the absolute value of the actual fMRI activation minus the predicted activation for every voxel in each participant's native space. MAEs were calculated by finding the average of all AEs across the whole brain for each participant. We repeated this procedure for the group average fMRI model (which also yielded voxelwise predictions). We then compared the prediction accuracy between the DTI connectivity and group average fMRI models. Figure 3.2 shows the fMRI activation of the most functionally specific voxels (i.e., top 5 percent; Osher et al., 2016) for each contrast of both the predicted and actual results for a single participant, in which the predicted results show a strikingly similar pattern to the actual fMRI response (see Appendix C for actual versus predicted results for all other participants). This suggests that individual subject activation patterns can be predicted from their DTI connectivity patterns. This is supported by our measures of prediction accuracy, reported below.

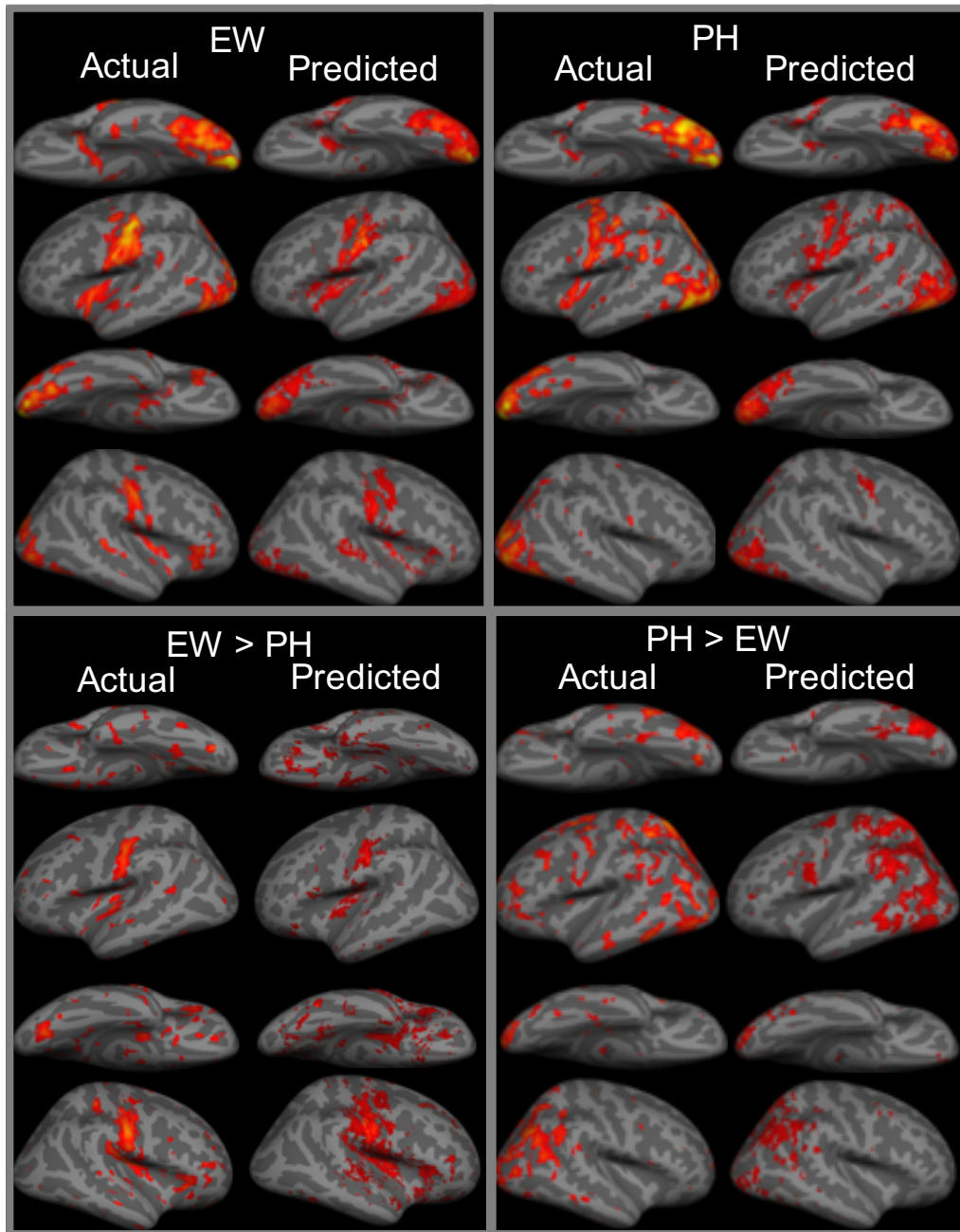


Figure 3.2. Representative actual versus predicted (from the connectivity model) activation for a single participant. Activation shows the most functionally selective voxels for each contrast (i.e., the top 5% of activation). The top two rows of brains for each contrast are the left hemisphere, the bottom two the right hemisphere.

EW Reading

EW reading typically elicits activation in a ventral occipito-temporal circuit of brain regions that includes the VWFA in the left fusiform gyrus, lateral extrastriate regions, and inferior temporal gyrus, as well as language and phonological output areas including the left IFG and TPJ (e.g., Experiments 1, 2, and 3; Borowsky et al., 2006, 2007; Cummine et al., 2012, 2015; Taylor et al., 2013). Figure 3.2 shows concordance between the predicted and actual responses, particularly in the left fusiform gyrus.

Comparison to group average activation. *Group 1:* Averaging across all grey matter voxels for all participants, the model created from DTI connectivity showed significantly lower MAEs than the model created from group fMRI activation, $t(14) = -29.08$, $p = 6.41 \times 10^{-14}$ (see Figure 3.3 for means and standard deviations for the EW contrast).

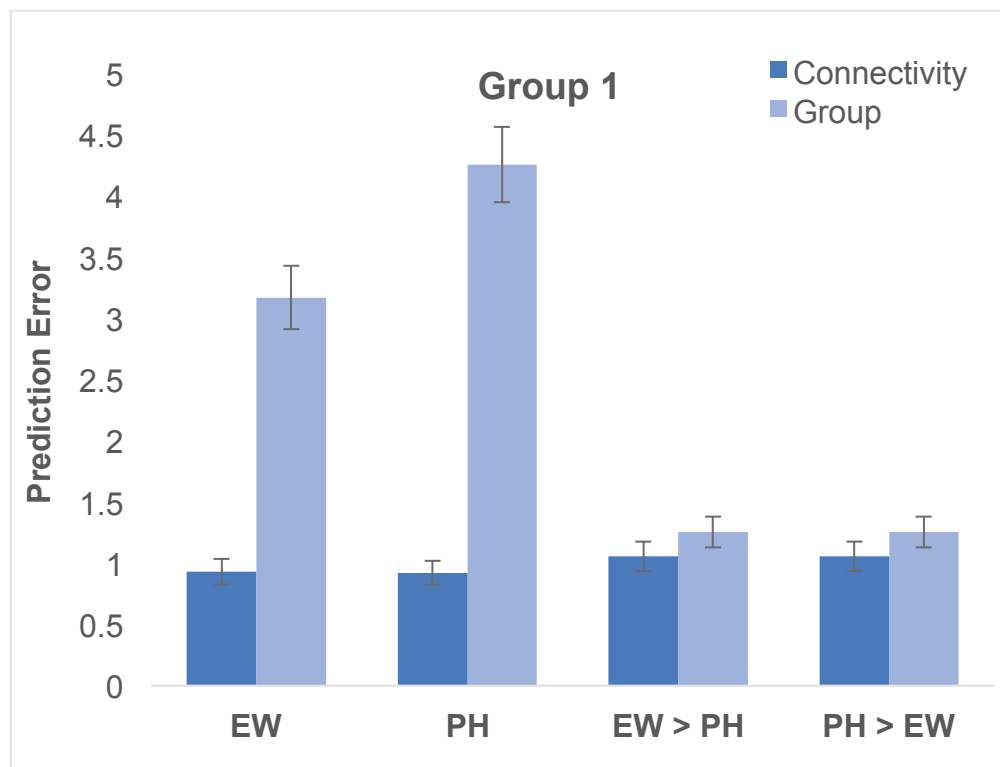


Figure 3.3. Mean prediction errors and comparison to the group average benchmark model as a function of predictive model (i.e., connectivity versus group fMRI average) for Group 1. Prediction error represents the mean absolute errors across all cortical voxels, error bars represent the standard deviation. Predictions from the connectivity models were significantly more accurate than predictions from the group-fMRI models in all conditions.

Group 2: Similar to Group 1, across all cortical voxels, the model created from DTI connectivity showed significantly lower MAEs than the model created from group fMRI activation, $t(14) = -35.04$, $p = 4.87 \times 10^{-15}$ (see Figure 3.4).

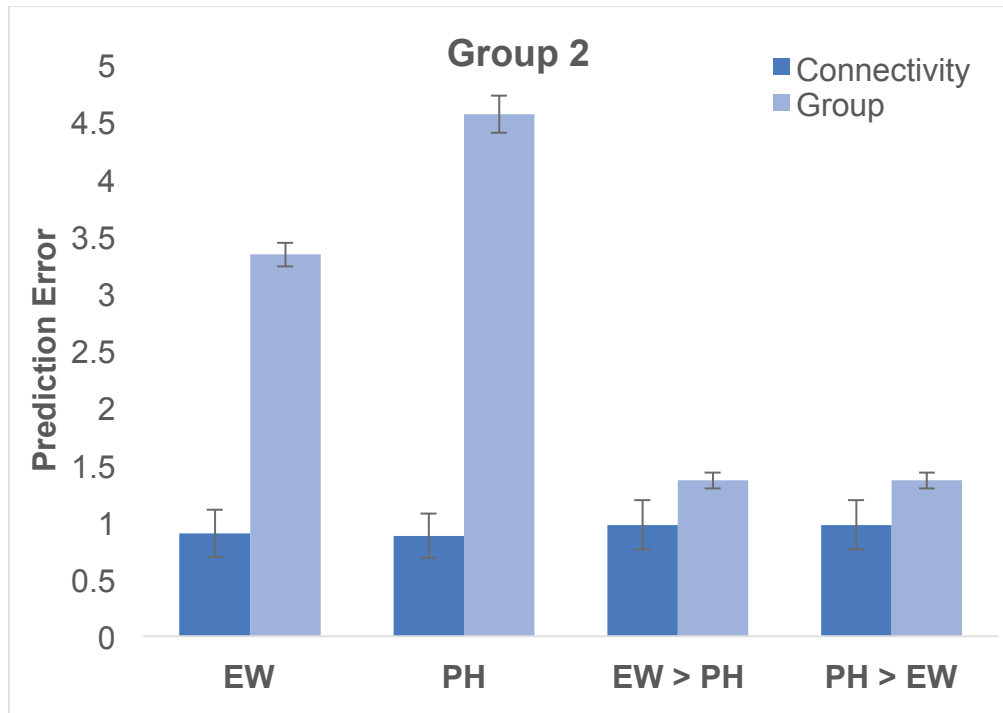


Figure 3.4. Mean prediction errors and comparison to the group average benchmark model as a function of predictive model (i.e., connectivity versus group fMRI average) for Group 2. Prediction error represents the mean absolute errors across all grey matter voxels. Predictions from the connectivity models were significantly more accurate than predictions from the group-fMRI models.

PH Reading

Phonetic decoding has been shown to rely more strongly on dorsal stream regions as well as the left IFG (i.e., Broca's area) and the posterior STG, angular gyrus, and supramarginal gyrus (see Experiments 1, 2, 3; Taylor et al., 2013; Cummine et al., 2012, 2015; Borowsky et al., 2006, 2007). Figure 3.2 shows highly similar activation in ventral stream areas including the left

fusiform gyrus, and dorsal stream areas including the angular and supramarginal gyri, and posterior parietal regions for the actual vs. predicted results of an example participant.

Comparison to group average activation. Group 1: Similar to the EW task, averaging across all grey matter voxels, the model created from DTI connectivity showed significantly lower MAEs than the model created from group fMRI activation, $t(14) = -35.37, p = 4.29 \times 10^{-15}$ (see Figure 3.3 for means and standard deviations).

Group 2: Similar to Group 1, across all grey matter voxels, the model created from DTI connectivity showed significantly lower MAEs than the model created from group fMRI activation, $t(14) = -44.72, p = 1.65 \times 10^{-16}$ (see Figure 3.4).

EW > PH

Contrasts between the EW and PH conditions were also assessed in order to determine whether DTI connectivity patterns are able to capture individual differences in lexical versus sublexical processing. Typically, lexical reading has been shown to elicit greater activation than sublexical reading in ventral stream areas including the parahippocampal and fusiform gyri, and MTG, as well as the posterior cingulum and precuneus, angular gyrus, gyrus rectus, and medial orbitofrontal cortex (Taylor et al., 2013; see also Carreiras, Armstrong, Perea, & Frost, 2014; see Price, 2012 for a review; see Figure 3.2).

Comparison to group average activation. Group 1: The model created from DTI connectivity showed significantly lower MAEs than the model created from group fMRI activation, $t(14) = -4.08, p = 1.13 \times 10^{-3}$ (see Figure 3.3 for means and standard deviations).

Group 2: Once again, the model created from DTI connectivity showed significantly lower MAEs than the model created from group fMRI activation, $t(14) = -8.22, p = 1.00 \times 10^{-6}$ (see Figure 3.4).

PH > EW

Pseudowords have been shown to elicit greater activation than real words in the posterior fusiform gyrus, occipitotemporal cortex, precentral gyrus, left IFG (i.e., Broca's area), SMA, superior temporal pole, left insula, left parietal cortex, and right inferior parietal cortex (e.g., Taylor et al., 2013). Further, PHs elicit greater activation in the left inferior/superior frontal and middle temporal gyri, left insula, and left SPL than pseudowords (Braun et al., 2015), as well as the angular and supramarginal gyri, and IPL (Borowsky et al., 2006). Figure 3.2 shows the voxels with t-statistics in the top 5 percent for the PH > EW contrast across the brain. Because this

contrast is the reverse of the EW > PH contrast, the MAE comparison statistics are the same for both groups as the EW > PH contrast.

3.2.3 Connectivity-based predictions of neural responses within regions of interest

Results from our ROI analysis in the most functionally specific regions showed that, when examining MAEs using a paired-sample t-test across all participants, the connectivity-based model outperformed the group average model for each ROI in the EW and PH contrasts for both Group 1 (Table 3.1) and Group 2 (Table 3.2). Further, when examining voxel-wise comparisons for each participant in each ROI, we found that, for Group 1, connectivity models outperformed the group average models for the majority of participants for ROIs in both word reading (see Figure 3.5) and attention areas (see Figure 3.6), with the majority of contrasts showing 100% of participants better predicted by connectivity models than group activation models. Group 2 showed similar results, with the majority of participants with lower AEs from the connectivity model than the group activation model in word reading areas (see Figure 3.7) and attention areas (see Figure 3.8), and the majority of contrasts showing 100% of participants fMRI activation being more accurately predicted by the connectivity based model.

Table 3.1. Results for Group 1 of the paired samples t-tests comparing connectivity MAEs to group activation MAEs for each ROI and contrast.

Contrast	ROI	Location	Function	Connectivity MAE (SD)	Group MAE (SD)	<i>t</i>	<i>p</i>
EW	16	R IFG	Ventral Attention	0.55 (0.09)	4.31 (1.42)	-10.03	9.02×10^{-8}
	19	R IFG	Ventral Attention	0.60 (0.19)	3.72 (1.38)	-8.68	5.21×10^{-7}
	32	R FEF	Dorsal Attention	0.75 (0.23)	4.72 (1.29)	-11.43	1.75×10^{-8}
	43	R SPL/IPS	Dorsal Attention	0.80 (0.34)	5.00 (0.91)	-16.69	1.23×10^{-10}
	47	R TPJ	Ventral Attention	0.75 (0.30)	2.86 (0.83)	-8.71	5.05×10^{-7}
	48	R TPJ	Ventral Attention	0.72 (0.42)	2.07 (0.52)	-6.54	1.31×10^{-5}
	151	L IFG	Speech Production	0.73 (0.28)	3.51 (1.00)	-10.20	7.33×10^{-8}
	156	L IFG	Speech Production	0.76 (0.19)	6.11 (1.81)	-10.37	5.93×10^{-8}
	182	L TPJ	Comprehension	0.90 (0.32)	2.89 (0.78)	-8.51	6.61×10^{-7}
	183	L TPJ	Comprehension	0.86 (0.21)	3.95 (1.62)	-6.97	6.52×10^{-6}
	198	L Fusiform	Word Recognition	1.00 (0.24)	2.86 (1.12)	-5.83	4.40×10^{-5}
	199	L Fusiform	Word Recognition	0.80 (0.31)	2.66 (1.78)	-3.86	1.74×10^{-3}

	200	L Fusiform	Word Recognition	1.01 (0.62)	4.90 (1.25)	-10.70	4.00×10^{-8}
	201	L Fusiform	Word Recognition	0.80 (0.42)	3.01 (1.48)	-4.96	2.11×10^{-4}
PH	16	R IFG	Ventral Attention	0.57 (0.15)	5.59 (1.53)	-12.53	5.36×10^{-9}
	19	R IFG	Ventral Attention	0.66 (0.25)	5.59 (1.62)	-11.60	1.45×10^{-8}
	32	R FEF	Dorsal Attention	0.86 (0.26)	7.32 (1.25)	-17.95	4.63×10^{-11}
	43	R SPL/IPS	Dorsal Attention	0.98 (0.43)	8.13 (1.12)	-19.53	1.48×10^{-11}
	47	R TPJ	Ventral Attention	0.90 (0.33)	4.79 (1.18)	-12.93	3.58×10^{-9}
	48	R TPJ	Ventral Attention	0.85 (0.37)	3.34 (0.80)	-10.19	7.39×10^{-8}
	151	L IFG	Speech Production	1.31 (1.63)	4.65 (1.49)	-5.18	1.38×10^{-4}
	156	L IFG	Speech Production	0.95 (0.32)	7.21 (1.84)	-12.30	6.80×10^{-9}
	182	L TPJ	Comprehension	0.97 (0.29)	3.81 (1.11)	-9.21	2.57×10^{-7}
	183	L TPJ	Comprehension	0.88 (0.31)	3.93 (1.98)	-5.67	5.78×10^{-5}
	198	L Fusiform	Word Recognition	0.97 (0.21)	3.58 (1.79)	-5.32	1.09×10^{-4}
	199	L Fusiform	Word Recognition	0.71 (0.17)	3.61 (2.19)	-4.95	2.14×10^{-4}
	200	L Fusiform	Word Recognition	1.08 (0.44)	6.62 (1.68)	-12.13	8.17×10^{-9}
	201	L Fusiform	Word Recognition	1.08 (0.57)	3.71 (1.99)	-4.63	3.87×10^{-4}
EW >	16	R IFG	Ventral Attention	0.65 (0.13)	1.33 (0.36)	-8.20	1.03×10^{-6}
PH	19	R IFG	Ventral Attention	0.79 (0.19)	1.59 (0.38)	-8.05	1.26×10^{-6}
PH >	32	R FEF	Dorsal Attention	0.86 (0.23)	1.88 (0.62)	-8.06	1.25×10^{-6}
EW	43	R SPL/IPS	Dorsal Attention	0.94 (0.30)	2.12 (0.47)	-10.11	8.18×10^{-8}
	47	R TPJ	Ventral Attention	1.11 (0.56)	1.92 (0.58)	-3.72	2.29×10^{-3}
	48	R TPJ	Ventral Attention	0.83 (0.15)	1.92 (0.47)	-8.13	1.14×10^{-6}
	151	L IFG	Speech Production	1.12 (1.29)	1.22 (0.30)	-0.33	<i>0.75 n.s.</i>
	156	L IFG	Speech Production	0.97 (0.33)	1.37 (0.29)	-3.07	8.37×10^{-3} <i>n.s.</i>
	182	L TPJ	Comprehension	0.87 (0.28)	1.64 (0.46)	-5.91	3.80×10^{-5}
	183	L TPJ	Comprehension	0.93 (0.26)	1.02 (0.20)	-1.99	<i>0.07 n.s.</i>
	198	L Fusiform	Word Recognition	0.92 (0.17)	1.49 (0.40)	-4.63	3.92×10^{-4}
	199	L Fusiform	Word Recognition	0.81 (0.12)	1.26 (0.44)	-3.63	2.73×10^{-3}
	200	L Fusiform	Word Recognition	1.07 (0.42)	1.54 (0.62)	-2.59	2.14×10^{-2} <i>n.s.</i>
	201	L Fusiform	Word Recognition	0.94 (0.43)	1.40 (0.38)	-3.16	6.98×10^{-3} <i>n.s.</i>

Note. SD = Standard deviation. Significance is assessed at a Bonferroni-corrected threshold of $p < 0.05/(14 \text{ ROIs}) = 3.57 \times 10^{-3}$.

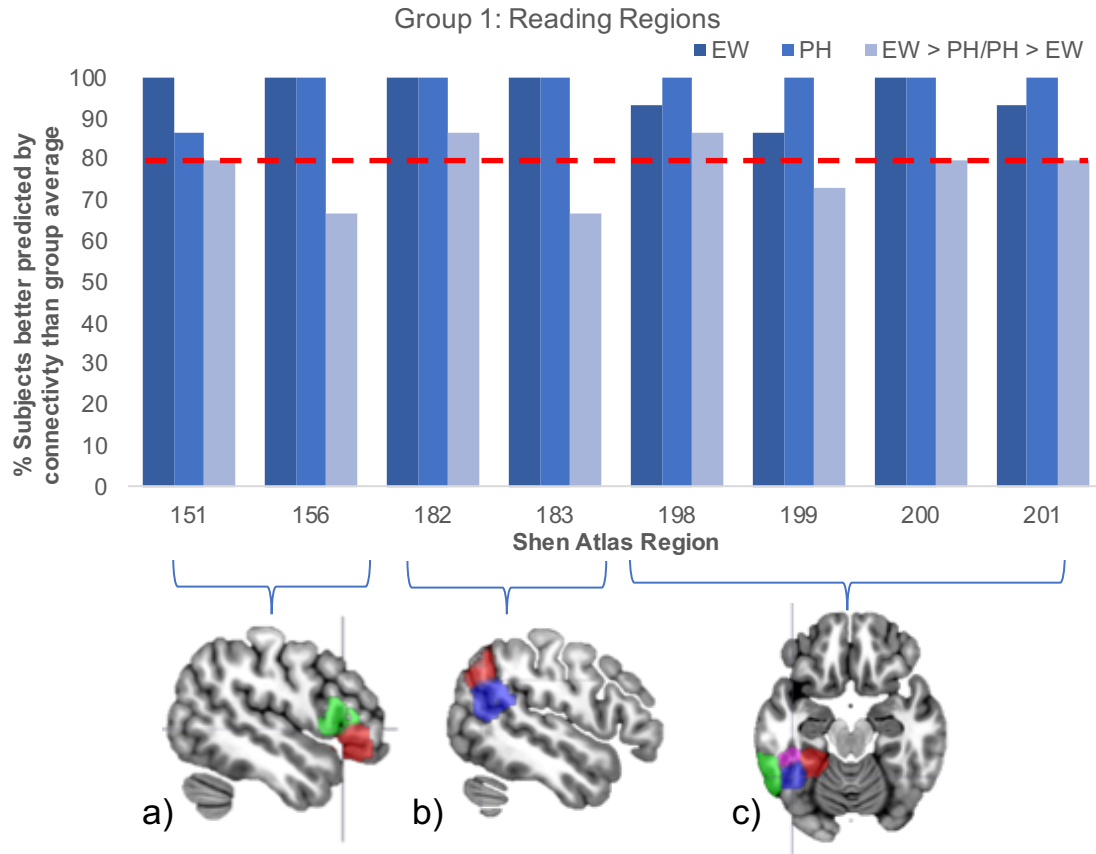


Figure 3.5. Predictive accuracy in ROIs associated with reading across subjects in Group 1 for the connectivity versus group activation average models. a) ROIs in the left IFG: Shen 151 shown in red, Shen 156 shown in green. b) ROIs in the left TPJ: Shen 182 shown in red, Shen 183 shown in blue. c) ROIs in the left fusiform gyrus: Shen 198 shown in red, 199 shown in green, 200 shown in blue, and 201 shown in purple. The red dashed line represents the percentage of participants necessary for a region to be significant based on our sign test (i.e., 80%).

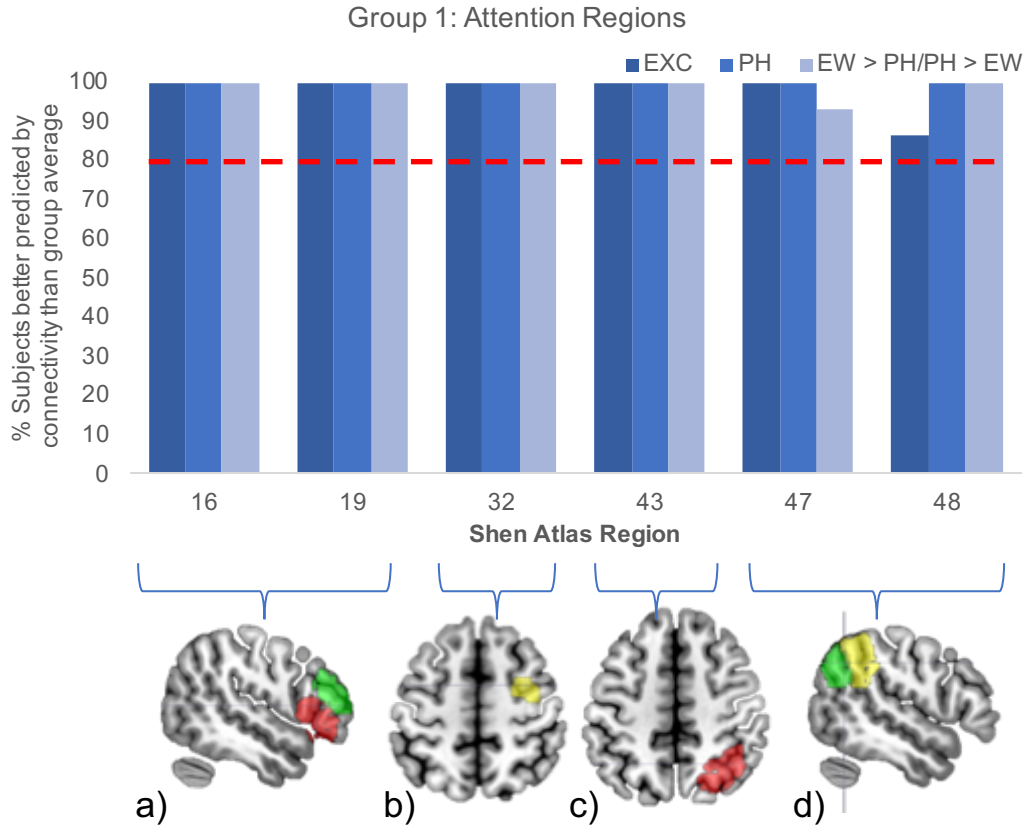


Figure 3.6. Predictive accuracy in ROIs associated with attention across subjects in Group 1 for the connectivity versus group activation average models. a) ROIs in the right IFG: Shen 16 shown in red, Shen 19 shown in green. b) ROI in the right FEF: Shen 32 shown in yellow. c) ROI in the right SPL/IPS: Shen 43 shown in red. d) ROIs in the right TPJ: Shen 47 shown in yellow, Shen 48 shown in green. The red dashed line represents the percentage of participants necessary for a region to be significant based on our sign test (i.e., 80%).

Table 3.2. Results for Group 2 of the paired samples t-tests comparing connectivity MAEs to group activation MAEs for each ROI and contrast.

Contrast	ROI	Location	Function	Connectivity MAE (SD)	Group MAE (SD)	<i>t</i>	<i>p</i>
EW	16	R IFG	Ventral Attention	0.66 (0.17)	4.90 (0.58)	-24.55	6.57×10^{-13}
	19	R IFG	Ventral Attention	0.61 (0.16)	3.95 (0.40)	-25.87	3.21×10^{-13}
	32	R FEF	Dorsal Attention	0.62 (0.23)	5.13 (0.42)	-31.49	2.13×10^{-14}

	43	R SPL/IPS	Dorsal Attention	0.73 (0.20)	6.00 (0.35)	-53.34	1.42×10^{-17}
	47	R TPJ	Ventral Attention	0.67 (0.22)	2.48 (0.25)	-17.48	6.59×10^{-11}
	48	R TPJ	Ventral Attention	0.72 (0.33)	1.52 (0.17)	-10.79	3.60×10^{-8}
	151	L IFG	Speech Production	0.66 (0.25)	3.77 (0.60)	-15.39	3.63×10^{-10}
	156	L IFG	Speech Production	0.73 (0.15)	6.22 (0.66)	-28.41	8.84×10^{-14}
	182	L TPJ	Comprehension	0.73 (0.16)	2.51 (0.18)	-37.33	2.03×10^{-15}
	183	L TPJ	Comprehension	0.79 (0.26)	3.53 (0.36)	-21.27	4.67×10^{-12}
	198	L Fusiform	Word Recognition	0.91 (0.29)	2.56 (0.29)	-15.07	4.80×10^{-10}
	199	L Fusiform	Word Recognition	0.62 (0.12)	2.01 (0.16)	-22.29	2.46×10^{-12}
	200	L Fusiform	Word Recognition	0.90 (0.24)	5.67 (0.38)	-35.02	4.91×10^{-15}
	201	L Fusiform	Word Recognition	0.72 (0.27)	3.09 (0.41)	-17.34	7.36×10^{-11}
PH	16	R IFG	Ventral Attention	0.64 (0.15)	6.10 (0.58)	-33.41	9.44×10^{-15}
	19	R IFG	Ventral Attention	0.62 (0.18)	6.44 (0.42)	-46.38	9.92×10^{-17}
	32	R FEF	Dorsal Attention	0.69 (0.21)	8.65 (0.61)	-45.73	1.21×10^{-16}
	43	R SPL/IPS	Dorsal Attention	0.78 (0.21)	9.67 (0.31)	-82.29	3.33×10^{-20}
	47	R TPJ	Ventral Attention	0.75 (0.18)	5.18 (0.39)	-37.98	1.60×10^{-15}
	48	R TPJ	Ventral Attention	0.86 (0.33)	3.16 (0.57)	-11.99	9.50×10^{-9}
	151	L IFG	Speech Production	0.60 (0.14)	4.70 (0.59)	-23.84	9.85×10^{-13}
	156	L IFG	Speech Production	0.70 (0.16)	7.96 (0.79)	-33.20	1.03×10^{-15}
	182	L TPJ	Comprehension	0.80 (0.17)	3.29 (0.60)	-16.60	1.32×10^{-10}
	183	L TPJ	Comprehension	0.72 (0.10)	3.69 (0.43)	-24.89	5.43×10^{-13}
	198	L Fusiform	Word Recognition	0.91 (0.27)	3.36 (0.55)	-13.21	2.70×10^{-9}
	199	L Fusiform	Word Recognition	0.74 (0.18)	3.06 (0.38)	-20.06	1.03×10^{-11}
	200	L Fusiform	Word Recognition	0.86 (0.18)	7.36 (0.43)	-44.72	1.65×10^{-16}
	201	L Fusiform	Word Recognition	0.76 (0.36)	3.35 (0.45)	-16.69	1.23×10^{-10}
EW >	16	R IFG	Ventral Attention	0.73 (0.23)	1.41 (0.27)	-10.81	3.52×10^{-8}
PH	19	R IFG	Ventral Attention	0.71 (0.17)	1.97 (0.33)	-18.78	2.52×10^{-11}
PH >	32	R FEF	Dorsal Attention	0.87 (0.39)	2.65 (0.38)	-11.91	1.03×10^{-8}
EW	43	R SPL/IPS	Dorsal Attention	0.87 (0.24)	2.29 (0.40)	-17.65	5.81×10^{-11}
	47	R TPJ	Ventral Attention	0.92 (0.34)	2.38 (0.43)	-23.69	1.07×10^{-12}
	48	R TPJ	Ventral Attention	1.02 (0.43)	2.45 (0.71)	-11.40	1.81×10^{-8}
	151	L IFG	Speech Production	0.75 (0.26)	1.15 (0.28)	-7.00	6.23×10^{-6}
	156	L IFG	Speech Production	0.86 (0.26)	1.45 (0.27)	-7.00	6.23×10^{-6}
	182	L TPJ	Comprehension	0.96 (0.56)	2.01 (0.76)	-4.83	2.68×10^{-4}
	183	L TPJ	Comprehension	0.83 (0.36)	1.09 (0.42)	-6.16	2.46×10^{-5}
	198	L Fusiform	Word Recognition	0.95 (0.23)	1.69 (0.32)	-7.46	3.07×10^{-6}
	199	L Fusiform	Word Recognition	0.78 (0.29)	1.48 (0.32)	-13.70	1.68×10^{-9}

200	L Fusiform	Word Recognition	0.93 (0.33)	1.39 (0.29)	-4.20	8.85×10^{-4}
201	L Fusiform	Word Recognition	0.80 (0.36)	0.98 (0.12)	-2.16	4.88×10^{-2} <i>n.s.</i>

Note. SD = Standard deviation. Significance is assessed at a Bonferroni-corrected threshold of $p < 0.05/(14 \text{ ROIs}) = 3.57 \times 10^{-3}$.

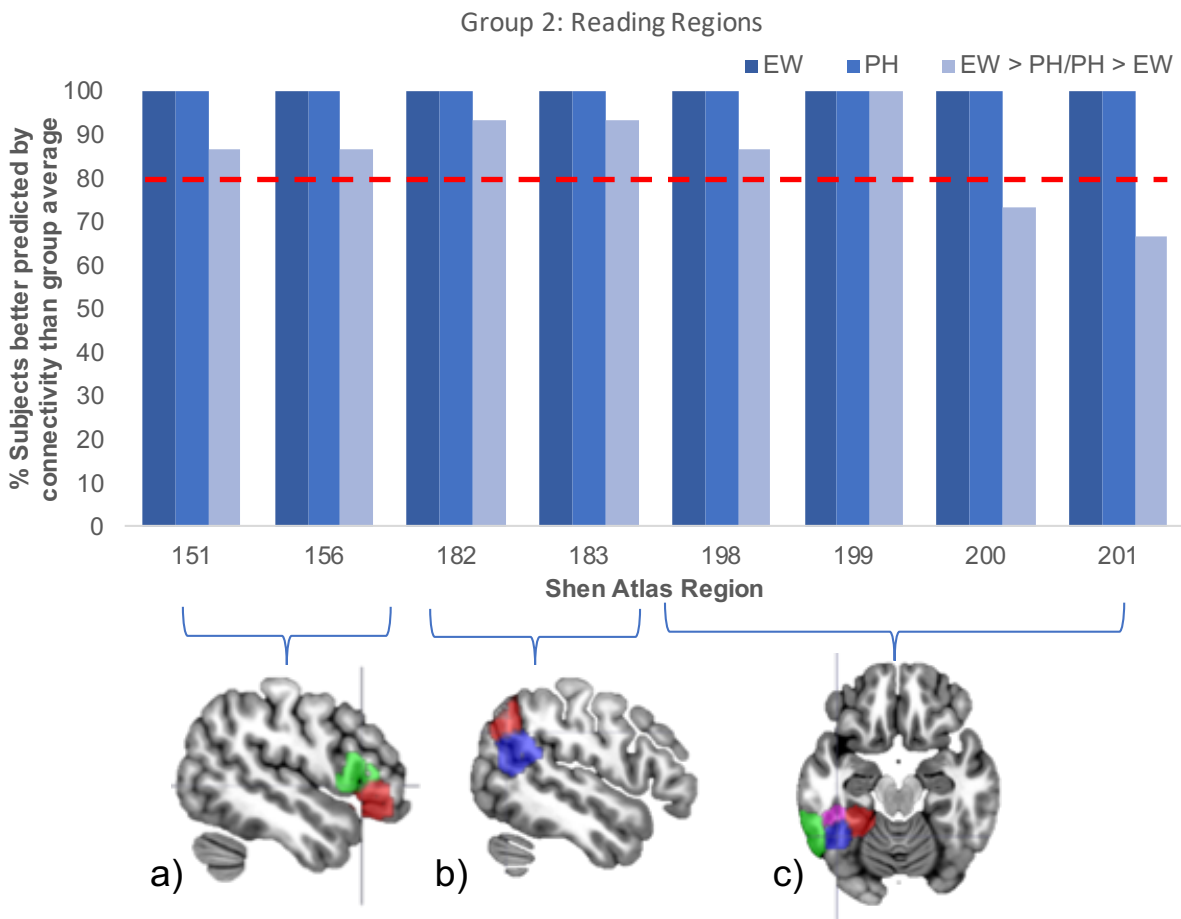


Figure 3.7. Predictive accuracy in ROIs associated with reading across subjects in Group 2 for the connectivity versus group activation average models. a) ROIs in the left IFG: Shen 151 shown in red, Shen 156 shown in green. b) ROIs in the left TPJ: Shen 182 shown in red, Shen 183 shown in blue. c) ROIs in the left fusiform gyrus: Shen 198 shown in red, 199 shown in green, 200 shown in blue, and 201 shown in purple. The red dashed line represents the percentage of participants necessary for a region to be significant based on our sign test (i.e., 80%).

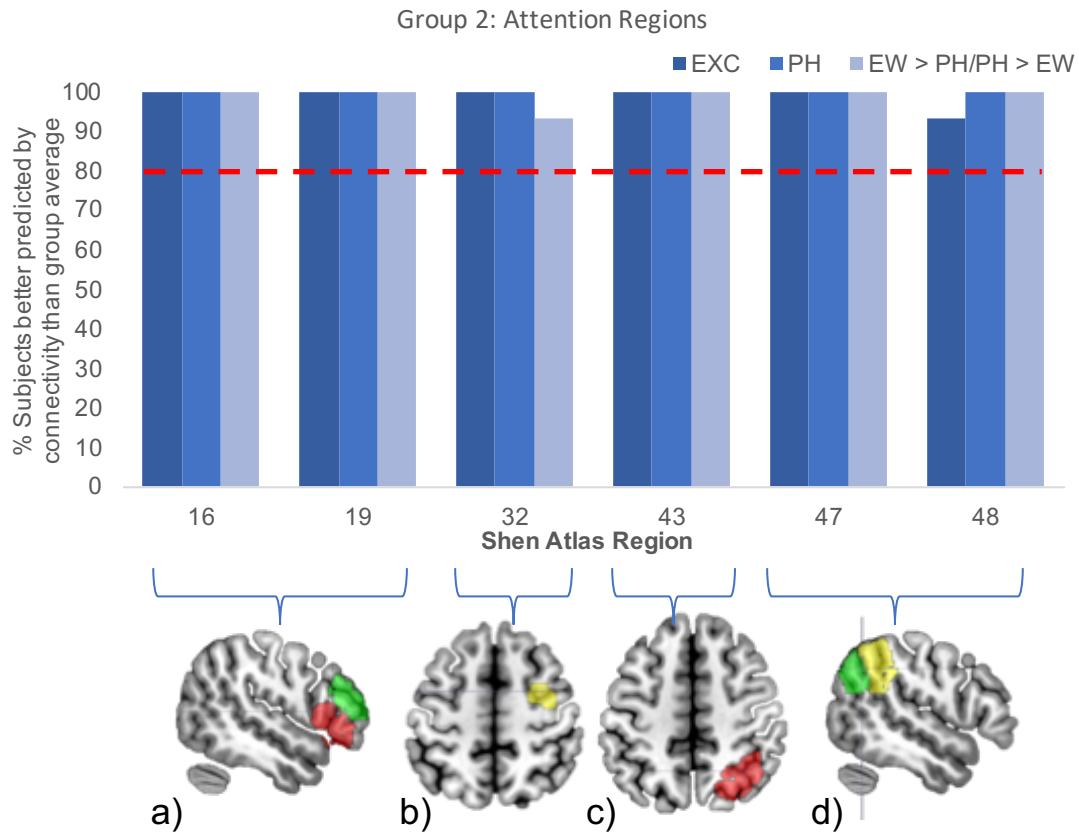


Figure 3.8. Predictive accuracy in ROIs associated with attention across subjects in Group 2 for the connectivity versus group activation average models. a) ROIs in the right IFG: Shen 16 shown in red, Shen 19 shown in green. b) ROI in the right FEF: Shen 32 shown in yellow. c) ROI in the right SPL/IPS: Shen 43 shown in red. d) ROIs in the right TPJ: Shen 47 shown in yellow, Shen 48 shown in green. The red dashed line represents the percentage of participants necessary for a region to be significant based on our sign test (i.e., 80%).

3.2.4 Interim Discussion: Chapter 3

3.2.4.1 Predicted neural responses from DTI modeling across all cortical voxels

Together, our findings suggest that fine-grained anatomical connectivity predicts the cognitive process of reading. When examining MAEs across all cortical voxels we found that predictions from the DTI connectivity model were significantly more accurate than predictions from the group fMRI activation model across all contrasts. This suggests that the voxelwise fMRI activation of an individual across the cortex can be predicted using only their structural connectivity. This corroborates the findings of Osher et al. (2016) suggesting that fine-grained structural connectivity fingerprints dictate functional activation (at least in part) and extends these findings into the domain of skilled word reading. These results were found not only for LOOCV participants in Group 1, but also for an independent group of subjects (Group 2). Results from each of our contrasts show that models created from DTI connectivity outperformed those created from group-average fMRI activation across the entire cortex and thus were better able to predict voxel-wise fMRI activity during both lexical and sublexical reading. A particularly exciting finding was that our connectivity model was also sensitive to differences between lexical and sublexical processing, suggesting that this technique is sensitive to detecting the differential structural networks that underlie lexical and sublexical reading.

3.2.4.2 Connectivity-based predictions of neural responses within ROIs

We also examined the performance of our connectivity-based model at predicting neural responses in ROIs. First, we examined ROIs in brain areas known to be involved in reading and language, which included the left fusiform gyrus (i.e., VWFA), IFG, and TPJ. When comparing mean ROI prediction accuracies from our connectivity model to the group activation model at the group level (i.e., MAEs across participants), we found that the connectivity model outperformed the group activation model for all of the ROIs during both lexical and sublexical reading for Group 1 (Table 3.1) and Group 2 (Table 3.2). For the lexical versus sublexical (EW > PH) reading contrast, all ROIs were significant at the group comparison level (Table 3.1), with the following exceptions: both ROIs in the left IFG (Shen 151 and 156; pars triangularis and pars opercularis of the IFG, respectively), one ROI in the left TPJ (Shen 183; angular gyrus), and two ROIs in the left fusiform gyrus (Shen 200 and 201). When examining voxel specific differences at the individual subject level (Figure 3.5), we found that for all reading ROIs, at least 66.7% of subjects' task-based fMRI activation was better predicted by the connectivity model than the

group activation model, with the majority of regions showing 100% of the participants better predicted by the connectivity model. Further, 21 of the 24 contrasts were found to be significant based on the sign test.

For Group 2, across all subjects, we found that connectivity based predictions outperformed group activation predictions for all ROIs in all contrasts except Shen region 201 in the left fusiform gyrus in the $EW > PH/PH > EW$ contrast (Table 3.2). When examining voxelwise differences at the individual level for each ROI (Figure 3.7), at least 66.7% of subjects showed better prediction accuracies for the connectivity model than the group activation model, again with the majority of regions showing 100% of the participants better predicted by the connectivity model. Further, 22 of the 24 contrasts were found to be significant based on the sign test. Together, these findings show that specific structural connectivity patterns to ROIs associated with reading and language play an important role in dictating subsequent fMRI activation during lexical and sublexical reading.

As the integral role of visuospatial attention in word reading has recently been stressed in the research literature, we also chose to examine whether connectivity models could better predict reading task based fMRI activation than group activation models in ROIs associated with spatial attentional processing in the right dorsal (right SPL/IPS and right FEF) and ventral (right TPJ and right IFG) streams. For Group 1, at the group level (Table 3.1), all regions showed significantly lower MAEs for connectivity model predictions versus group activation model predictions. This is supported by findings at the individual subjects level (Figure 3.6), whereby all ROIs had at least 86.7% of participants better predicted by the connectivity model than the group activation model, with most ROIs having 100% of subjects better predicted by connectivity than group activation. Findings from Group 2 were similar, whereby all regions showed significantly lower MAEs for the connectivity model versus the group activation model (Table 3.2), and at least 93.3% of participants better predicted by connectivity than group activation for all ROIs and contrasts (Figure 3.8). Further, all ROIs and contrasts were found to be significant based on the sign test. These findings highlight the importance of spatial attention in reading, as activation in these regions can be accurately predicted from models of lexical and sublexical reading.

These results extend the work of Saygin et al. (2012) that examined face processing in the fusiform gyrus, and Osher et al. (2016) that examined face, body, scene, and object processing

across the cortex, into the processing domain of skilled reading. They are also in concordance with the findings of Saygin et al. (2016), which showed that connectivity to the VWFA (even prior to reading development) can predict subsequent fMRI activation in that area. We extend these findings not only to the entire cortex (i.e., by modeling 268 different brain regions that spanned cortical grey matter), but importantly, to skilled, adult readers. In addition, the atlas used in our experiment (i.e., the Shen et al., 2013 268 node parcellation) provides a higher resolution parcellation than the Destrieux 148 node atlas (Destrieux, Fischl, Dale, & Halgren, 2010) used by Osher et al. (2016), thus providing a more fine-grained examination of structure and function. Results from our region of interest analysis of the left fusiform gyrus show that distinct connectivity patterns exist in adulthood that account for a significant amount of variance in reading fMRI activation. As this region is critically important for reading, this suggests that a distinct structural connectivity pattern to this region underlies word processing. Further, we also show that activation of other regions integral to language and reading (i.e., the left IFG and TPJ) have connectivity biomarkers that allow for accurate prediction from DTI connectivity alone.

Our findings support the idea that reading ability is reliant on adequate development of the underlying structural connectivity to regions that make up the language and reading networks. This conclusion is supported by the work of Vanderauwera et al. (2018) and Wang et al. (2016) who found that pre-reading tract integrity is an important predictor of subsequent reading outcomes, as well as Saygin et al. (2013) who found that white matter tract volume in key language pathways played an important role in reading development. Further, our model provides exciting insights into the nature of reading impairments by uncovering patterns in structural connectivity associated with skilled reading in adult readers that can serve as biomarkers for identifying reading deficits. Thus, our model may have the potential to help identify those at risk for reading impairments based on their early structural connectivity biomarkers (similar to Saygin et al., 2016), which may have implications for targeting remediation strategies (e.g., through spatial attentional training, see Franceschini et al., 2015, 2017).

Our connectivity model was also able to successfully predict activation in known attention areas in the dorsal and ventral streams, lending support to the idea that spatial attention is an integral component of reading. This is in concordance with the findings of Experiments 1, 2, and 3 showing that spatial attention is differentially associated with reading strategy (i.e., lexical versus sublexical). Our results provide evidence that the underlying structural network

architecture involving attention related regions predicts the involvement of attentional orienting regions (as indexed by fMRI activation in reading tasks) during lexical and sublexical reading. This supports research that has found that white matter connectivity in the right hemisphere plays an important role in reading (Catani & Mesulam, 2008; Horowitz-Kraus et al., 2015), as well as research using spatial attentional training as an effective reading intervention (Franceschini et al., 2015, 2017). Future research should continue to examine the roles that right hemisphere connectivity and the attentional system play in skilled reading.

Importantly, these connectivity based models can better account for individual variability in fMRI activation than group models, which has a myriad of implications for both basic research and clinical applications. For example, this technique of modeling DTI connectivity with task-based fMRI activation may help to uncover characteristic structural connectivity associated with specific cognitive functions that accommodates individual differences. This technique could also be used to develop universal models relating brain structure to function using large databases such as the Human Connectome Project (<http://www.humanconnectome.org>) in order to characterize consistent patterns of structural connectivity that underlie specific neural responses. Further, it may provide a valuable clinical tool for uncovering language and reading networks in patients for whom which functional imaging cannot be performed (e.g., patients who require sedation in the MRI, who are unresponsive/comatose, or are unable to perform the tasks required for functional scanning) from their DTI connectivity alone. Future research should assess the efficacy of these models for predicting functional brain responses in patient groups, including those who may have irregular or compromised network connectivity.

In summary, we show that brain activation during both lexical and sublexical reading in skilled readers can be accurately predicted using DTI connectivity. This finding extends to known reading and language areas including the left IFG (i.e., Broca's area), left TPJ, and the VWFA, as well as important spatial attentional areas including the right TPJ, IFG, IPS/SPL, and FEF. This research broadens our understanding of the underlying structural biomarkers that potentiate skilled reading and has important implications for understanding reading impairment. It may also have clinical implications for aiding localization of language and reading function in patients where functional neuroimaging is not possible. Thus, this research suggests that there is a fine-grained relationship between skilled reading and extrinsic brain connectivity, suggesting that functional organization of reading and language can be determined (at least in part) by structural

connectivity patterns. We hope this work will serve as an impetus to examining the structural biomarkers of skilled reading to help broaden our understanding of this essential cognitive process.

CHAPTER 4

GENERAL DISCUSSION

Portions of this chapter have been previously published or submitted for publication. Redundant information has been removed:

Ekstrand, C., Neudorf, J., Gould, L., Mickleborough, M., & Borowsky, R. (2019). Where words and space collide: The overlapping neural activation of lexical and sublexical reading with voluntary and reflexive spatial attention. *Brain Research, 1706*, 1-12. © 2018 Elsevier B.V. All rights reserved.

Reading is a relatively recent human invention that, unlike other cognitive skills (such as speech), requires effortful, explicit instruction in order to be successful. Interestingly, however, while there might be great variability in reading instruction, writing systems, and even processing modality (e.g., alphabetic scripts versus Braille), the cognitive and neural architecture of the reading network appears to develop approximately the same across individuals (e.g., Perfetti, 2011; Rueckl et al., 2015). This suggests that there is a consistent underlying functional and structural neural architecture that potentiates the development of skilled reading. However it is also clear that, even amongst skilled readers, there is heterogeneity of reading processes (Andrews, 2012) that are associated with consistent differences in neural activation (Welcome & Joanisse, 2012). This suggests that there is not a simple, unitary definition of skilled reading, and, instead, that skilled reading may come in many different forms. Thus, this thesis sought to investigate the differential cognitive and structural contributions to single word reading in skilled readers, with a specific focus on lexical and sublexical processing, visuospatial attention (voluntary and reflexive), and individual DTI connectivity.

4.1 Summary of results from Chapter 2

Chapter 2 focused on unraveling the complex relationship between voluntary and reflexive attention and lexical and sublexical reading. Experiment 1 used a voluntary attentional cuing paradigm to examine the overlapping neural correlates of voluntary attention and lexical

reading of EWs and sublexical reading of PHs. PHs represent the optimal matched stimuli, as they do not differ from their real word counterparts on phonology or semantics, thus ensuring that any processing differences are due solely to reading strategy. Results from this experiment showed that sublexical reading of PHs led to unique overlapping activation with voluntary attention in known voluntary attentional orienting regions outlined by Corbetta and Shulman (2002). Specifically, sublexical reading overlapped with voluntary attention in the bilateral SPL and IPS. The SPL has been primarily implicated in voluntarily tracking the locus of spatial attention (see Chica et al., 2013). Therefore, results from Experiment 1 support our hypothesis that sublexical reading requires phonemic assembly of the stimulus that is reliant on voluntary spatial attention in the dorsal stream. In contrast, lexical reading of EWs led to unique overlapping activation with voluntary attention in reflexive attentional orienting areas, specifically the right TPJ and IFG. This result may be due to our use of a voluntary arrow cue, whereby arrows represent an overlearned stimulus that activates both voluntary and reflexive attentional networks (see Ristic & Kingstone, 2012). We addressed this possibility in Experiment 3 by utilizing a purely voluntary colour-changing fixation cross as the voluntary cue, rather than an arrow cue. Further, both EWs and PHs were shown to overlap with voluntary attention in the left fusiform gyrus (i.e., VWFA), suggesting that this attentional strategy may be critically involved at early stages of reading.

Experiment 2 used a reflexive attentional cuing paradigm to examine the neural overlap of reflexive attention and lexical and sublexical reading. Results from this experiment showed that EWs had unique overlapping activation with reflexive attention in the right TPJ. The right TPJ has been primarily implicated as a ‘circuit-breaker’ of attention, such that it is involved in automatic shifts of attention to behaviorally relevant stimuli (see Chica et al., 2013 for a review). Thus, we suggest that lexical stimuli automatically recruit reflexive attention based on their behaviourally relevant properties. In addition, PHs did not show unique overlapping activation with reflexive attention, suggesting that phonetic decoding may not automatically recruit reflexive attention to the same extent as lexical reading. Experiments 1 and 2 provided valuable insight into the overlapping neural correlates of reading and attention that may potentiate their relationship in behavioural and neuroimaging studies.

When comparing the results from Experiments 1 and 2, we found support for our conclusion that the voluntary arrow cue used in Experiment 1 may have been recruiting both the

reflexive and voluntary attentional systems. This conclusion is based on the activation overlap found in the right TPJ for the EWs with both voluntary and reflexive attention. However, there was still evidence of unique activation between the voluntary and reflexive attention tasks used in Experiments 1 and 2, as EWs were shown to overlap uniquely with reflexive attention in the right IFG, and uniquely with voluntary attention in the bilateral IPS. For the PHs, areas of unique overlapping activation with the voluntary task included the bilateral IPS/SPL and the left fusiform gyrus (i.e., the VWFA). Unique overlapping activation of PHs with the reflexive attention task was found in the bilateral primary motor cortices. Overall, results from our comparative analysis of Experiments 1 and 2 support the conclusion that our attention tasks were, in fact, recruiting separable attentional systems, however the voluntary arrow cue may also (to some degree) recruit parts of the reflexive attentional orienting system.

Experiment 3 sought to combine reading and attention into novel hybrid tasks to investigate the relationships, and possible interaction, between lexical and sublexical reading and voluntary and reflexive attention. Based on the results of Experiment 1 that showed overlapping activation of EWs with voluntary attention in the right TPJ and IFG that may have been due to our use of an arrow cue, we altered our design to include a purely endogenous spatial cue, in order to separate the effects of voluntary attention. Results from this study isolated the contribution of the right TPJ to lexical processing of EWs, showing that even in the voluntary orienting condition, lexical reading still elicited activation in this region. Further, the IPS and SPL were shown to be more associated with phonetic decoding of PHs than lexical reading of EWs, even in the reflexive attention condition, suggesting that PHs recruit voluntary attentional regions even when it is not required by the task demands. In addition, we also found an area in the left middle occipital gyrus that showed an interaction between reading and attention. This interaction appeared to be driven by decreased percent signal change in this region for the Reflexive-cued-EW task compared to the Voluntary-cued-EW, Voluntary-cued-PH, and Reflexive-cued-PH tasks, suggesting that EW reading does not necessarily require contributions from the dorsal stream. Overall, results from Experiment 3 corroborate the findings of Experiments 1 and 2 and isolate the relationship between reading and attention to parietal (i.e., the right TPJ and IPS/SPL), rather than frontal (i.e., the right FEF and IFG), attentional orienting areas.

These findings have important implications for extending our understanding of word reading and how spatial attention may play an integral and differential role in reading based on reading strategy. Our results support the idea that lexical reading is largely automatic, based on the right TPJ activation found for EWs greater than PHs. Increased activation in the right TPJ for lexical versus sublexical reading suggests that real-words are more behaviorally relevant (based on their familiarity) than PHs with unfamiliar orthography. Support for this conclusion comes from the well-characterized Stroop effect (see MacLeod, 1991 for a review and Lorentz et al., 2015 for thresholds of consciousness effects), whereby lexical stimuli are processed automatically, even when participants are instructed to ignore them. However, in contrast to Experiment 2, we did not find an effect for lexical versus sublexical reading in the right IFG, a reflexive attentional orienting region associated with stimulus-driven reorienting when reorienting is unexpected, or when responses are suppressed (see Chica et al., 2013 for a review). This may be due in part to the predictive validity of the color changing voluntary cue used in the current experiment (i.e., 75%, which is often used in order to optimize cue effectiveness in attention research) versus the 50% validity of the arrow cue used in Experiment 1. In addition, the color changing fixation used in this study provides a purely endogenous cue to spatial location, in contrast to the arrow cue used in Experiment 1, whereby arrow cues have been suggested to recruit both voluntary and reflexive attentional mechanisms (e.g., Ristic & Kingstone, 2006, 2012). Further, these results support the voxel-based morphometry results of He et al. (2013), who found a significant positive correlation between cortical volume in the right TPJ and word naming speed, a task strongly associated with lexical reading ability. Thus, ventral attentional stream contributions from the right TPJ appear to be more specific to lexical processing than those from the right IFG.

Overall, the results from Chapter 2 lend support to the idea that lexical and sublexical reading strategies are differentially associated with attention, whereby lexical reading relies more strongly on ventral, reflexive attentional orienting areas, whereas sublexical reading relies more strongly on dorsal, voluntary orienting areas. In addition, our results suggest that phonetic decoding, to a greater extent than lexical reading, is reliant on contributions from dorsal attentional stream regions (i.e., the SPL and IPS). At the level of skilled reading, our results suggest that parietal attention regions become critically involved in lexical and sublexical reading. This is congruent with the view that sublexical processing requires conscious assembly

of orthographic units via a moving spotlight of attention (e.g., Vidyasagar & Pammer, 2010; see also Montani et al., 2014), as the right SPL has been implicated in controlled shifting of attention between local features (see Chica et al., 2013). Similarly, the IPS is involved in sustained maintenance of attention at peripheral locations as well as coding visual saliency maps, which is required for coherent visual exploration and control of visually guided behavior (including the saccadic eye movements required for reading). Thus, we propose that the interplay between attentional shifting via the right SPL and attentional focusing via the right IPS is involved in phonetic decoding. Further, based on the interaction between reading and attention, we suggest that a pathway through the middle occipital gyrus may be involved in both sublexical reading and voluntary attention, but lexical reading does not necessarily recruit this region, particularly under conditions of reflexive attention.

4.2 Summary of results from Chapter 3

In Chapter 3, we focused on uncovering the underlying structural connectivity architecture associated with skilled reading of EWs and PHs using the computational modeling approach of Saygin et al. (2012, 2016) and Osher et al. (2016). To do this, we modeled the relationship between fine-grained DTI connectivity and voxelwise fMRI activation on independent groups of participants and applied them to participants outside the model using LOOCV and by applying the model from one group of participants to an independent group of participants. We then calculated prediction accuracies for both the entire cortex, as well as for specific ROIs associated with reading, language, and attention. To quantify the accuracy of our models, we compared prediction accuracies from the DTI connectivity model to accuracies from a group average fMRI model. Results from this study showed that across the cortex, we were able to predict voxelwise fMRI activation based on the participants structural connectivity profiles alone. This model outperformed group fMRI average activation models for each of the contrasts for both the LOOCV group, as well as an independent group of subjects (Group 2). For the reading and language related ROIs (i.e., the left IFG, TPJ, and fusiform gyrus), we found that the DTI connectivity model outperformed the group fMRI model for the lexical and sublexical reading tasks, as well as the majority of the regions in the EW > PH/PH > EW contrast. Interestingly, the attention ROIs (i.e., the right TPJ, IFG, FEF, and IPS/SPL) showed even better prediction performance than the reading ROIs, whereby activation in all regions was better predicted by the DTI connectivity model than the group average fMRI model for both groups.

A particularly exciting finding from this study is the ability of our model to predict relatively subtle differences in lexical and sublexical processing (i.e., the $EW > PH/PH > EW$ contrast). Although there is some specialization for lexical and sublexical reading processes, there is also a large amount of overlap in the reading and language networks (for example, in phonological output areas, as well as visual and semantic processing regions, which can be seen in the conjunction analyses from Experiments 1 and 2), particularly between real words and PHs. Comparatively, Osher et al. (2016) examined four different object categories that each have distinct specialization across the cortex and, in particular, the fusiform gyrus (i.e., faces, objects, scenes, and bodies). Further, processing these different object categories occurs naturally and does not require explicit instruction. Thus, the presence of unique structural connectivity patterns underlying these different types of object processing may be more intuitive from an evolutionary perspective. In contrast, the distinction between lexical and sublexical reading is much more subtle, yet our connectivity model was still able to identify distinct structural connectivity patterns that underlie this distinction. Thus, there appears to be unique underlying architecture that subserves lexical versus sublexical processing. It is possible that this lexical versus sublexical system may be based on the structural development of other cognitive networks (consistent with Dehaene & Cohen's (2007) cortical recycling hypothesis, whereby new cognitive processes overtake evolutionarily older brain circuits), including those for spatial attention.

Our findings are in concordance with the work of Saygin et al. (2016) showing that activation in the left fusiform gyrus can be predicted from DTI connectivity alone. Further, we extended these findings to 268 regions across the entire brain, as well as to skilled lexical and sublexical reading, and showed that structural connectivity models outperformed group fMRI activation models. These findings are particularly interesting, as they suggest that individual differences can be accurately captured based on DTI connectivity patterns, thus offering a window into how consistent structural differences dictate differences in brain function. This is in contrast to group average fMRI techniques, which seek to identify consistent patterns of activation in specific regions in a standardized space when, in reality, the location of these regions may vary to large degree across individuals. Thus, structural connectivity biomarkers associated with specific fMRI activation may be able to provide important insight into how individual variations in cortical architecture potentiate the same cognitive outcomes.

4.3 Implications for models of reading

Together, these studies have important implications for informing models of reading. First, we propose that spatial attentional processes should be taken into account when modeling reading ability. Based on the findings of Experiment 1, we showed overlapping activation in the left fusiform gyrus (a critical word reading area) for both lexical and sublexical reading with only the voluntary attention task, rather than the reflexive task. This suggests that voluntary attention may play an important role in skilled reading, particularly in relation to early word processing in the VWFA. Further, based on Experiments 1 and 3, voluntary attentional skill appears to be associated with skilled phonetic decoding. In addition, based on the results of Experiments 2 and 3, we suggest that reflexive attentional skill is associated with successful lexical reading. Thus, our results provide interesting implications for developing a model of reading that incorporates how individual variability of spatial attentional skill may play a role in reading, such that skilled readers with better reflexive attentional skills may show more reliance (and possibly enhanced) lexical reading skills. In comparison, readers with better voluntary attentional skills may show enhanced, and perhaps greater reliance, on phonetic decoding in everyday reading.

This conclusion may offer valuable insight into recent work from Fischer-Baum et al. (2018) who used patterns of fMRI activation to classify skilled readers into two groups (referred to here as G1 and G2) based on their brain's response to word stimuli. Their results showed that although the two groups had similar reading skill (i.e., comparable reading comprehension, vocabulary scores, reading rates, sight word and phonetic decoding efficiency), G2 had significantly greater activation for pseudowords than real words in the left IFG, left angular gyrus, and left IPL. In addition, G1 was slower at processing PHs compared to pseudowords than G2, whereas G2 was slower at reading pseudowords compared to word stimuli than G1. Of particular interest, a dissociation between G1 and G2 was also shown in the right angular gyrus (including the right TPJ), whereby G1 showed greater activation in this area for words than pseudowords, whereas G2 showed greater activation for pseudowords than words. This suggests that participants in G1 had superior sublexical reading ability (and thus more efficient processing) compared to participants in G2, that coincided with greater activation in the right angular gyrus. Thus, this work suggests that there are at least two subtypes of skilled reading, one that relies more strongly on lexical processing, and the other that relies more strongly on sublexical processing. We propose that spatial attention may play an important role in

establishing reading dominance and may contribute to the development of these different subtypes of reading. Thus, development of a functional reading system may be first reliant on adequate development of the visuospatial attentional systems on which they are built.

In line with this, our findings also allow us to make several predictions about the role of spatial attention in reading development. First, we hypothesize that development of word reading ability is reliant, at least in part, on spatial attentional ability and adequate development of both reading and spatial attentional structural networks. As spatial attentional skills develop prior to reading acquisition, these networks may play an important preliminary role in providing the architecture on which skilled reading can be developed. This hypothesis may provide an interesting perspective on the work of Saygin et al. (2016), who showed that DTI connectivity to the left fusiform gyrus (i.e., VWFA) prior to reading acquisition can predict subsequent fMRI activation in this region after reading acquisition. Thus, pre-reading structural connectivity patterns play an important role in dictating subsequent reading development. We suggest that structural connectivity between the visual system and the attentional network may provide part of the scaffolding that allows for skilled reading development in the fusiform gyrus. Thus, we propose that, based on our findings, the development of the spatial attentional system may play an important role in establishing a functional reading system, as structural connectivity was able to predict functional activation in lexical and sublexical reading tasks. Further research is necessary to begin to understand the specific facets and connectivity of the spatial attentional system that are most involved in reading processes.

4.4 Implications for understanding reading impairments

This research also provides interesting insight into the diversity of reading impairments by considering how low-level attentional impairments may impact subsequent reading development. Our results suggest that activation related to reflexive orienting in the right TPJ may be associated with lexical reading ability. This conclusion is supported by the findings of Yamada et al. (2011) who showed that while children with normal reading development showed increased involvement of the bilateral temporo-parietal regions during letter identification, children at risk of developing reading impairments did not exhibit right TPJ activation. After reading intervention for the at-risk group, like the normal reading development group, activation was found in the right TPJ. However, greater activation in right IFG regions was also found for the at-risk group, suggesting possible compensatory mechanisms compared to the normally

developing group (see also Hoeft et al., 2011, who found that improvement in reading ability in children with dyslexia was associated with increased activation in the right IFG using multi-voxel pattern analysis). Similarly, impairments to voluntary orienting in the SPL/IPS may impair subsequent sublexical reading ability. This is supported by the findings of Reilhac, Peyrin, Démonet, & Valdois (2013), who showed that dyslexic adults with letter string processing deficits, unlike controls, did not exhibit activation in the right SPL during a letter substitution task.

Our results may suggest a role of targeted attentional training for reading remediation based on an individual's specific reading deficits. For example, an intervention targeting voluntary attentional orienting may be beneficial for individuals exhibiting phonetic decoding difficulties in the absence of whole-word reading deficits (e.g., phonological dyslexia, see McDougall et al., 2005). Further, an intervention targeting reflexive orienting may improve lexical reading impairments, thus aiding reading impaired populations who exhibit deficits in whole-word reading but not phonetic decoding (e.g., surface dyslexia, see McDougall et al., 2005). This is congruent with research such as Franceschini et al. (2013, 2017), whereby attentional training via first-person video games in children with dyslexia led to significant reading improvements, such that navigating a complex, virtual environment had the ability to enhance the spatial resolution of visual processing (see Green & Bavelier, 2007), potentially reducing detrimental visual crowding effects associated with reading impairments (e.g., Gori & Facoetti, 2015; Whitney & Levi, 2011; Pelli, 2008; Pelli & Tillman, 2008). Importantly, Saygin et al. (2016) provided evidence that anatomical connectivity precedes word selectivity in the VWFA, suggesting that factors such as spatial attention may have a very early influence in shaping subsequent word reading ability, and thus early spatial attentional interventions (both voluntary and reflexive) may lead to enhanced reading development.

In addition, underlying structural connectivity patterns may provide a valuable tool for evaluating reading impairments by taking into account individual differences in normal structural organization. Establishing the bounds of normal structural connectivity may help to more accurately identify deviations in the reading structural network that are associated with reading impairments. Further, it may be possible to develop a structural model of impaired reading that can be used to identify biomarkers of those at risk for reading impairments. This would allow for early remediation strategies to be put into effect, such as visuospatial attentional training, which

may help to improve cognitive outcomes. Thus, we propose that it is increasingly important to take a network perspective when investigating cognitive processes, as examination of discrete brain regions does not provide a comprehensive picture of how abnormalities in underlying structural and functional network architecture play a role in neural disorders.

4.5 Limitations and future directions

In these experiments, in order to examine sublexical reading we used PHs rather than non-words. This decision was made in order to maximize experimental control and to isolate orthographic differences in lexical versus sublexical decoding. However, PHs have been shown to have different neural activation than non-words (i.e., words with no semantic meaning and unfamiliar phonological output). For example, PHs often lead to enhanced activation in the left fusiform gyrus and inferior frontal gyrus than words as well as non-words (e.g., Edwards et al., 2005; Braun et al., 2015). Indeed, some researchers have argued that PHs may actually recruit orthographic, phonological, and semantic processing to an equal or greater extent than reading normal words (e.g., Newman & Joanisse, 2011). In everyday life, we are often exposed to misspelled words that we have no difficulty processing, and thus the use of PHs may tap into similar word processing areas as normal words, therefore diminishing the differences between the two. This may contribute to the results from Experiment 3, such that PHs may activate many of the same semantic and phonological processing areas as their real word counterparts, dampening our ability to identify differences between lexical and sublexical processing and their relationship with reflexive and voluntary attention. Thus, while PHs provided maximal experimental control and comparability with their real-world counterparts, and perhaps greater ecological validity than non-words, we propose that future research should incorporate non-words into the current paradigms to examine how semantics and phonology may have played a role in the current findings. As well, it would be interesting to examine how the relationship between reading and attention differs between skilled readers and individuals with dyslexia, thus future research should examine the neural overlap and interaction of lexical and sublexical reading with reflexive and voluntary attention in this population.

In addition, attentional processes have been shown to operate at a very early time course (Müller & Rabbitt, 1989) that is difficult to adequately capture using fMRI. It is possible that lexical and sublexical reading are being influenced by spatial attention at several different time points that are unable to be picked up by the relatively low temporal resolution of fMRI. Future

research should adapt the current paradigms to EEG, which allows for examination of the fast cerebral event of spatial attentional orienting as well as early reading processes. Further, the findings of Laycock et al. (2009) discussed in Chapter 1 show that transcranial magnetic stimulation to the occipitotemporal junction to prevent interaction between the dorsal and ventral streams led to both early (i.e., 4 ms post-stimulus) and late (i.e., 99 ms post stimulus) disruptions in word reading. Thus, the influence of spatial attention on lexical and sublexical reading processes may be occurring at multiple time points, which could be optimally investigated using EEG.

In regards to our computational model, there is a wealth of information still to be gleaned from the model coefficients that would help to unravel the nature of the underlying structural network that is able to predict skilled reading. Specifically, by examining the significant coefficients from each of the 268 models, information about the characteristics of the entire network can be examined. For example, graph theoretical approaches can be utilized to assess network features, such as nodal degree (i.e., the number of times each target was predictive of the functional response of the other seed regions), clustering coefficient (i.e., the interconnectedness of the network neighbourhoods of a specific target region), and k-core decomposition (i.e., identifying the central core(s) of a network; see Osher et al., 2016 for an example using graph theoretical techniques to identify characteristics of their structural connectivity model). Therefore, future research should focus on disentangling the complex network architecture that underlies lexical and sublexical reading in order to identify the structural connectivity backbone that significantly predicts fMRI activation in reading tasks. Further, future research should examine the ability of underlying resting state connectivity to predict task-based fMRI, which would provide insight into how the functional architecture of the brain dictates functional activation during cognitive tasks.

4.6 Conclusions

The experiments outlined in this thesis provide valuable insight into how spatial attention and underlying white matter structural architecture contribute to skilled reading. We show that spatial attention plays an important and differential role depending on reading strategy, whereby lexical reading appears to be more strongly associated with reflexive spatial attention and sublexical reading appears to be more strongly associated with voluntary spatial attention. Further, we show that consistent structural connectivity patterns underlie lexical and sublexical

reading that can be used to predict fMRI activation in reading tasks. This work represents a new and notable contribution to the field of cognitive neuroscience by providing an important first step to uncovering the functional and structural biomarkers of lexical and sublexical reading. This can be used to not only inform models of word reading, but also to help unravel the complex nature of reading impairments. By understanding the functional and structural neural architecture of reading processes we can begin to unravel how early disruptions to the developing reading system are associated with specific reading outcomes, which will in turn inform remediation strategies of reading impairments. This research also underscores the importance of taking into account the network architecture of the brain when examining cognitive processes, as distinct structural connectivity patterns were shown to be predictive of brain activation patterns during reading tasks. In conclusion, the experiments presented in this thesis provide valuable insight into functional and structural contributions to skilled word reading that broaden our collective understanding of this essential cognitive process.

References

- Amaro Jr., E., & Barker, G. J. (2006). Study design in fMRI: Basic principles. *Brain and Cognition*, 60(3), 220-232.
- Andrews, S. (2012). "Individual differences in skilled visual word recognition and reading," in *Visual Word Recognition*, ed. J. S. Adelman (New York, NY: Psychology Press), 151–172.
- Antzaka, A., Lallier, M., Meyer, S., Diard, J., Carreiras, M., & Valdois, S. (2017). Enhancing reading performance through action video games: The role of visual attention span. *Scientific Reports*, 7, 14563.
- Arrington, C. N., Kulesz, P. A., Juranek, J., Cirino, P. T., & Fletcher, J. M. (2017). White matter microstructure integrity in relation to reading proficiency. *Brain and Language*, 174, 103-111.
- Astafiev, S. V., Shulman, G. L., & Corbetta, M. (2006). Visuospatial reorienting signals in the human temporo-parietal junction are independent of response selection. *European Journal of Neuroscience*, 23(2), 591-596.
- Baeck, A., Kravitz, D., Baker, C., & Op de Beeck, H. P. (2015). Influence of lexical status and orthographic similarity on the multi-voxel response of the Visual Word Form Area. *NeuroImage*, 111, 321-328.
- Boden, C., & Giaschi, D. (2007). M-stream deficits and reading-related visual processes in developmental dyslexia. *Psychological Bulletin*, 133, 346–366.
- Boersma, P., & Weenink, D. (2009) "Praat: doing phonetics by computer (version 5.1.07)" (computer program), <http://www.praat.org/> (last viewed 25/06/2018).
- Bohn, R., & Short, J. (2012). Measuring consumer information. *International Journal of Communication*, 6, 980-1000.
- Borowsky, R. & Besner, D. (1993). Visual word recognition: A multistage activation model. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 19, 813-840.
- Borowsky, R. & Besner, D. (2006). Parallel Distributed Processing and Lexical-Semantic Effects in Visual Word Recognition: Are a Few Stages Necessary? *Psychological Review*, 113, 181-195.

- Borowsky, R. & Esopenko, C., Cummine, J., & Sarty, G.E. (2007). Neural representations of visual words and objects: A functional MRI study on the modularity of reading and object processing. *Brain Topography*, 20, 89-96.
- Borowsky, R., Cummine, J., Owen, W. J., Friesen, C. K., Shih, F., & Sarty, G. E. (2006). FMRI of ventral and dorsal processing streams in basic reading processes: Insular sensitivity to phonology. *Brain Topography*, 18, 233-239.
- Borowsky, R., Esopenko, C., Gould, L., Kuhlmann, N., Sarty, G. & Cummine, J. (2012). Localisation of function for noun and verb reading: Converging evidence for shared processing from fMRI activation and reaction time. *Language and Cognitive Processes*, 28, 789-809.
- Bosse, M., & Valdois, S. (2009). Influence of the visual attention span on child reading performance: A cross-sectional study. *Journal of Research in Reading*, 32(2), 230-253.
- Bosse, M., Tainturier, M. J., & Valdois, S. (2007). Developmental dyslexia: The visual attention span deficit hypothesis. *Cognition*, 104(2), 198-230.
- Braun, M., Hutzler, F. Munte, T. F., Rotte, M., Dambacher, M., Richlan, F., & Jacobs, A. M. (2015). The neural bases of the pseudohomophone effect: Phonological constraints on lexico-semantic access in reading. *Neuroscience*, 295, 151-163.
- Canadian Council on Learning (2008). State of learning in Canada: Toward a learning future. *Report on Learning in Canada*, 1-143.
- Carreiras, M., Armstrong, B. C., Perea, M., & Frost, R. (2014). The what, when, where, and how of visual word recognition. *Trends in Cognitive Sciences*, 18(2), 90-98.
- Carter, J. C., Lanham, D. C., Cutting, L. E., Clements-Stephens, A. M., Chen, X., Hadzipasic, M., Kim, J., Denckla, M. B., & Kaufmann, W. E. (2009). A dual DTI approach to analyzing white matter in children with dyslexia. *Psychiatry Research*, 172(3), 215-219.
- Catani, M., & de Schotten, M. T. (2008). A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex*, 44, 1105-1132.
- Catani, M., & Mesulum, M. (2008). The arcuate fasciculus and the disconnection theme in language and aphasia: History and current state. *Cortex*, 44(8), 953-961.
- Catani, M., Jones, D. K., & Ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Annals of Neurology*, 57, 8-16.

- Chica, A. B., Bartolomeo, P., & Lupiáñez, J. (2013). Two cognitive and neural systems for endogenous and exogenous spatial attention. *Behavioral Brain Research*, 237, 107-123.
- Cohen, L., Dehaene, S., Vinckier, F., Jobert, A., & Montavont, A. (2008). Reading normal and degraded words: Contribution of the dorsal and ventral visual pathways. *NeuroImage*, 40, 353-366.
- Collis, N. L., Kohnen, S., & Kinoshita, S. (2013). The role of visual spatial attention in adult developmental dyslexia. *Quarterly Journal of Experimental Psychology*, 66(2), 245-260.
- Coltheart, M. (2005). Modeling reading: The dual-route approach. In M. J. Snowling, & C. Hulme (Eds.), *The science of reading: A handbook*. (pp. 6-23. Oxford: Blackwell.
- Coltheart, M. (2006). Dual route and connectionist models of reading: An overview. *London Review of Education*, 4, 5-17.
- Coltheart, M., & Rastle, K. (1994). Serial processing in reading aloud: Evidence for dual-route models of reading. *Journal of Experimental Psychology: Human Perception and Performance*, 20(6), 1197-1211.
- Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: A dual route cascaded model of visual word recognition and reading aloud. *Psychological Review*, 108, 204-256.
- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, 3, 201-215.
- Culham, J., & Valyear, K. F. (2006). Human parietal cortex in action. *Current Opinion in Neurobiology*, 16(2), 205-212.
- Cummine, J., Dai, W., Borowsky, R., Gould, L., Rollans, C., & Boliek, C. (2015). Investigating the ventral-lexical, dorsal-sublexical model of basic reading processes using diffusion tensor imaging. *Brain Structure and Function*, 220, 445-455.
- Cummine, J., Gould, L., Zhou, C., Hrybouski, S., Siddiqi, Z., Chouinard, B., & Borowsky, R. (2012). Manipulating instructions strategically affects reliance on the ventral-lexical reading stream: Converging evidence from neuroimaging and reaction time. *Brain & Language*, 125, 203-214.
- Thiebaut De Schotten, M. T., Dell'Acqua, F., Forkel, S. J., Simmons, A., Vergani, F., Murphy, D. G., & Catani, M. (2011). A lateralized brain network for visuospatial attention. *Nature Neuroscience*, 14(10), 1245.

- Dehaene, S., & Cohen, L. (2007). Cultural recycling of cortical maps. *Neuron*, 56(2), 384-398.
- Dehaene S., & Cohen, L. (2011). The unique role of the visual word form area in reading. *Trends in Cognitive Science*, 15, 252-262.
- Destrieux, C., Fischl, B., Dale, A., & Halgren, E. (2010). Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. *Neuroimage*, 53, 1-15.
- Diehl, J. J., Frost, S. J., Sherman, G., Mencl, W. E., Kurian, A., Molfese, P., Landi, N., Preston, J., Soldan, A., Fulbright, R. K., Rueckl, J. G., Seidenberg, M. S., Hoeft, F., & Pugh, K. R. (2014). Neural correlates of language and non-language visuospatial processing in adolescents with reading disability. *NeuroImage*, 101, 653-666.
- Dietz, N. A., Jones, K. M., Gareau, I., Zeffiro, T. A., Eden, G. F. (2005). Phonological decoding involves left posterior fusiform gyrus. *Human Brain Mapping*, 26, 81-93.
- Edwards, J. D., Pexman, P. M., Goodyear, B. G., & Chambers, C. G. (2005). An fMRI investigation of strategies for word recognition. *Cognitive Brain Research*, 24, 648-662.
- Ekstrand, C., Gould, L., Mickleborough, M., Lorentz, E., & Borowsky, R. (2016). When words and space collide: Spatial attention interacts with lexical access during word recognition. *Visual Cognition*, 3, 284-291.
- Epstein, J. N., Conners, C., K., Erhardt, D., Marsh, J. S., & Swanson, J. M. (1997). Asymmetrical hemispheric control of visual-spatial attention in adults with attention deficit hyperactivity disorder. *Neuropsychology*, 11, 467-473.
- Eriksen, C., & Hoffman, J. E. (1972). Temporal and spatial characteristics of selective encoding from visual displays. *Perception and Psychophysics*, 12(2), 201-204.
- Facoetti, A., Paganoni, P., Turatto, M., Marzola, V., & Mascetti, G. G. (2000). Visual-spatial attention in developmental dyslexia. *Cortex*, 36, 109-123.
- Facoetti, A., Trussardi, A. N., Ruffino, M., Lorusso, M. L., Cattaneo, C., Galli, R., Molteni, M., & Zorzi, M. (2009). Multisensory spatial attention deficits are predictive of phonological decoding skills in developmental dyslexia. *Journal of Cognitive Neuroscience*, 22(5), 1011-1025.
- Facoetti, A., Zorzi, M., Cestnick, L., Lorusso, M. L., Molteni, M., Paganoni, P., Umiltà, C., & Mascetti, G. G. (2007). The relationship between visuo-spatial attention and nonword reading in developmental dyslexia. *Cognitive Neuropsychology*, 23(6), 841-855.

- Feng, G., Chen, H. C., Zhu, Z., He, Y., & Wang, S. (2015). Dynamic brain architectures in local brain activity and functional network efficiency associate with efficient reading in bilinguals. *NeuroImage*, 119, 103-118.
- Finn, E. S., Shen, X., Holahan, J. M., Scheinost, D., Lacadie, C., Papademetris, X., Shaywitz, S. E., Shaywitz, B. A., & Constable, R. T. (2013). Disruption of functional networks in dyslexia: A whole-brain, data-driven analysis of connectivity. *Biological Psychiatry*, 76, 397-404.
- Fischer-Baum, S., Kook, J. H., Lee, Y., Ramos-Nuñez, A., & Vannucci, M. (2018). Individual differences in the neural and cognitive mechanisms of single word reading. *Frontiers in Human Neuroscience*, eCollection 2018.
- Franceschini, S., Bertoni, S., Ronconi, L., Molteni, M., Gori, S., & Facoetti, A. (2015). “Shall we play a game?”: Improving reading through action video games in developmental dyslexia. *Current Developmental Disorders Reports*, 2(4), 318-329.
- Franceschini, S., Gori, S., Ruffino, M., Pedrolli, K., & Facoetti, A. (2012). A causal link between visual spatial attention and reading acquisition. *Current Biology*, 22(9), 814-819.
- Franceschini, S., Gori, S., Ruffino, M., Viola, S., Molteni, M., & Facoetti, A. (2013). Action video games make dyslexic children read better. *Current Biology*, 23(6), 462-466.
- Franceschini, S., Trevisan, P., Ronconi, L., Bertoni, S., Colmar, S., Double, K., Facoetti, A., & Gori, S. (2017). Action video games improve reading abilities and visual-to-auditory attentional shifting in English-speaking children with dyslexia. *Scientific Reports*, 7, 5863.
- Friedrich, F. J., Rafal, R. D., & Beck, D. M. (1998). Spatial attention deficits in humans: A comparison of superior parietal and temporal-parietal junction lesions. *Neuropsychology*, 12(2), 193-207.
- Frye, R. E., Hasan, K., Malmberg, B., Desouza, L., Swank, P., Smith, K., & Landry, S. (2010). Superior longitudinal fasciculus and cognitive dysfunction in adolescents born preterm and at term. *Developmental Medicine and Child Neurology*, 52(8), 760-766.
- Gabrieli, J. D. E., & Norton, E. S. (2012). Reading abilities: Importance of visual-spatial attention. *Current Biology*, 9, R298-R299.

- Ge, H., Yin, X., Xu, J., Tang, Y., Han, Y., Xu, W., Pang, Z., Meng, H., & Liu, S. (2013). Fiber pathways of attention subnetworks revealed with tract-based spatial statistics (TBSS) and probabilistic tractography. *PLoS One*, 8(11), e78831.
- Giraldo-Chica, M., Hegarty II, J. P., & Schneider, K. A. (2015). Morphological differences in the lateral geniculate nucleus associated with dyslexia. *NeuroImage: Clinical*, 7, 830-836.
- Glezer, L. S., Jiang, X., & Riesenhuber, M. (2009). Evidence for highly selective neuronal tuning to whole words in the “visual word form area”. *Neuron*, 62, 199–204.
- Glezer, L. S., Kim, J., Rule, J., Jiang, X., & Riesenhuber, M. (2015). Adding words to the brain’s visual dictionary: Novel word learning selectively sharpens orthographic representation in the VWFA. *The Journal of Neuroscience*, 35(12), 4965-4972.
- Goodale, M., & Milner, A. D. (1992). Separate visual pathways for perception and action. *Trends in Neuroscience*, 15, 20-25.
- Gori, S., & Facoetti, A. (2014). Perceptual learning as a possible new approach for remediation and prevention of developmental dyslexia. *Vision Research*, 99, 78–87.
- Gori, S., & Facoetti, A. (2015). How the visual aspects can be crucial in reading acquisition: The intriguing case of crowding and developmental dyslexia. *Journal of Vision*, 15(8), 1-20.
- Gould, L., Mickleborough, M. J. S., Ekstrand, C., Lorentz, E., & Borowsky, R. (2017). Examining the neuroanatomical and the behavioural basis of the effect of basic rhythm on reading aloud. *Language, Cognition, and Neuroscience*, 32(6), 724-742.
- Gould, L., Mickleborough, M. J. S., Wu, A., Tellez, J., Ekstrand, C., Lorentz, E., Ellchuk, T., Babyn, P., & Borowsky, R. (2016). Presurgical language mapping in epilepsy: Using fMRI of reading to identify functional reorganization in a patient with long-standing temporal lobe epilepsy. *Epilepsy and Behavior Case Reports*, 5, 6-10.
- Grahn, J. A., & Brett, M. (2007). Rhythm and beat perception in motor areas of the brain. *Journal of Cognitive Neuroscience*, 19(5), 893-906.
- Grainger, J., Dufau, S., Ziegler, J. C. (2016). A vision of reading. *Trends in Cognitive Sciences*, 20(3), 171-179.
- Green, C. S., & Bavelier, D. (2003). Action video game modifies visual selective attention. *Nature*, 423, 534-537.
- Green, C. S., & Bavelier, D. (2007). Action-video-game experience alters the spatial resolution of vision. *Psychological Science*, 18, 88-94.

- Habib, M. (2000). The neurological basis of developmental dyslexia: An overview and working hypothesis. *Brain*, 123(12), 2373-2399.
- Hari, R., & Renvall, H. (2001). Impaired processing of rapid stimulus sequences in dyslexia. *Trends in Cognitive Science*, 5, 525–532.
- Hayward, D. A., & Ristic, J. (2016). Automated symbolic orienting is not modulated by explicit temporal attention. *Acta Psychologica*, 171, 93-98.
- He, Q., Xue, G., Chen, C., Chen, C., Lu, Z., & Dong, Q. (2013). Decoding the neuroanatomical basis of reading ability: A multivoxel morphometric study. *The Journal of Neuroscience*, 33(31), 12835-12843.
- Hernandez-Fernandez, M., Reguly, I., Giles, M., Jbabdi, S., Smith, S., & Sotiropoulos, S. N. (2016). A fast and flexible toolbox for tracking brain connections in diffusion MRI datasets using GPUs. Presented at the 22nd Annual Meeting of the Organization for Human Brain Mapping (OHBM), Geneva, Switzerland.
- Hernandez, A. E., & Fiebach, C. J. (2006). The brain bases of reading late learned words: Evidence from functional MRI. *Visual Cognition*, 13, 1027-1043.
- Hernandez, M., Guerrero, G. D., Cecilia, J. M., Garcia, J. M., Inuggi, A., Jbabdi, S., Behrens, T. E. J., & Sotiropoulos, S. N. (2013). Accelerating fibre orientation from diffusion weighted magnetic resonance imaging using GPUs. *PLoS ONE*, 8(4), e61892.
- Hoeft, F., McCandliss, B. D., Black, J. M., Gantman, A., Zakerani, N., Hulme, C., Lyytinen, H., Whitfield-Gabrieli, S., Glover, G. H., Reiss, A. L., & Gabrieli, J. D. E. (2011). Neural systems predicting long-term outcome in dyslexia. *PNAS*, 108, 361-366.
- Hoeft, F., McCandliss, B. D., Black, J. M., Gantman, A., Zakerani, N., Hulme, C., ... Gabrieli, J. D. E. (2011). Neural systems predicting long-term outcome in dyslexia. *Proceedings of the National Academy of Sciences*, 108, 361-366.
- Hopfinger, J., Buonocore, M., & Mangun, G. (2000). The neural mechanisms of top-down attentional control. *Nature Neuroscience*, 3, 284-291.
- Horowitz-Kraus, T., Wang, Y., Plante, E., & Holland, S. K. (2015). Involvement of the right hemisphere in reading comprehension: A DTI study. *Brain Research*, 1582, 34-44.
- Jenkinson, M., & Smith, S. M. (2001). A global optimization method for robust affine registration of brain images. *Medical Image Analysis*, 5(2), 143-156.

- Jenkinson, M., Bannister, P., Brady, M., & Smith, S. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage*, 17(2), 825-841.
- Jones, E., Oliphant, E., Peterson, P. et al. (2001). Scipy: Open source scientific tools for python. <http://www.scipy.org/>.
- Karnath, H. O., Himmelbach, M., & Rorden, C. (2002). The subcortical anatomy of human spatial neglect: Putamen, caudate nucleus and pulvinar. *Brain*, 125, 350-360.
- Kelley, T. A., Serences, J. T., Giesbrecht, B., & Yantis, S. (2008). Cortical mechanisms for shifting and holding visuospatial attention. *Cerebral Cortex*, 18, 114-125.
- Krauzlis, R. J., Bollimunta, A., Arcizet, F., & Wang, L. (2014). Attention as an effect not a cause. *Trends in Cognitive Sciences*, 18(9), 457-464.
- Laycock, R., Crewther, D. P., Fitzgerald, P. B., & Crewther, S. G. (2009). TMS disruption of V5/MT+ indicates a role for the dorsal stream in word recognition. *Experimental Brain Research*, 197, 69–79.
- Lebel, C., Shaywitz, B., Holahan, J., Shaywitz, S., Marchione, K., & Beaulieu, C. (2013). Diffusion tensor imaging correlates of reading ability in dysfluent and non-impaired readers. *Brain and Language*, 215-222.
- Levy, J., Pernet, C., Treserras, S., Boulanouar, K., Aubry, F., Démonet, J., & Celsis, P. (2009). Testing for the dual-route cascade reading model in the brain: An fMRI effective connectivity account for an efficient reading style. *PLoS One*, 4(8), e6675.
- Livingstone M. S. Rosen G. D. Drislane F. W. Galaburda A. M. (1991). Physiological and anatomical evidence for a magnocellular defect in developmental dyslexia. *Proceedings of the National Academy of Sciences, USA*, 88, 7943–7947.
- Loftus, G. R. & Masson, M. E. (1994). Using confidence intervals in within-subject designs. *Psychonomic Bulletin and Review*, 1(4), 476-490.
- Lorentz, E., McKibben, T., Ekstrand, C., Gould, L., Anton, K., & Borowsky, R. (2016). Disentangling genuine semantic Stroop effects in reading from contingency effects: On the need for two neutral baselines. *Frontiers in Psychology*, 7, 386.
- MacLeod, C. M. (1991). Half a century of research on the Stroop effect: An integrative review. *Psychological Bulletin*, 109(2), 163-203.

- Mahon, B. Z., Kumar, N., & Almeida, J. (2013). Spatial frequency tuning reveals interactions between the dorsal and ventral visual systems. *Journal of Cognitive Neuroscience*, 25(6), 862-871.
- Martelli, M., Filippo, G. D., Spinelli, D., & Zoccolotti, P. (2009). Crowding, reading, and developmental dyslexia. *Journal of Vision*, 9, 14.
- Martin, A., Schruz, M., Kronbichler, M., & Richlan, F. (2015). Reading in the brain of children and adults: A meta-analysis of 40 functional magnetic resonance imaging studies. *Human Brain Mapping*, 36(5), 1963-1981.
- McCann, R. S., Folk, C. L., & Johnston, J. C. (1992). The role of spatial attention in visual word processing. *Journal of Experimental Psychology: Human Perception and Performance*, 18(4), 1015-1029.
- McDougall, P., Borowsky, R., MacKinnon, G. E., & Hymel, S. (2005). Process dissociation of sight vocabulary and phonetic decoding in reading: A new perspective on surface and phonological dyslexia. *Brain and Language*, 92(2), 185-203.
- Mickleborough, M. J., Ekstrand, C., Gould, L., Lorentz, E. J., Ellchuk, T., Babyn, P., & Borowsky, R. (2016). Attentional network differences between migraineurs and non-migraine controls: fMRI evidence. *Brain Topography*, 29(3), 419-428.
- Milner, A. D., & Goodale, M. (1995). *The visual brain in action*. Oxford, England: Oxford University Press.
- Montani, V., Facoetti, A., & Zorzi, M. (2014). Spatial attention in written word perception. *Frontiers in Human Neuroscience*, 8, 42.
- Moore, E., Cassim, R., & Talcott, J. B. (2011). Adults with dyslexia exhibit large effects of crowding, increased dependence on cues, and detrimental effects of distractors in visual search tasks. *Neuropsychologia*, 49(14), 3881-3890.
- Müller, H. J., & Rabbitt, P. M. (1989). Reflexive and voluntary orienting of visual attention: Time course of activation and resistance to interruption. *Journal of Experimental Psychology: Human Perception and Performance*, 15(2), 315-330.
- Murakami, T., Hama, S., Yamashita, H., Onoda, K., Hibino, S., Sato, H., Ogawa, S., Yamawaki, S., & Kurisu, K. (2014). Neuroanatomic pathway associated with attentional deficits after stroke. *Brain Research*, 1544, 25-32.

- Newman, R. L., & Joanisse, M. F. (2011). Modulation of brain regions involved in word recognition by homophonous stimuli: An fMRI study. *Brain Research*, 1367, 250-264.
- Nichols, T. (2007). Easythresh_conj—quick method of getting conjunction stats outside of Feat [web page]. Available at http://www2.warwick.ac.uk/fac/sci/statistics/staff/academic-research/nichols/scripts/fsl/easythresh_conj.sh. (accessed 13 Sept 2017).
- Norton, E. S., & Wolf, M. (2012). Rapid automatized naming (RAN) and reading fluency: Implications for understanding and treatment of reading disabilities. *Annual review of psychology*, 63, 427-452.
- Oberhuber, M., Jones, O. P., Hope, T. M. H., Prejawa, S., Seghier, M. L., Green, D. W., & Price, C. J. (2013). Functionally distinct contributions of the anterior and posterior putamen during sublexical and lexical reading. *Frontiers in Human Neuroscience*, 7, 787.
- Odegard, T. N., Farris, E. A., Ring, J., McColl, R., & Black, J. (2009). Brain connectivity in non-reading impaired children and children diagnosed with developmental dyslexia. *Neuropsychologia*, 47(8-9), 1972-1977.
- Osher, D. E., Saxe, R. R., Koldewyn, K., Gabrieli, J. D. E., Kanwisher, N., & Saygin, Z. M. (2016). Structural connectivity fingerprints predict cortical selectivity for multiple visual categories across cortex. *Cerebral Cortex*, 26, 1668-1683.
- Owen, W.J. & Borowsky, R. (2003). Examining the interactivity of lexical orthographic and phonological processing. *Canadian Journal of Experimental Psychology*, 57, 290-303.
- Patterson, K., & Hodges, J. R. (1992). Deterioration of word meaning: Implications for reading. *Neuropsychologia*, 30(12), 1025-1040.
- Pedregosa, F., Varoquaux, G., Gramfort, A., Michel, V., Thirion, B., Grisel, O., Blondel, M., Prettenhofer, P., Weiss, R., Dubourg, V., Vanderplas, J., Passos, A., Cournapeau, D., Brucher, M., Perrot, M., & Duchesnay, E. (2011). Scikit-learn: Machine learning in python. *JMLR*, 12, 2825-2830.
- Pelli, D. G. (2008). Crowding: A cortical constraint on object recognition. *Current Opinion in Neurobiology*, 18(4), 445–451.
- Pelli, D. G., & Tillman, K. A. (2008). The uncrowded window of object recognition. *Nature Neuroscience*, 11(10), 1129–1135.

- Perfetti, C. A. (2011). "Phonology is critical in reading," in *Explaining Individual Differences in Reading: Theory and Evidence*, eds S. A. Brady, D. Braze and C. A. Fowler (New York, NY: Psychology Press), 153–171.
- Peyrin, C., Lallier, M., Demonet, J. F., Pernet, C., Baciú, M., Le Bas, J. F., & Valdois, S. (2012). Neural dissociation of phonological and visual attention span disorders in developmental dyslexia: fMRI evidence from two case reports. *Brain and Language*, 120(3), 381-394.
- Pleger, B., & Timmann, D. (2018). The role of the human cerebellum in linguistic prediction, word generation and verbal working memory: Evidence from brain imaging, non-invasive cerebellar stimulation and lesion studies. *Neuropsychologia*, in press.
- Posner, M. I. (1980). Orienting of attention. *Quarterly Journal of Experimental Psychology*, 32, 3-25.
- Price, C. J. (2012). A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage*, 62, 816-847.
- Price, C. J., & Devlin, J. T. (2004). The pro and cons of labelling a left occipitotemporal region: "The visual word form area". *NeuroImage*, 22, 477-479.
- Price, C. J., Moore, C. J., Frackowiak, C. (1996). The effect of varying stimulus rate and duration on brain activity during reading. *NeuroImage*, 3, 40-52.
- Price, C. J., Wise, R. J., Watson, J. D., Patterson, K., Howard, D., Frackowiak, R. S. (1994). Brain activity during reading. The effects of exposure duration and task. *Brain*, 117(6), 1255-1269.
- Rauschecker, J. P. (2012). Ventral and dorsal streams in the evolution of speech and language. *Frontiers in Evolutionary Neuroscience*,
- Reilhac, C., Peyrin, C., Démonet, J., & Valdois, S. (2013). Role of the superior parietal lobules in letter-identity processing within strings: fMRI evidence from skilled and dyslexic readers. *Neuropsychologia*, 51(4), 601-612.
- Richardson, F. M., Seghier, M. L., Leff, A. P., Thomas, M. S. C., & Price, C. J. (2011). Multiple routes from occipital to temporal cortices during reading. *Journal of Neuroscience*, 31(22), 8239-8247.
- Riecker, A., Wildgruber, D., Dogil, G., Grodd, W., & Ackermann, H. (2002). Hemispheric lateralization effects of rhythm implementation during syllable repetitions: An fMRI study. *NeuroImage*, 16, 169-176.

- Ristic, J., & Kingstone, A. (2006). Attention to arrows: Pointing to a new direction. *The Quarterly Journal of Experimental Psychology*, 59(11), 1921-1930.
- Ristic, J., & Kingstone, A. (2012). A new form of human spatial attention: Automated symbolic orienting. *Visual Cognition*, 20(3), 244-264.
- Ristic, J., Landry, M., & Kingstone, A. (2012). Automated symbolic orienting: The missing link. *Frontiers in Psychology*, 17(3), 560.
- Rizzolatti, G., & Matelli, M. (2003). Two different streams form the dorsal visual system: Anatomy and functions. *Experimental Brain Research*, 153(2), 146-157.
- Rollans, C., & Cummine, J. (2018). One tract, two tract, old tract, new tract: A pilot study of the structural and functional differentiation of the inferior fronto-occipital fasciculus. *Journal of Neurolinguistics*, 46, 122-137.
- Rueckl, J. G., Paz-Alonso, P. M., Molfese, P. J., Kuo, W. J., Bick, A., Frost, S. J., et al. (2015). Universal brain signature of proficient reading: evidence from four contrasting languages. *Proceedings of the National Academy of Sciences*, 112, 15510–15515.
- Ryherd, K., Jasinska, J. A., Van Dyke, J. A., Hung, Y. H., Baron, E., Mencl, W. E., Zevin, J., & Landi, N. (2018). Cortical regions supporting reading comprehension skill for single words and discourse. *Brain and Language*, 186, 32-43.
- Saalman, Y. B., Pinsk, M. A., Wang, L., Li, X., & Kastner, S. (2012). The pulvinar regulates information transmission between cortical areas based on attention demands. *Science*, 337, 753-756.
- Saur, D., Kreher, D. W., Schnell, S., Kümmerer, D., Kellmeyer, P., Vry, M., Umarova, R., Musso, M., Glauche, V., Abel, S., Rijntjes, M., Hennig, J., & Weiller, C. (2008). Ventral and dorsal pathways for language. *PNAS*, 105(46), 18035-18040.
- Saygin, Z. M., Norton, E. S., Osher, D. E., Beach, S. D., Cyr, A. B., Ozernov-Pakchik, O., Yendiki, A., Fischl, B., Gaab, N., & Gabrieli, J. D. E. (2013). Tracking the roots of reading ability: White matter volume and integrity correlate with phonological awareness in prereading and early-reading kindergarten children. *The Journal of Neuroscience*, 33(33), 13251-13258.
- Saygin, Z. M., Osher, D. E., Koldewyn, K., Reynolds, G., Gabrieli, J. D. E., & Saxe, R. R. (2012). Anatomical connectivity patterns predict face-selectivity in the fusiform gyrus. *Nature Neuroscience*, 15(2), 321-327.

- Saygin, Z. M., Osher, D. E., Norton, E. S., Youssoufian, D. A., Beach, S. D., Feather, J., Gaab, N., Gabrieli, J. D. E., & Kanwisher, N. (2016). Connectivity precedes function in the development of the visual word form area. *Nature Neuroscience*, 19(9), 1250-1255.
- Schneps, M. H., Brockmole, J. R., Sonnert, G., & Pomplun, M. (2012). History of reading struggles linked to enhanced learning in low spatial frequency scenes. *PLoS One*, 7(4), e35724.
- Seghier, M. L., & Price, C. J. (2010). Reading aloud boosts connectivity through the putamen. *Cerebral Cortex*, 20(3), 570-582.
- Shen, X., Tokoglu, F., Papademetris, X., & Constable, R. T. (2013). Groupwise whole-brain parcellation from resting-state fMRI data for network node identification. *Neuroimage*, 82, 403-415.
- Silva-Pereyra J, Bernal J, Rodríguez-Camacho M, Yáñez G, Prieto-Corona B, et al. (2010) Poor reading skills may involve a failure to focus attention. *Neuroreport* 21: 34–38.
- Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping*, 17(3), 143-155.
- Sprenger-Charolles, L., Siegel, L. S., Jimenez, J. E., & Ziegler, J. C. (2011). Prevalence and reliability of phonological, surface, and mixed profiles in dyslexia: A review of studies conducted in languages varying in orthographic depth. *Scientific Studies of Reading*, 15(6), 498-521.
- Stevens, W. D., Kravitz, D. J., Peng, C. S., Tessler, M. H., & Martin, A. (2017). Privileged functional connectivity between the visual word form area and the language system. *Journal of Neuroscience*, 37(21), 5288-5297.
- Stuart, M., & Coltheart, M. (1988). Does reading develop in a sequence of stages? *Cognition*, 30(2), 139-181.
- Stolz, J. A., & McCann, R. S. (2000). Visual word recognition: Reattending to the role of spatial attention. *Journal of Experimental Psychology: Human Perception and Performance*, 26(4), 1320-1331.
- Striemer, C. L., Cantelmi, D., Cusimano, M. D., Danckert, J. A., & Schweizer, T. A. (2015). Deficits in reflexive covert attention following cerebellar injury. *Frontiers in Human Neuroscience*. doi: 10.3389/fnhum.2015.00428.

- Strijkers, K., Bertrand, D., & Grainger, J. (2015). Seeing the same words differently: The time course of automaticity and top-down intention in reading. *Journal of Cognitive Neuroscience*, 27(8), 1-10.
- Taylor, J. S. H., Rastle, K., & Davis, M. H. (2013). Can cognitive models explain brain activation during word and pseudoword reading? A meta-analysis of 36 neuroimaging studies. *Psychological Bulletin*, 139(4), 766-791.
- The Nielsen Company. (2018). The Nielsen total audience report: Q1 2018. Retrieved from <https://radioconnects.ca/wp-content/uploads/2018/08/Nielsen-Q1-2018-Total-US-Audience-Report.pdf>.
- Theibaut de Schotten, M. T., Dell'Acqua, F., Forkel, S. J., Simmons, A., Vergani, F., Murphy, D., & Catani, M. (2011). A lateralized brain network for visuospatial attention. *Nature Neuroscience*, 14, 1245-1246.
- Tommasi, G., Fiorio, M., Yelnik, J., Krack, P., Sala, F., Schmitt, E., Fraix, V., Bertolasi, L., Le Bas, J., Ricciardi, G. K., Fiaschi, A., Theeuwes, J., Pollak, P., & Chelazzi, L. (2015). Disentangling the role of cortico-basal ganglia loops in top-down and bottom-up visual attention: An investigation of attention deficits in Parkinson Disease. *Journal of Cognitive Neuroscience*, 27(6), 1215-1237.
- Ueno, T., Meteyard, L., Hoffman, P., & Murayama, K. (2018). The ventral anterior temporal lobe has a necessary role in exception word reading. *Cerebral Cortex*, 28(8), 3035-3045.
- Ungerleider, L. G., & Haxby, J. V. (1994). 'What' and 'where' in the human brain. *Current Opinion in Neurobiology*, 4(2), 157-165.
- Ungerleider, L. G., & Mishkin, M. (1982). Two cortical visual systems. In Ingle D. J., Goodale M. A., & Manfield R. J. W., eds. *Analysis of Visual Behavior*. MIT Press, Cambridge, MA.
- Valdois, S., Bosse, M. L., & Tainturier, M. J. (2004). The cognitive deficits responsible for developmental dyslexia: Review of evidence for a selective visual attentional disorder. *Dyslexia*, 10(4), 339– 363.
- van Schouwenburg, M. R., den Ouden, H. E. M., & Cools, R. (2013). Selective attentional enhancement and inhibition of fronto-posterior connectivity by the basal ganglia during attention switching. *Cerebral Cortex*, 25(6), 1527-1534.

- Vanderauwera, J., De Vos, A., Forkel, S. J., Catani, M., Wouters, J., Vandermosten, M., & Ghesquière, P. (2018). Neural organization of ventral white matter tracts parallels the initial steps of reading development: A DTI tractography study. *Brain and Language*, 183, 32-30.
- Vandermosten, M., Boets, B., Wouters, J., & Ghesquière, P. (2012). A qualitative and quantitative review of diffusion tensor imaging studies in reading and dyslexia. *Neuroscience and Biobehavioral Reviews*, 36, 1532-1552.
- Vidyasagar, T. R., & Pammer, K. (1999). Impaired visual search in dyslexia relates to the role of the magnocellular pathway in attention. *Neuroreport*, 10(6), 1283-1287.
- Vidyasagar, T. R., & Pammer, K. (2010). Dyslexia: A deficit in visuo-spatial attention, not in phonological processing. *Trends in Cognitive Science*, 14, 57– 63.
- Vigneau, M., Beaucousin, V., Hervé, P. Y., Duffau, H., Crivello, F., Houdé, O., ... & Tzourio-Mazoyer, N. (2006). Meta-analyzing left hemisphere language areas: Phonology, semantics, and sentence processing. *NeuroImage*, 30(4), 1414-1432.
- Wang, Y., Mauer, M. V., Raney, T., Peysakhovich, B., Becker, B. L. C., Sliva, D. D., & Gaab, N. (2017). Development of tract-specific white matter pathways during early reading development in at-risk children and typical controls. *Cerebral Cortex*, 27(4), 2469-2485.
- Welcome, S. E., and Joanisse, M. F. (2012). Individual differences in skilled adult readers reveal dissociable patterns of neural activity associated with component processes of reading. *Brain and Language*, 120, 360–371.
- Whitney, D., & Levi, D. M. (2011). Visual crowding: A fundamental limit on conscious perception and object recognition. *Trends in Cognitive Science*, 15(4), 160–168.
- Wile, T. L., & Borowsky, R. (2004). What does rapid automatized naming measure? A new RAN task compared to naming and lexical decision. *Brain and Language*, 90, 47-62.
- Wingerak, S., Neudorf, J., Gould, L., & Borowsky, R. (2017). On the Dissociation Between Reaction Time and Response Duration as a Function of Lexical and Sublexical Reading: An Examination of Phonetic Decoding and Computational Models. *Visual Cognition*, 25, 913-927.
- Woolrich, M. W., Ripley, B. D., Brady, M., & Smith, S. M. (2001). Temporal autocorrelation in univariate linear modeling of FMRI data. *Neuroimage*, 14(6), 1370-1386.

- Worsley, K.J., 2001. Statistical analysis of activation images. In: Jezzard, P., Matthews, P.M., Smith, S.M. (Eds.), *Functional MRI: An Introduction to Methods*. Oxford University Press, New York.
- Yamada, Y., Stevens, C., Dow, M., Ham, B. A., Chard, D. J., & Neville, H. J. (2011). Emergence of the neural network for reading in five-year-old beginning readers of different levels of pre-literacy abilities: An fMRI study. *NeuroImage*, 57(3), 704-713.
- Yeatman, J. D., Dougherty, R. F., Ben-Schachar, M., & Wandell, B. A. (2012). Development of white matter and reading skills. *Proceedings of the National Academy of Sciences*, 109(44), E3045-E3053.
- Yeh, F. C., & Tseng, W. Y. (2011). NTU-90: A high angular resolution brain atlas constructed by q-space diffeomorphic reconstruction. *NeuroImage*, 58, 91-99.
- Zemmoura, I., Herbet, G., Moritz-Gasser, S., & Duffau, H. (2015). New insights into the neural network mediating reading processes provided by cortico-subcortical electrical mapping. *Human Brain Mapping*, 36, 2215-2230.

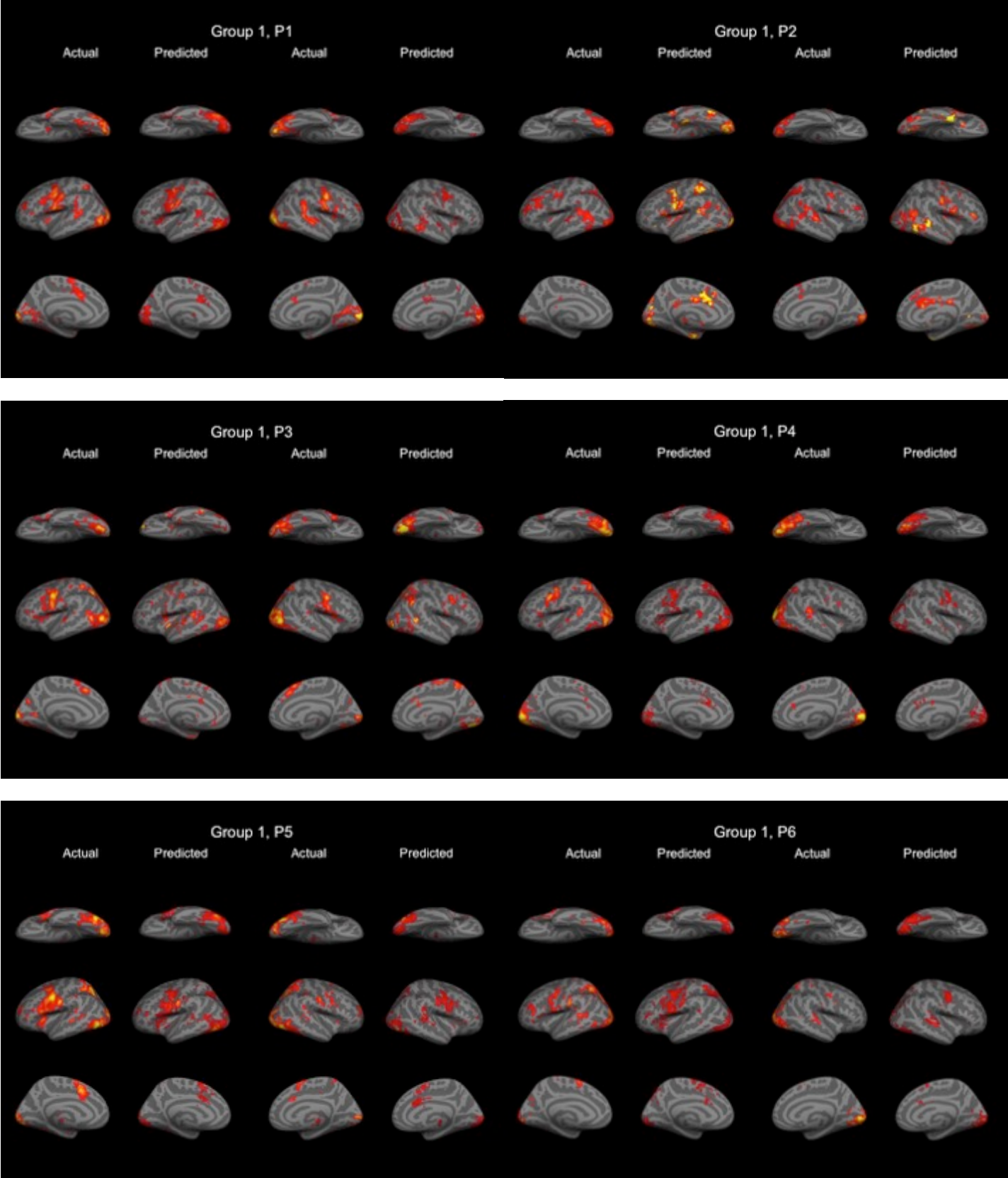
Appendix A
Reading Stimuli from Experiments 1, 2, and 3

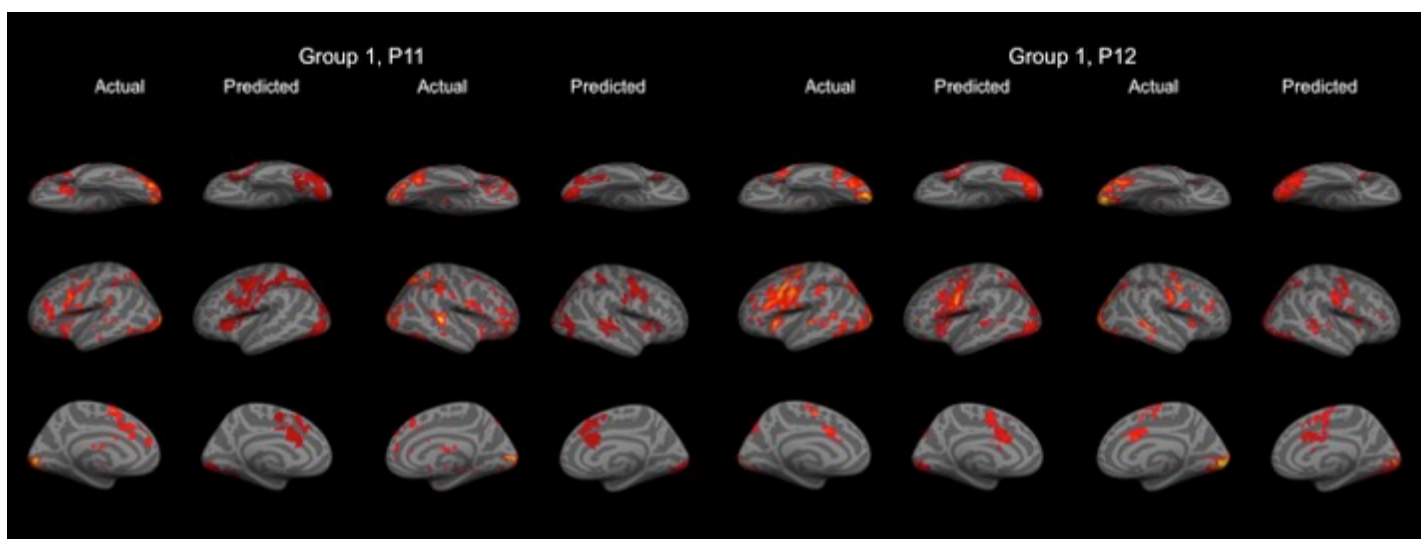
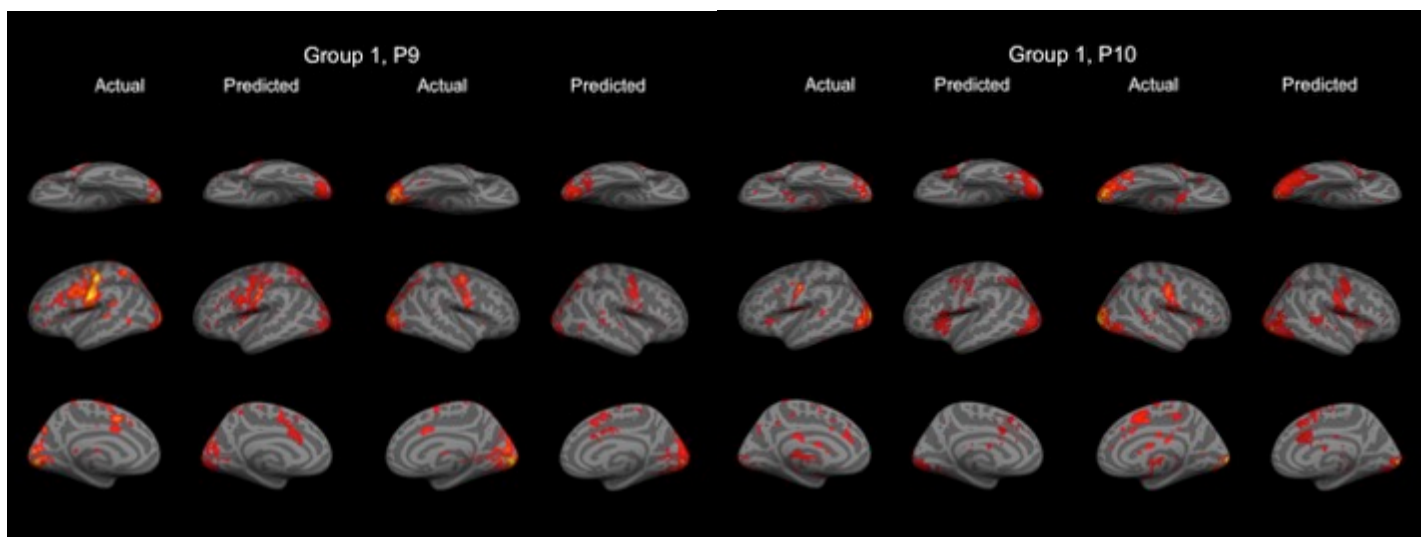
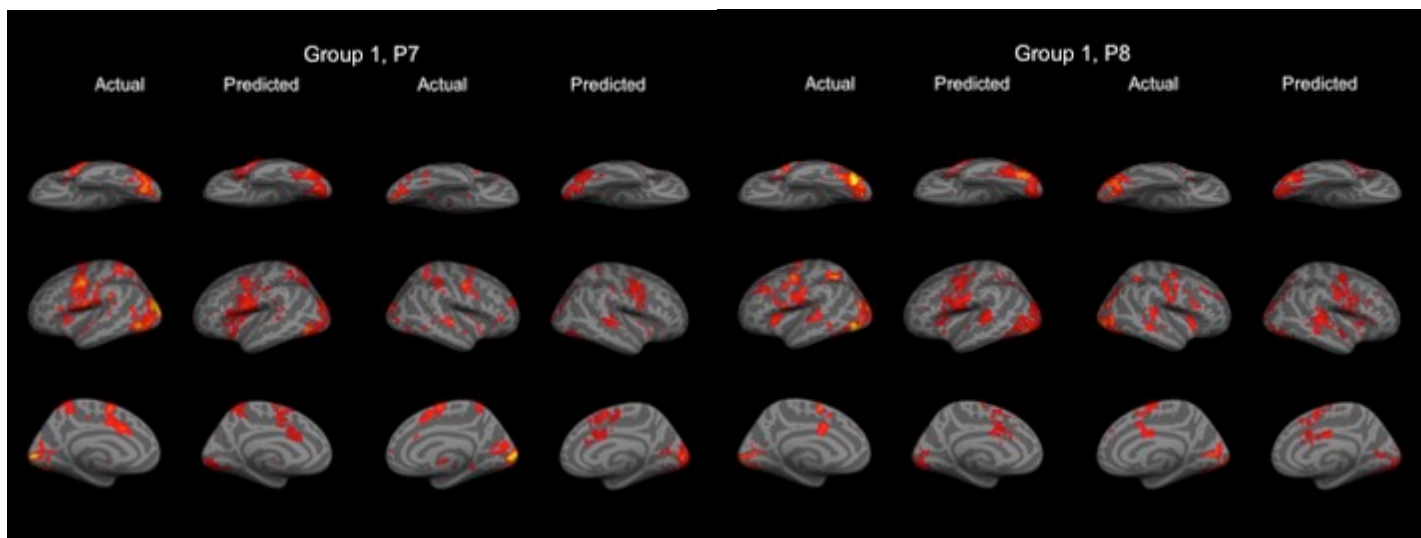
EW	Length	Log_Freq_HAL	PH	Length	Baseword Log_Freq_HAL
bear	4	10.066	bair	4	10.066
blood	5	10.855	blud	4	10.855
bowl	4	9.28	bohl	4	9.28
bread	5	9.112	brayn	5	10.899
bull	4	9.025	bul	3	9.025
comb	4	7.386	coam	4	8.76
door	4	10.893	coyn	4	7.386
foot	4	10.095	flaim	5	7.155
geese	5	6.461	gurl	4	10.453
glove	5	7.764	hupe	4	10.605
heart	5	10.732	krib	4	7.154
hook	4	9.36	leef	4	8.861
mould	5	6.817	mhug	4	10.439
pear	4	6.878	mowth	5	7.404
pint	4	7.293	poap	4	7.293
shoe	4	8.558	pynt	4	9.005
soup	4	8.707	shedd	5	8.737
sponge	6	7.376	shue	4	8.558
steak	5	7.32	spunge	5	7.376
thread	6	10.954	staik	5	7.32
wasp	4	6.667	thred	5	10.954
wolf	4	9.979	tohste	6	8.027
wood	4	10.087	tuthe	5	8.048
wool	4	7.633	werld	5	7.633
world	5	12.597	wull	4	12.597

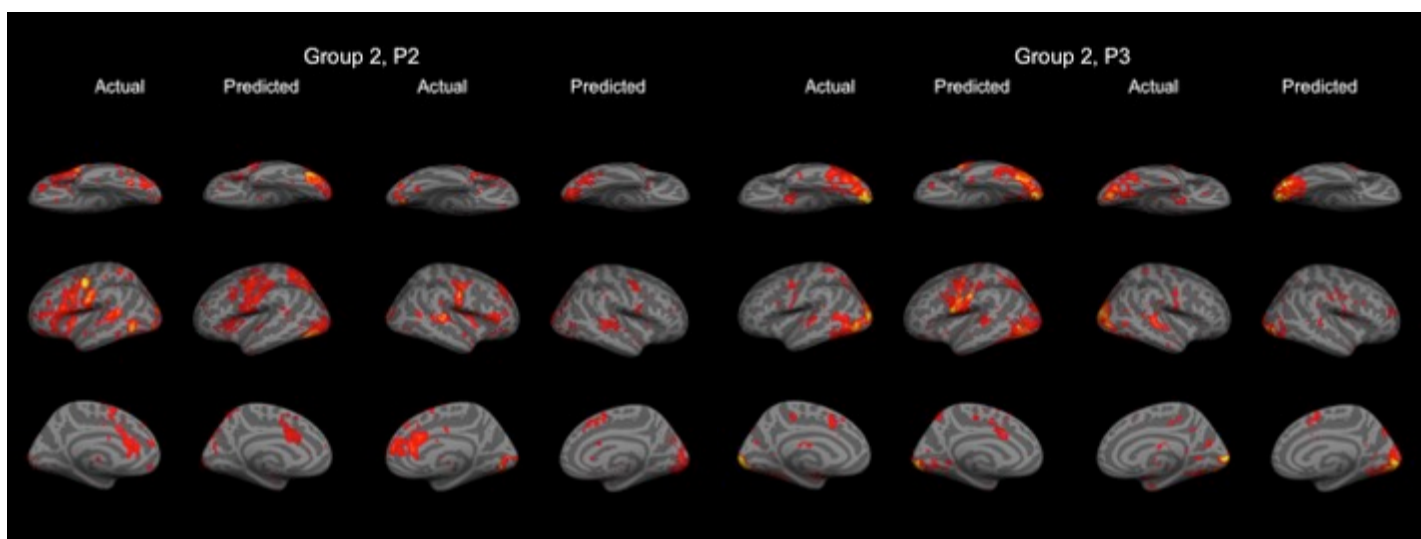
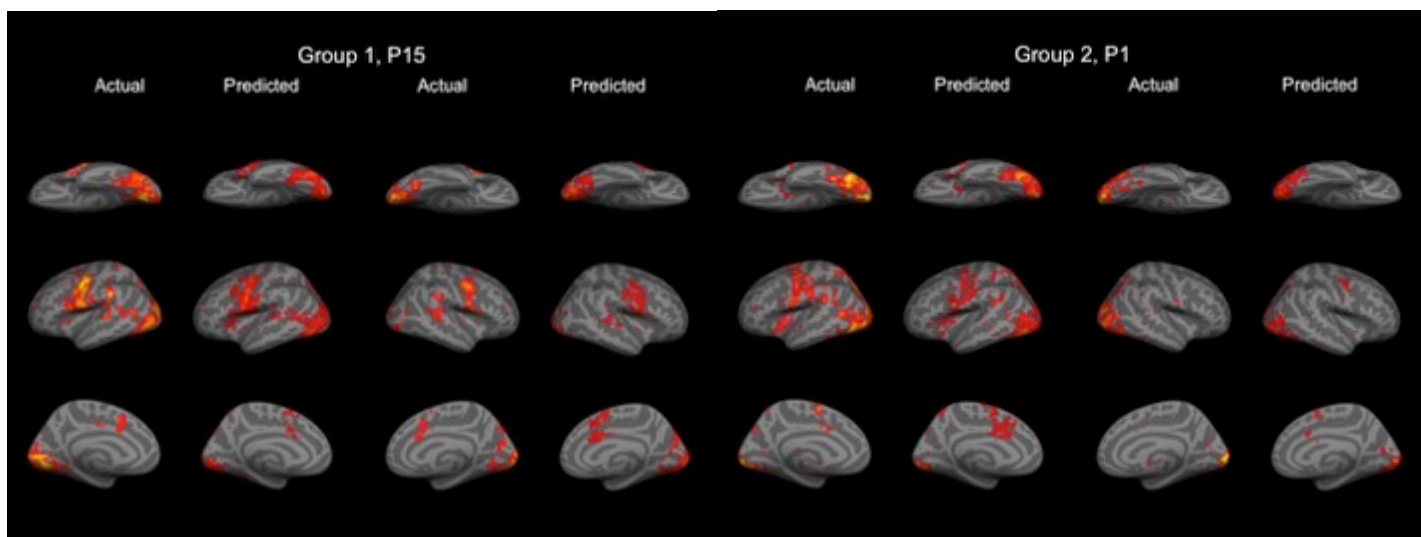
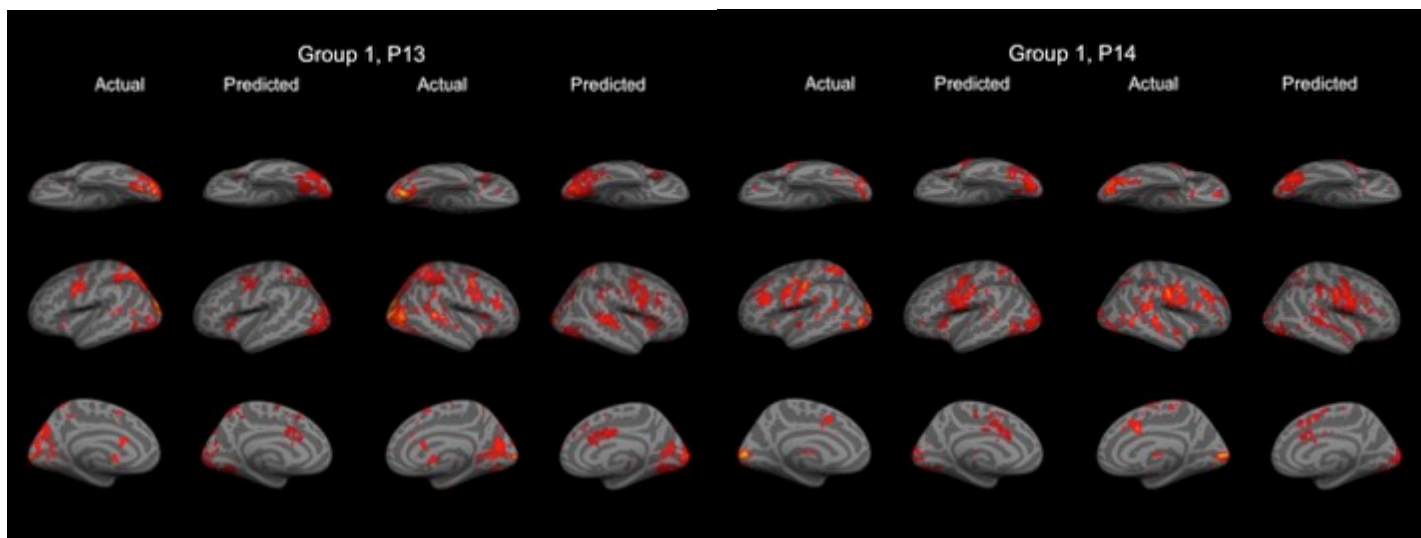
Appendix B
Reading Stimuli from Experiment 4

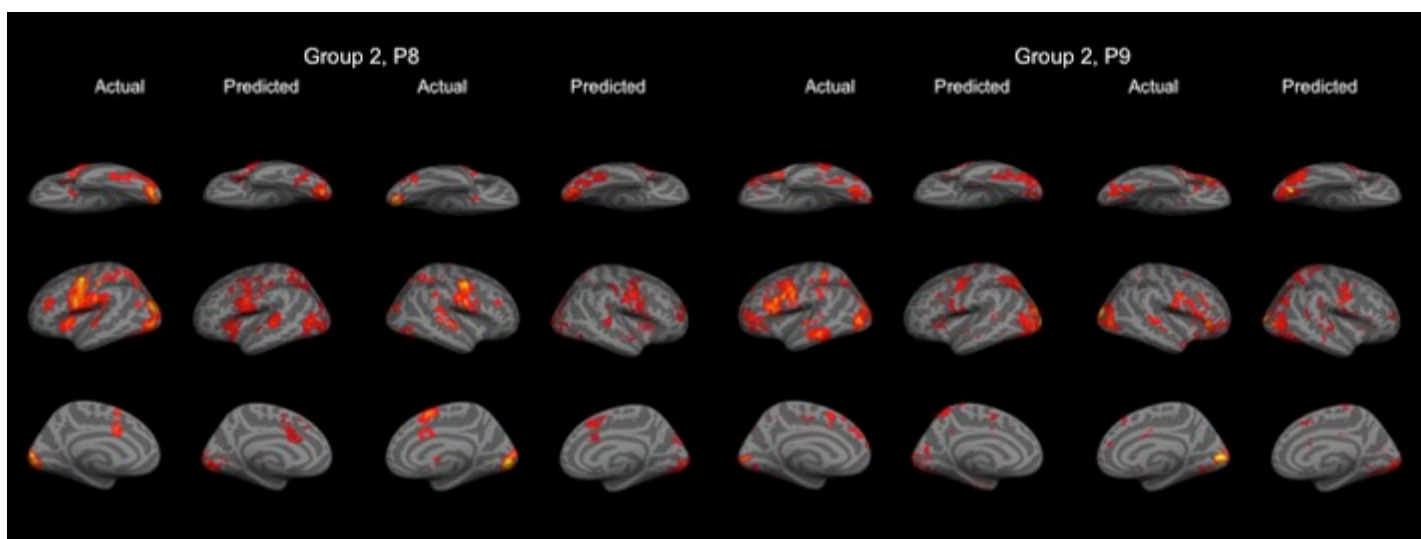
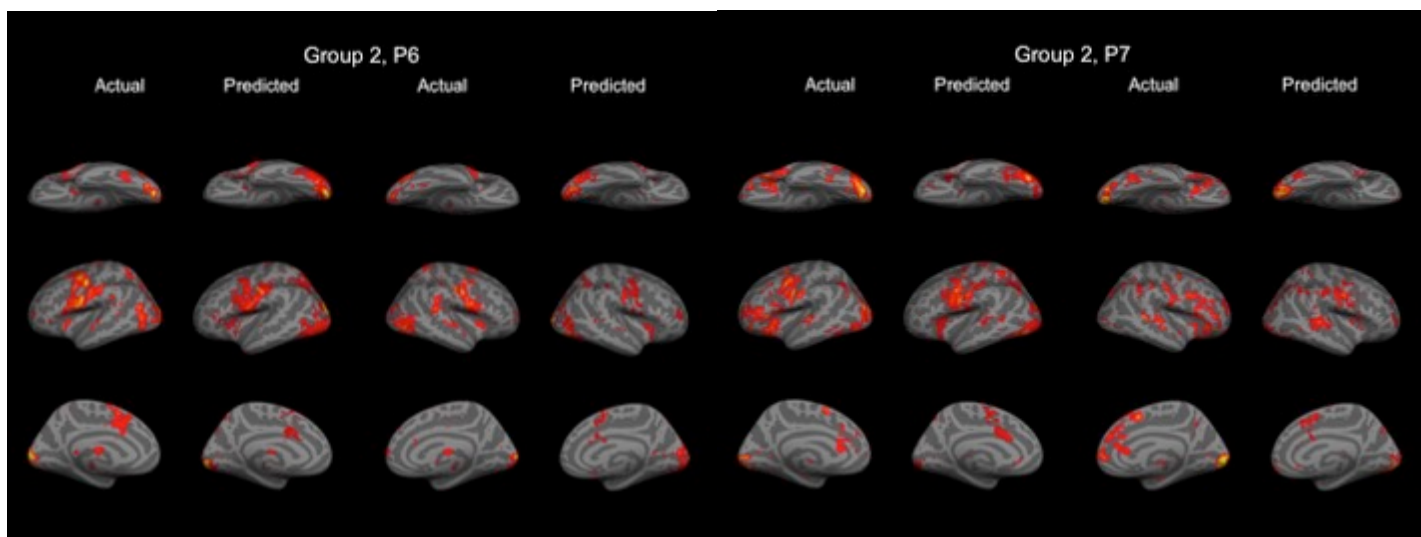
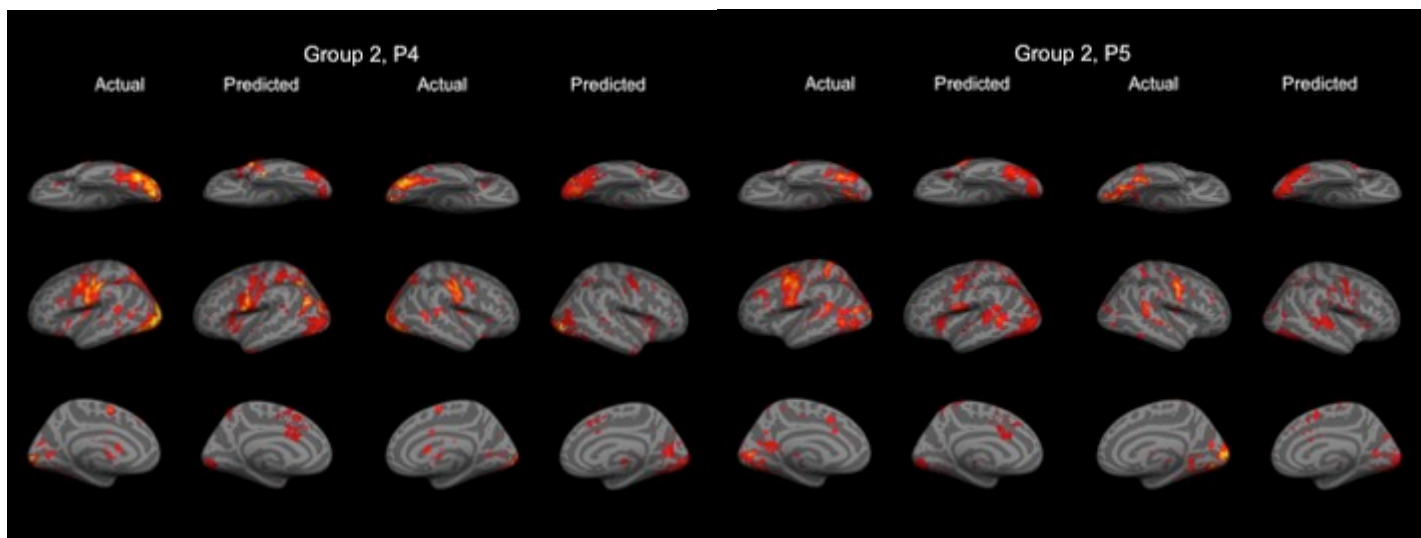
EW	Length	Log_Freq_HAL	PH	Length	Baseword Log_Freq_HAL
bear	4	10.066	bair	4	10.066
blood	5	10.855	blud	4	10.855
bowl	4	9.28	bohl	4	9.28
bread	5	9.112	braik	5	10.899
break	5	10.774	brayn	5	10.774
bull	4	9.025	bul	3	9.025
comb	4	7.386	coam	4	8.76
door	4	10.893	coyn	4	7.386
foot	4	10.095	flaim	5	7.155
geese	5	6.461	gurl	4	10.453
glove	5	7.764	hupe	4	10.605
heart	5	10.732	krib	4	7.154
hook	4	9.36	leef	4	8.861
mould	5	6.817	mhug	4	10.439
pear	4	6.878	mowth	5	7.404
pint	4	7.293	poap	4	7.293
pull	4	10.247	puhl	4	9.005
shoe	4	8.558	pynt	4	10.247
soup	4	8.707	shedd	5	8.737
sponge	6	7.376	shue	4	8.558
steak	5	7.32	spunge	6	7.376
tear	4	8.797	staik	5	7.32
thread	6	10.954	tare	4	8.797
took	4	11.377	thred	5	10.954
wasp	4	6.667	tohste	6	8.027
wolf	4	9.979	toohk	5	11.377
wood	4	10.087	tuthe	5	8.048
wool	4	7.633	werld	5	7.633
world	5	12.597	wull	4	12.597
yacht	5	6.914	yawt	4	6.914

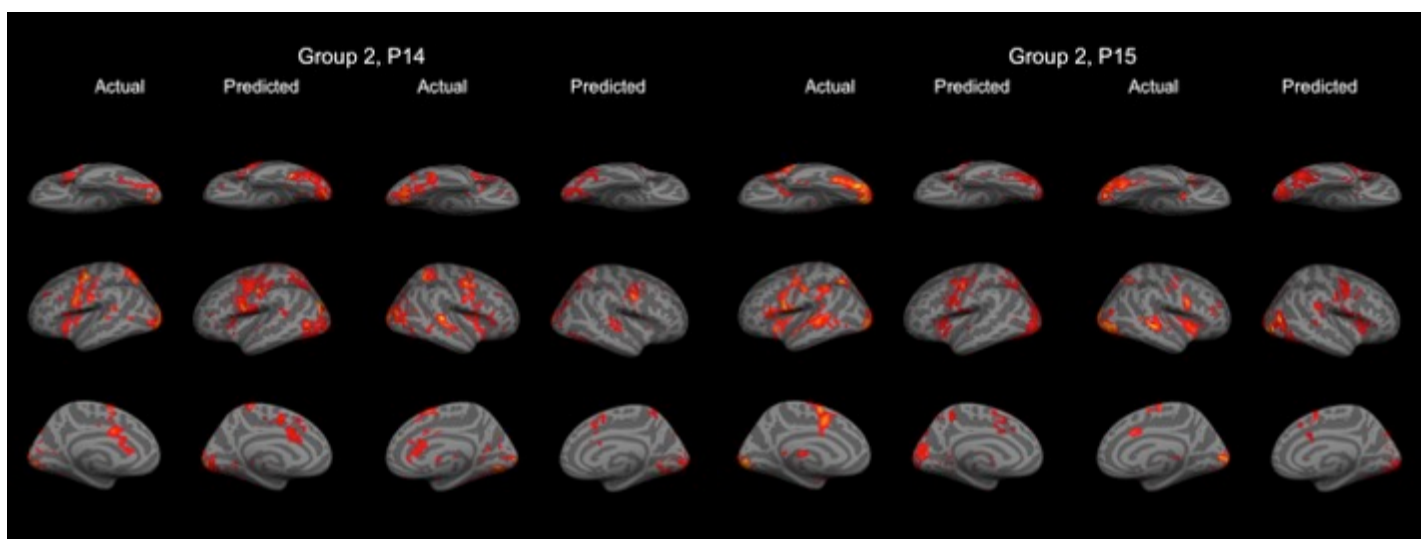
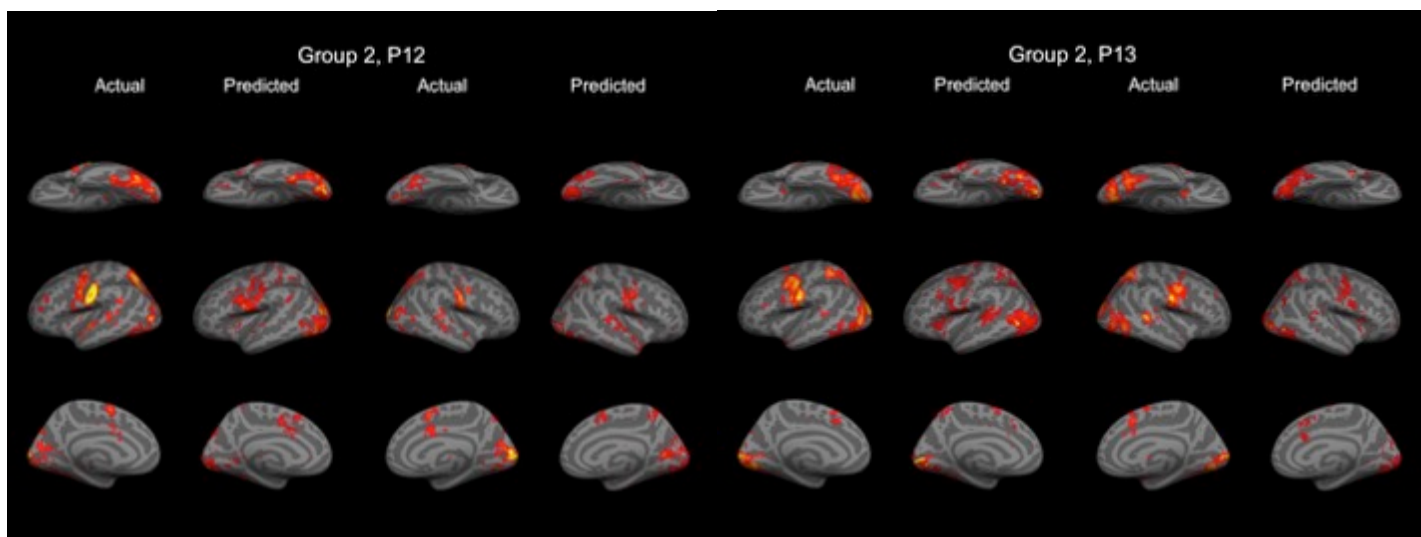
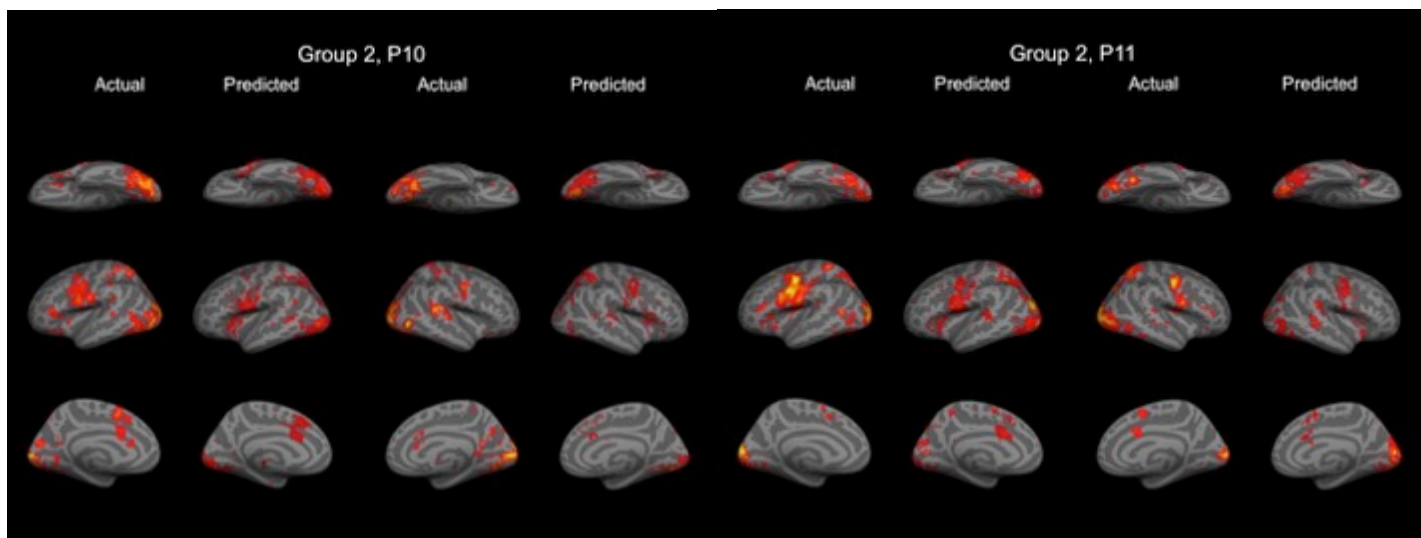
Exception Words



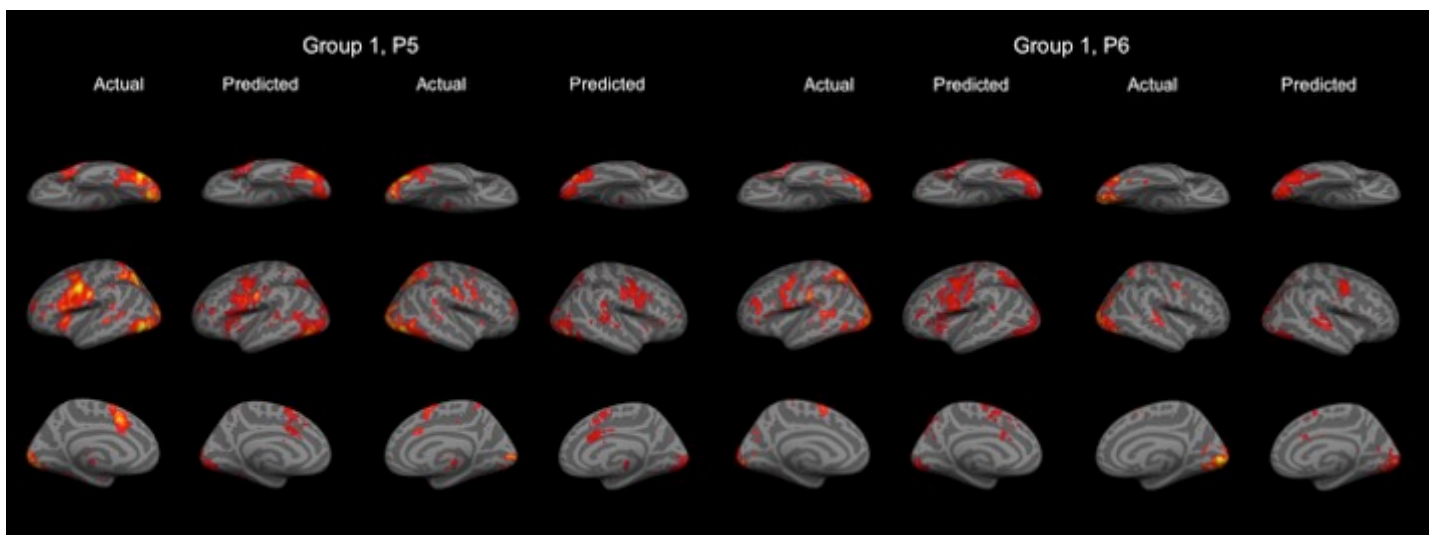
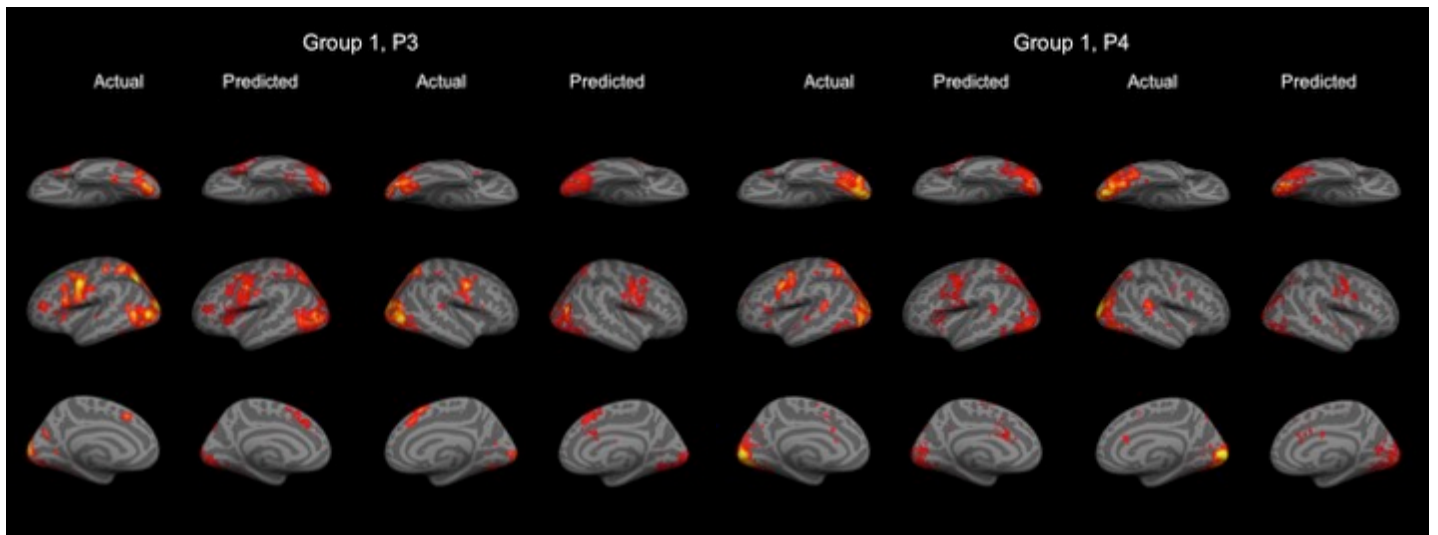
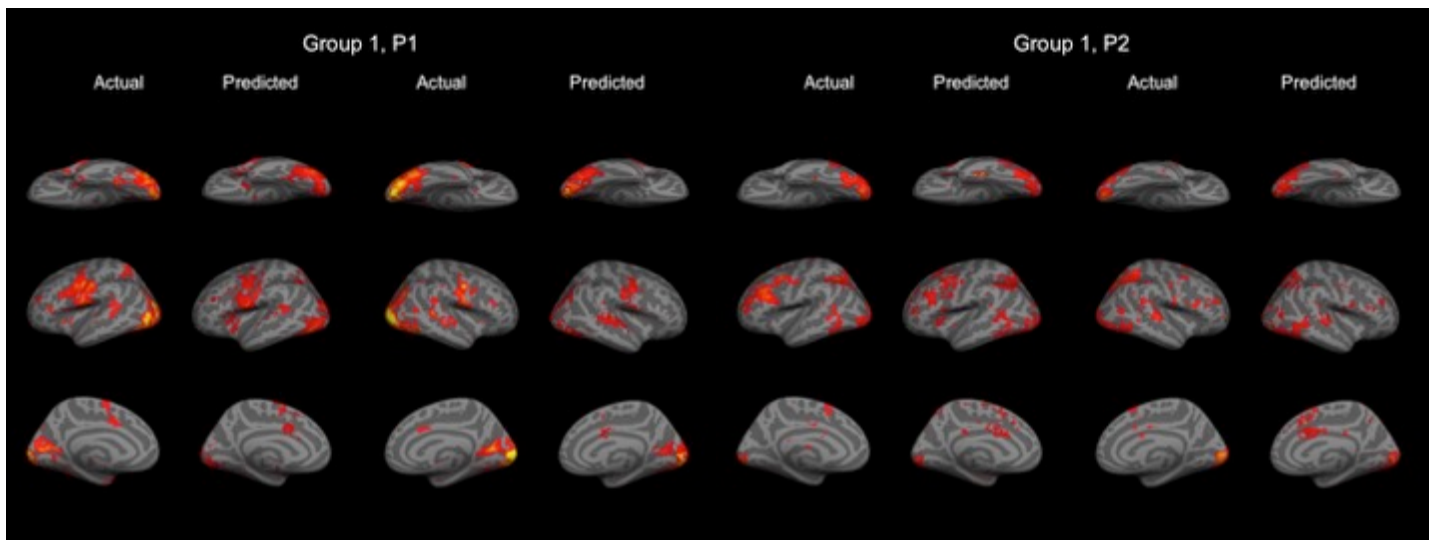


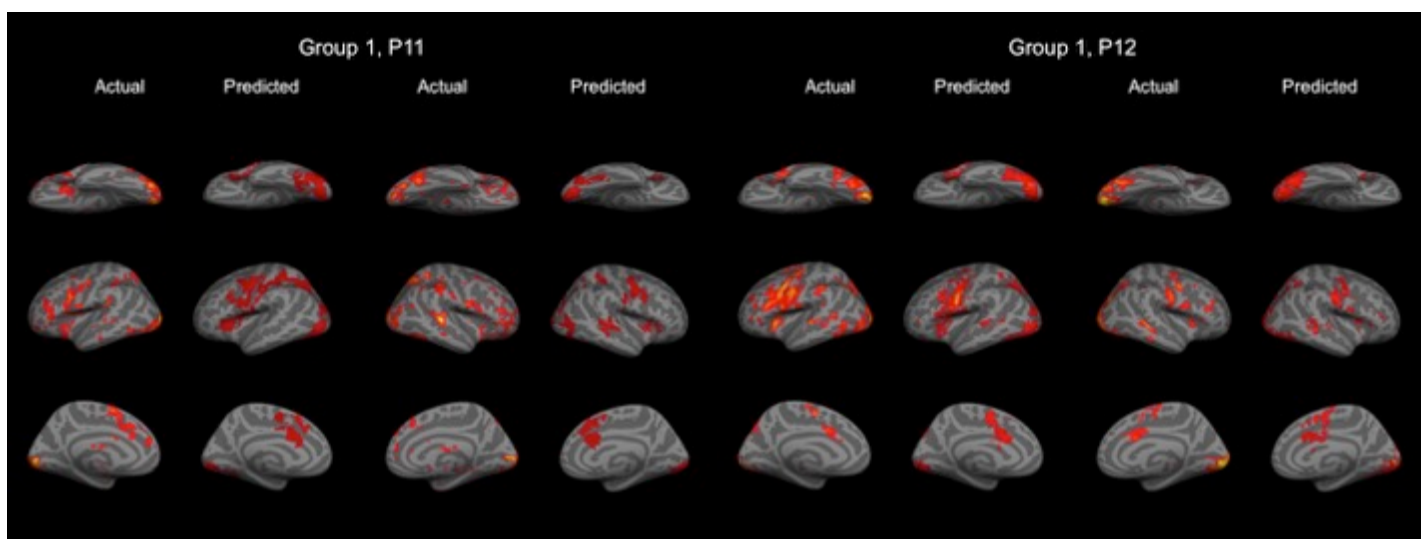
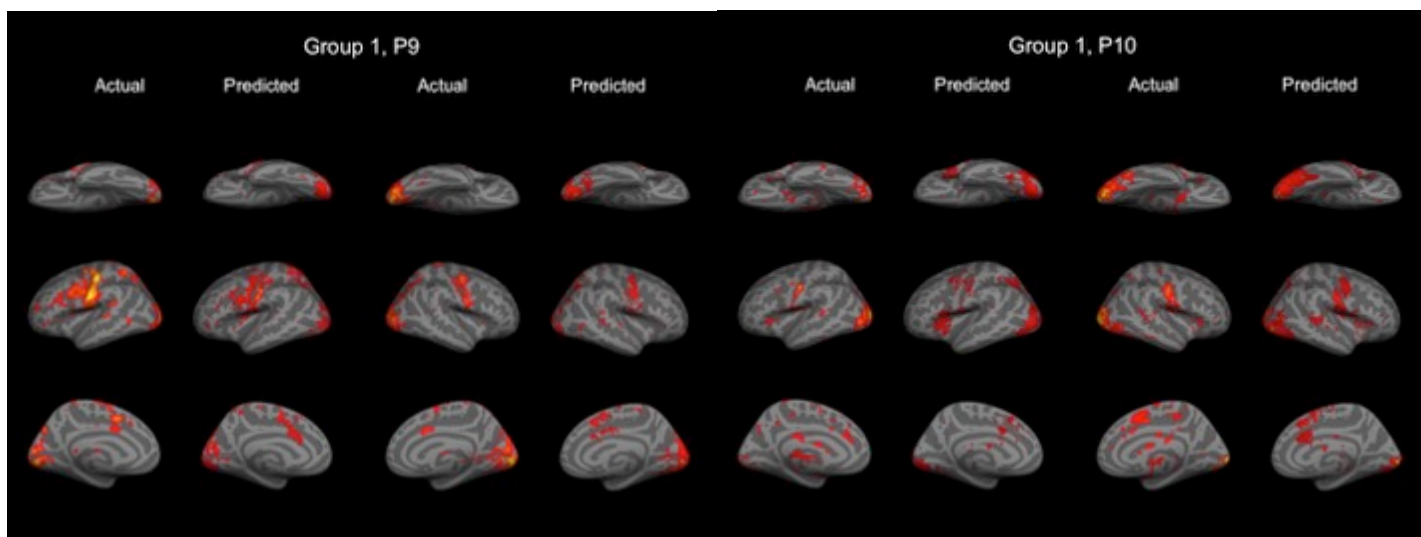
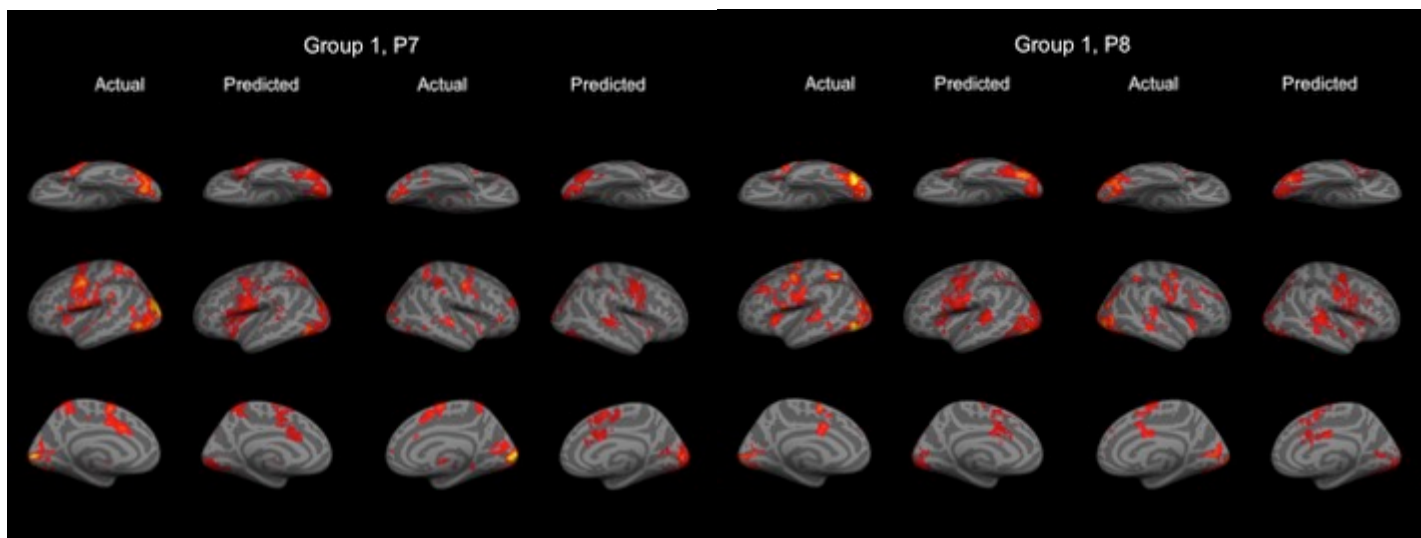


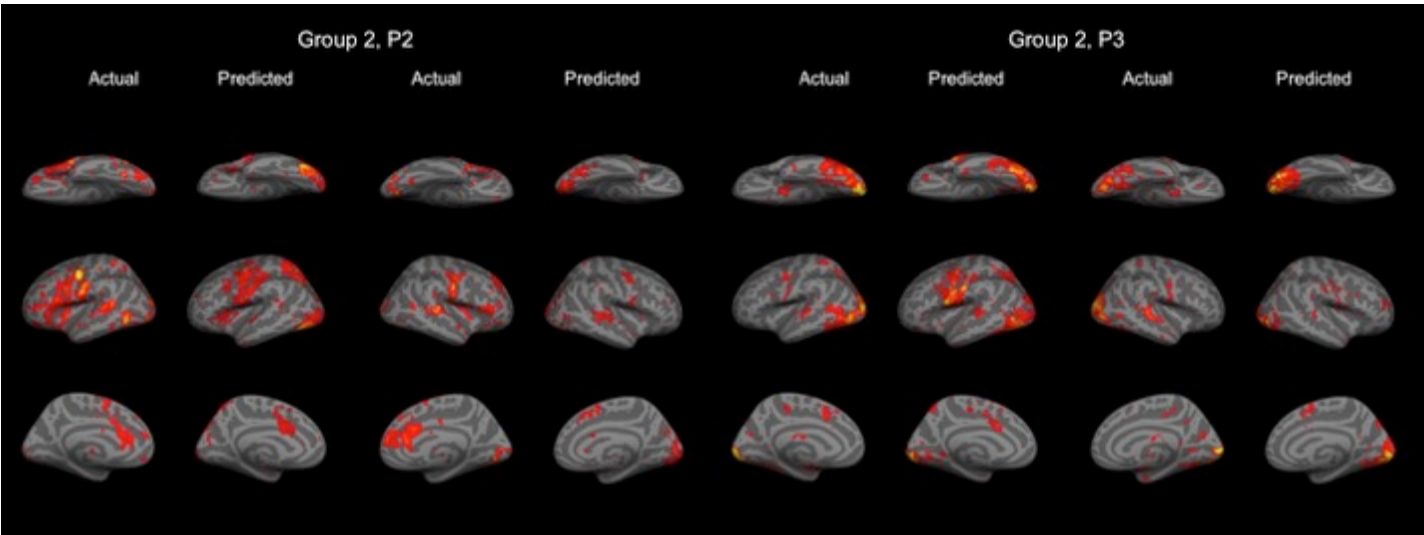
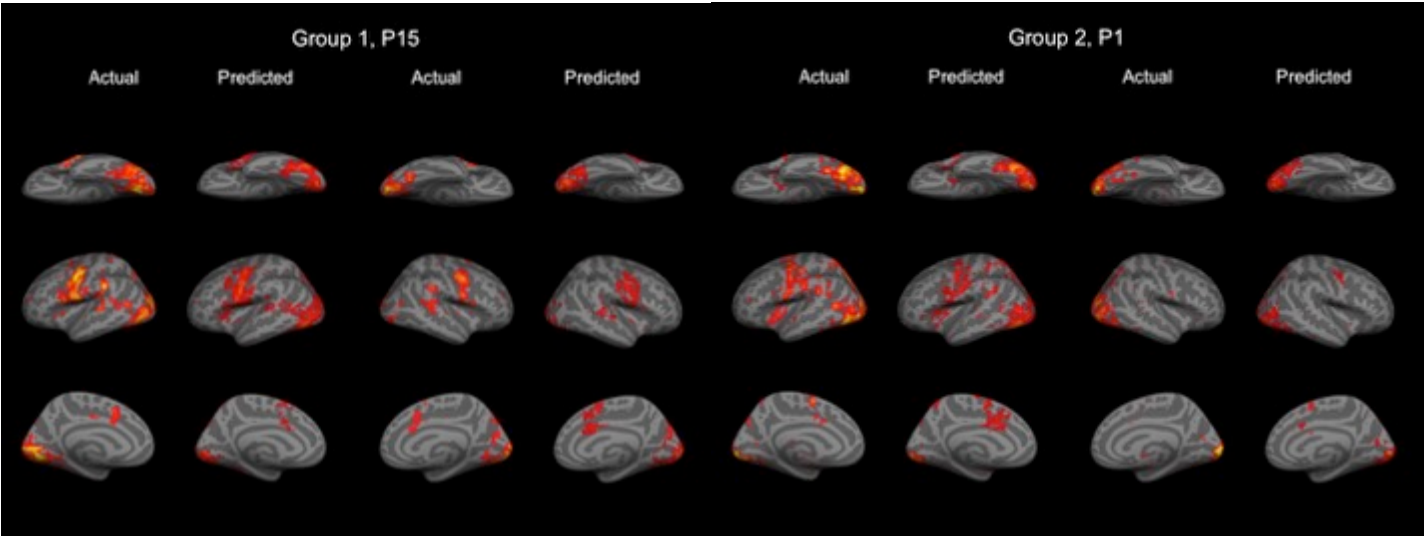
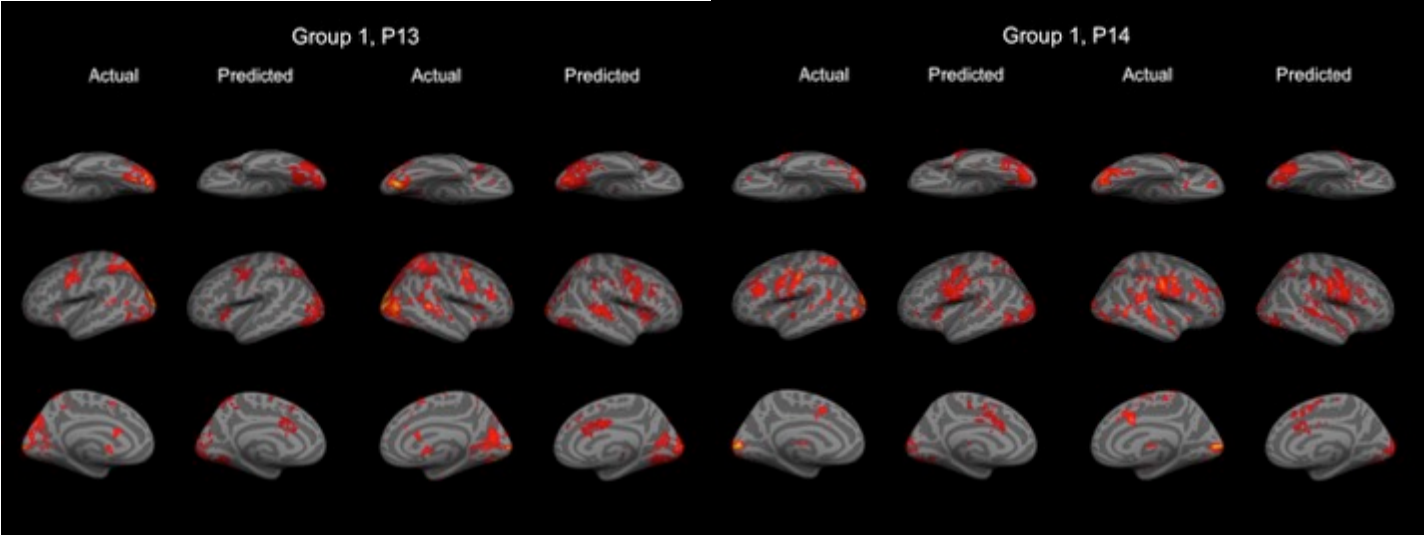


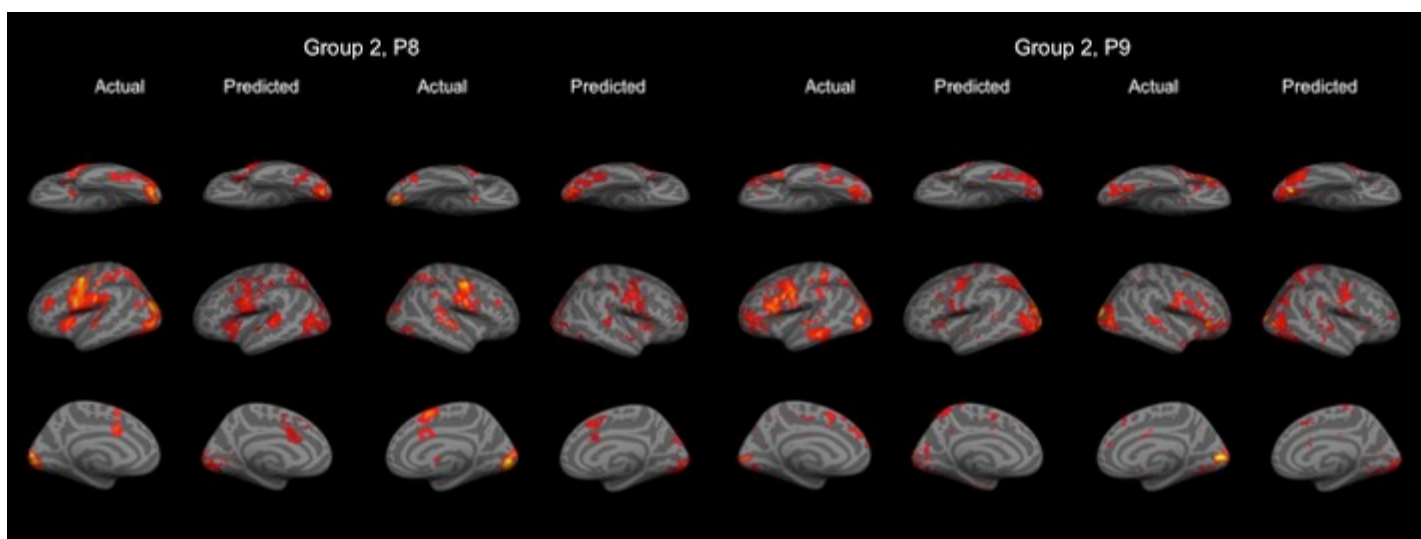
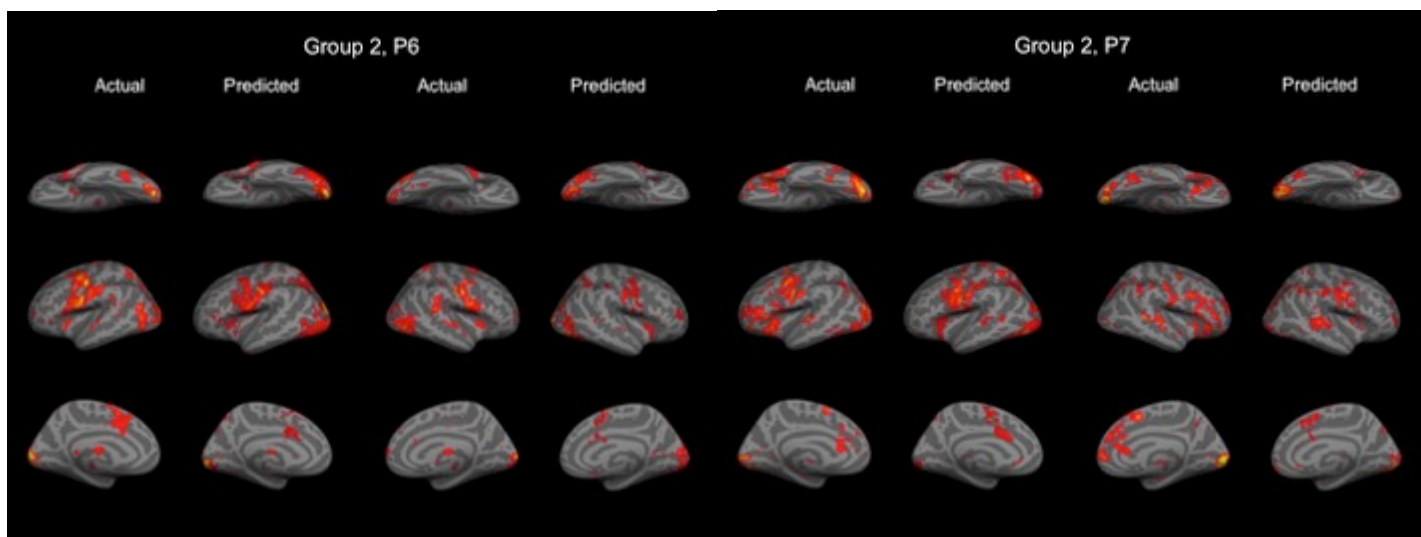
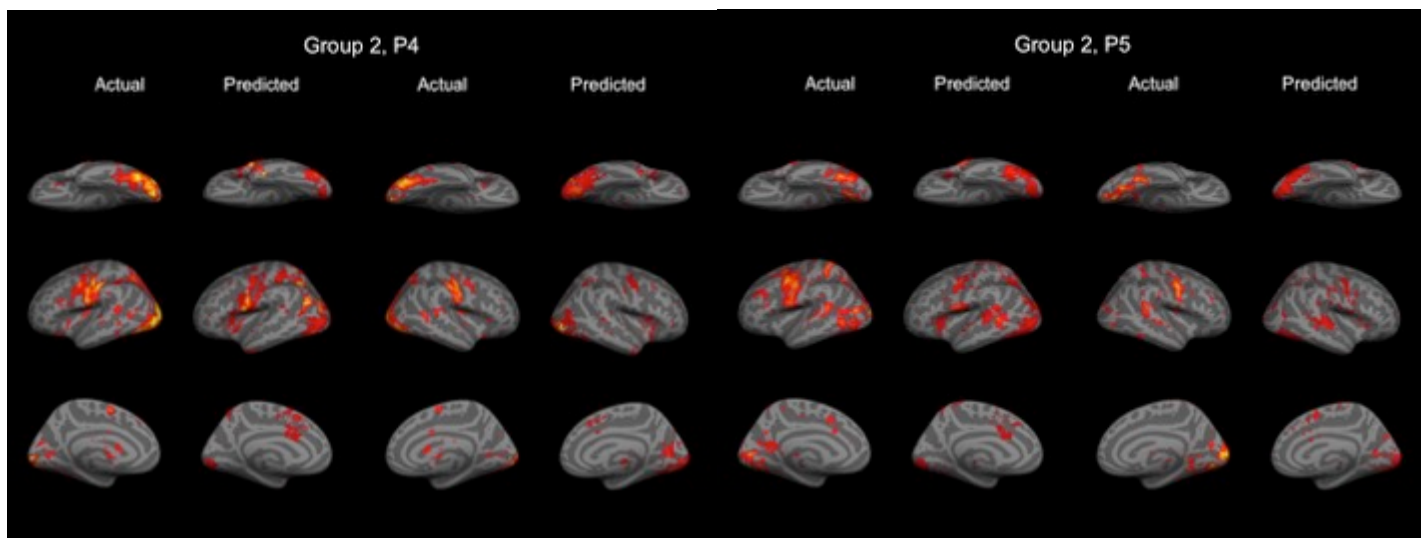


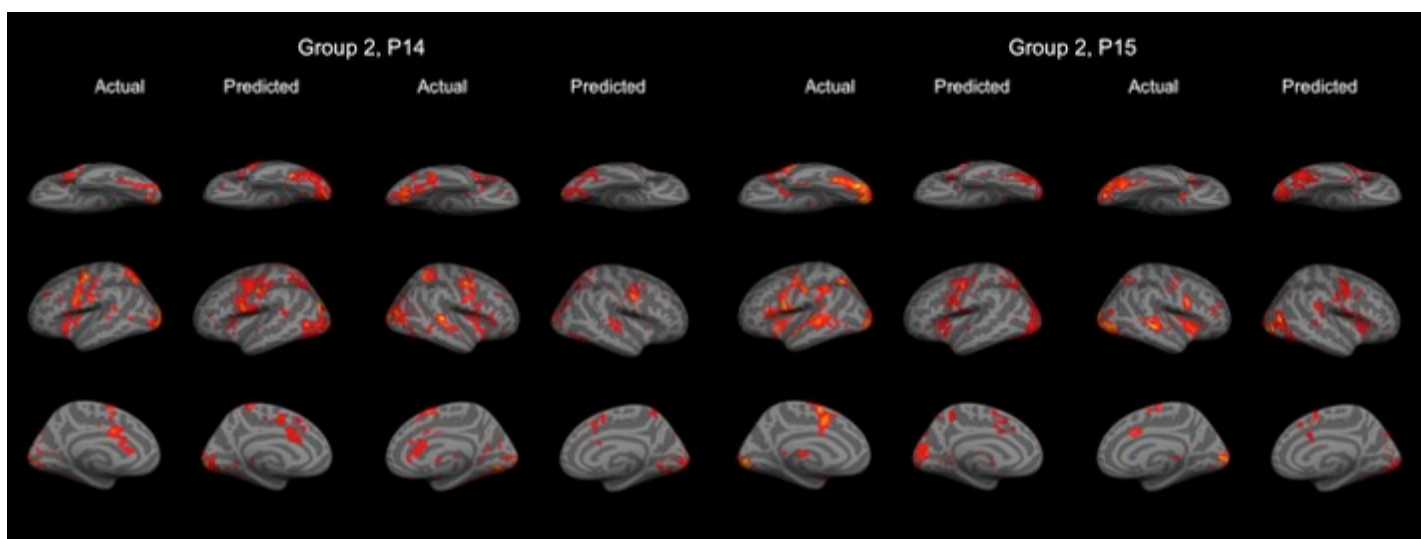
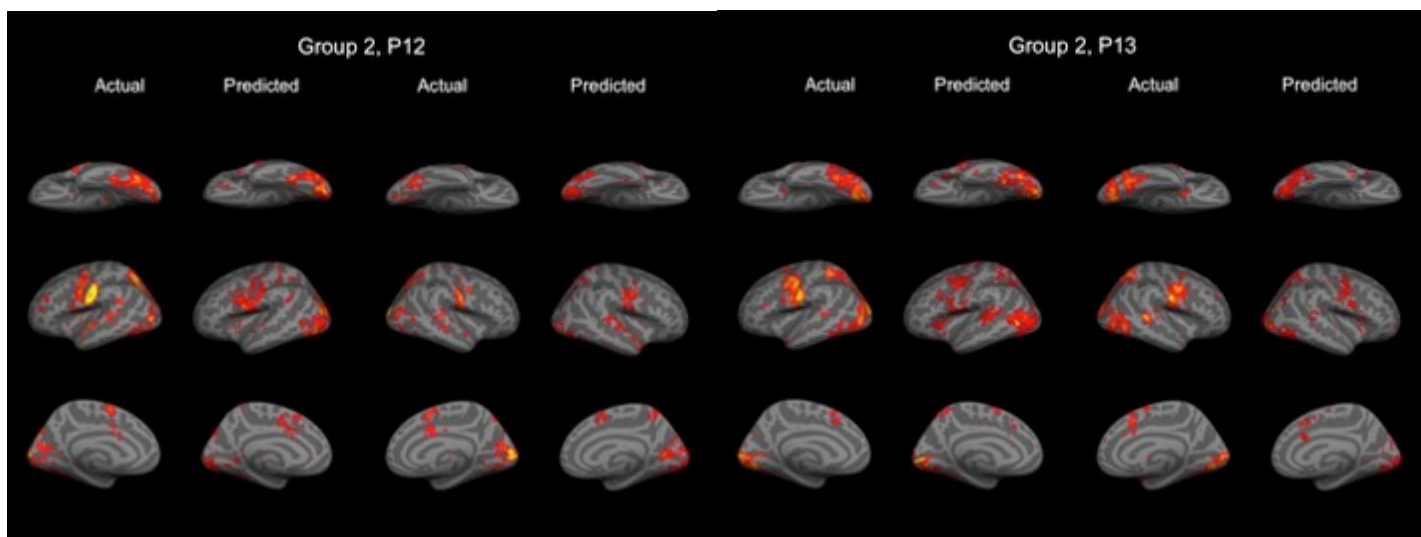
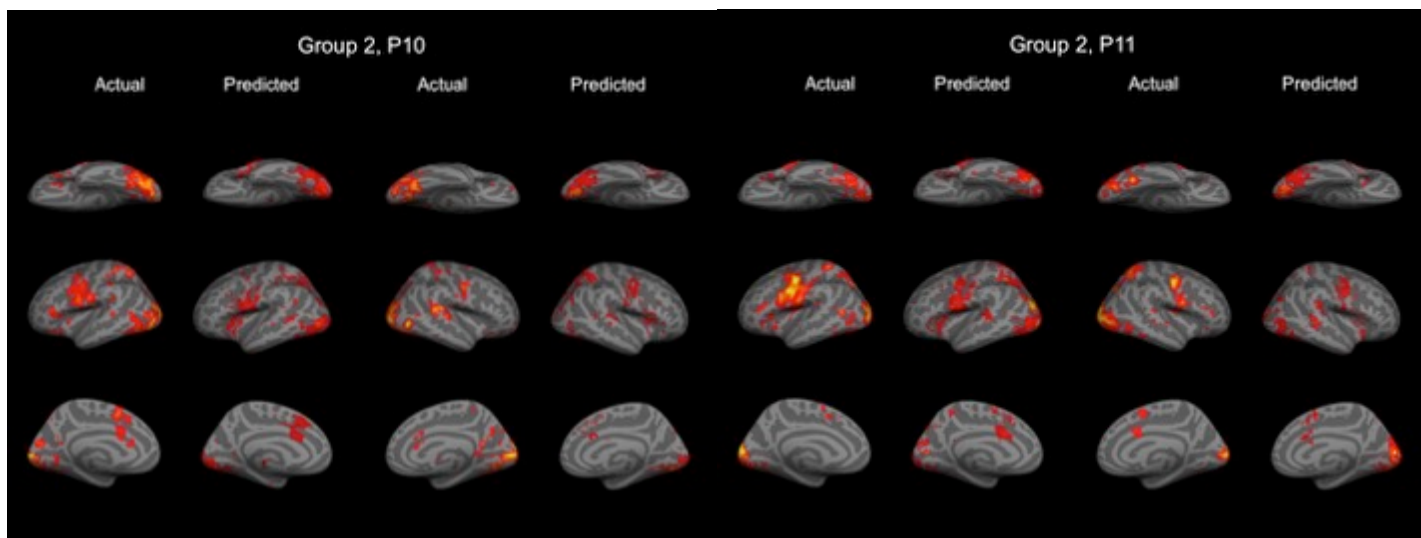
Pseudohomophones



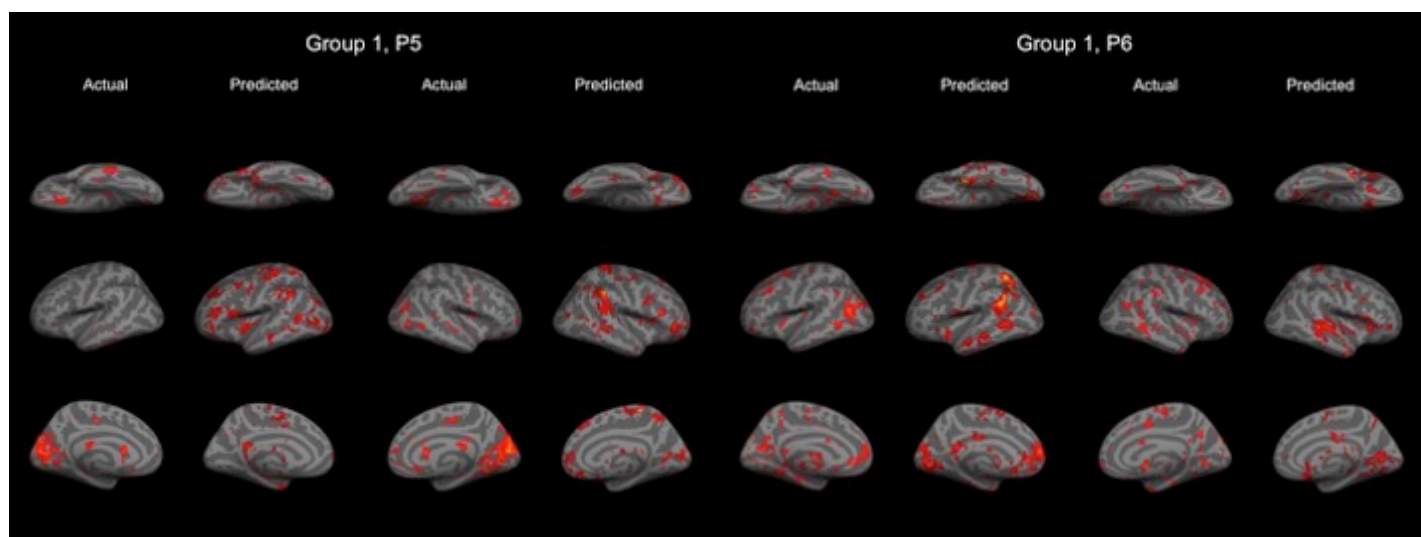
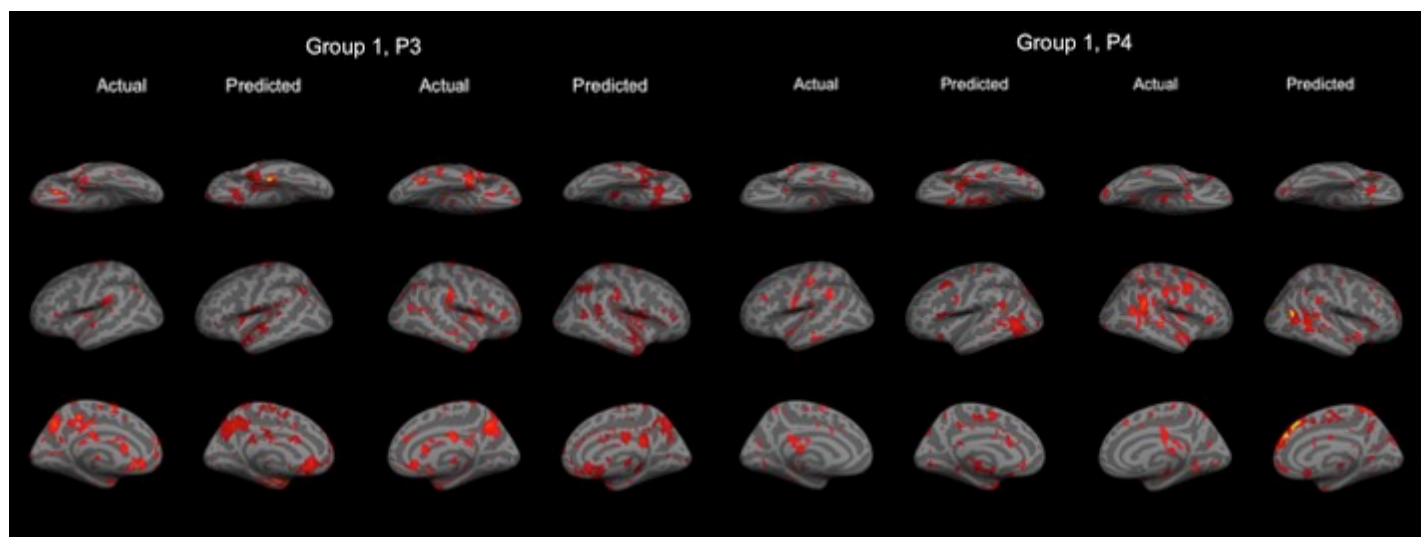
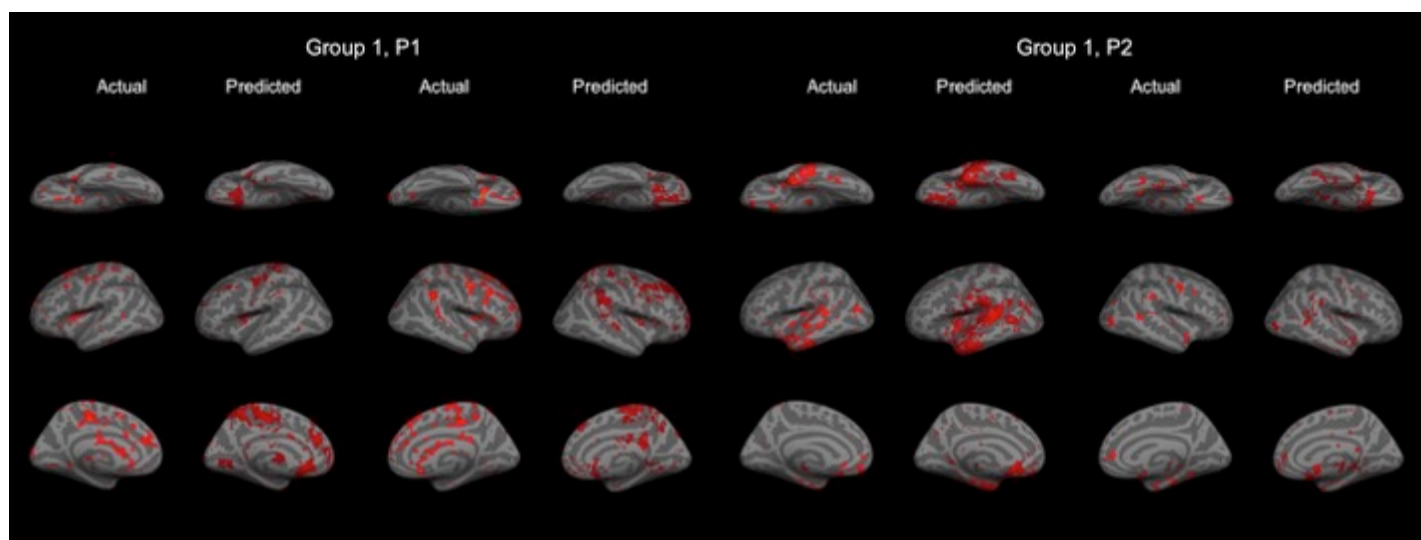


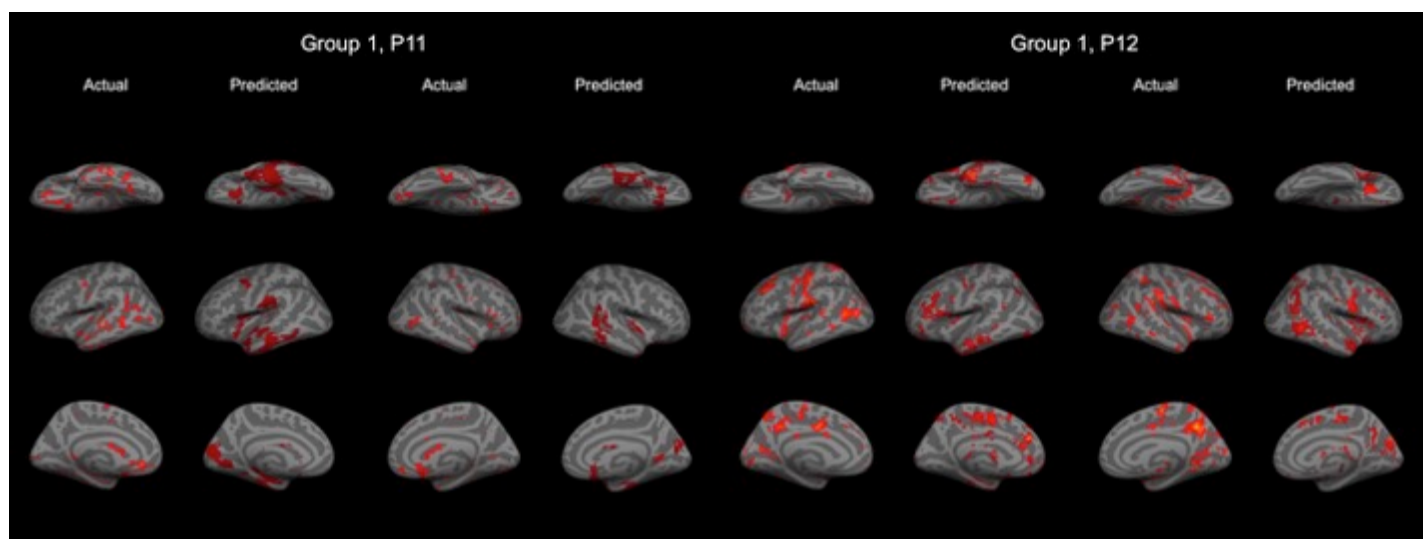
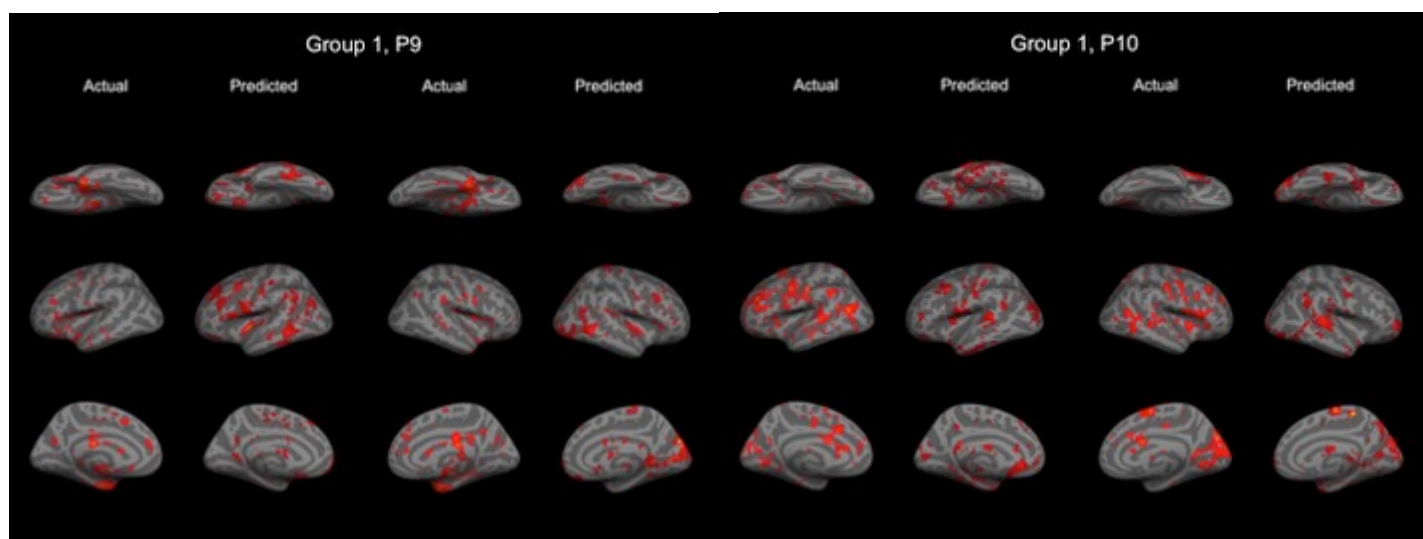
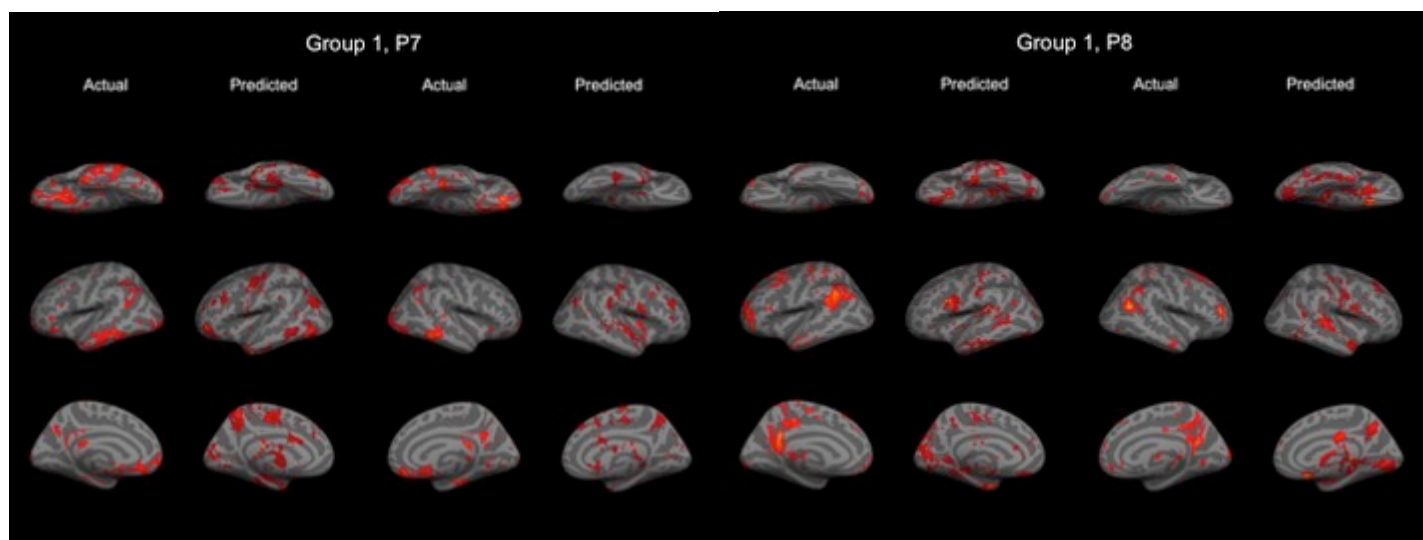


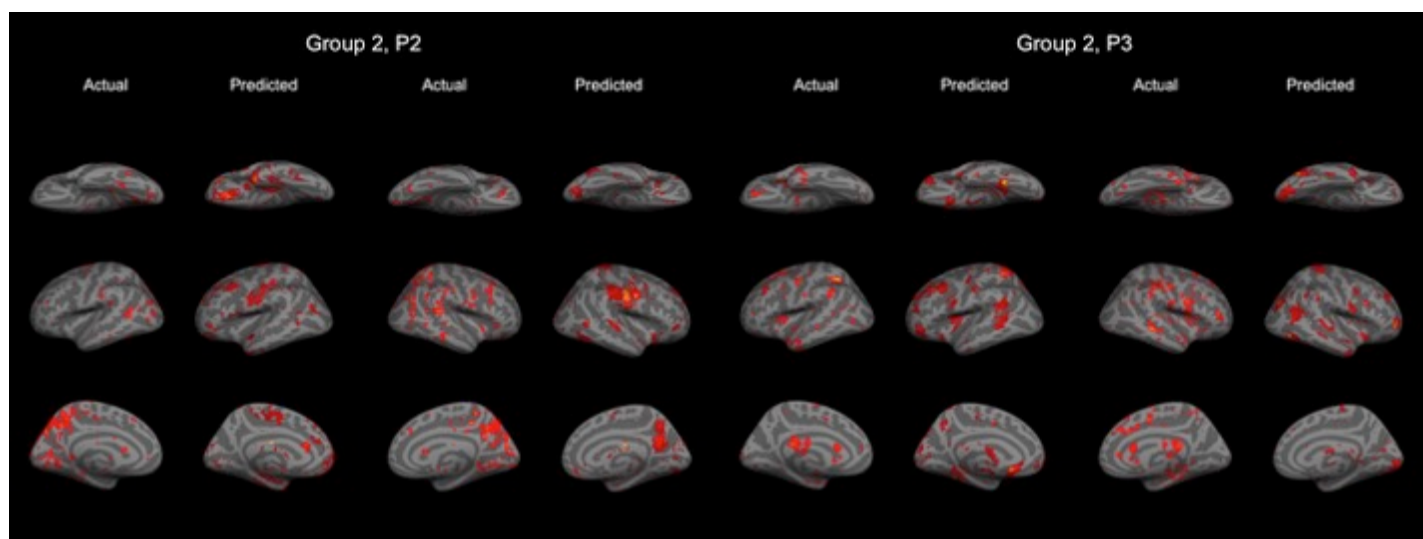
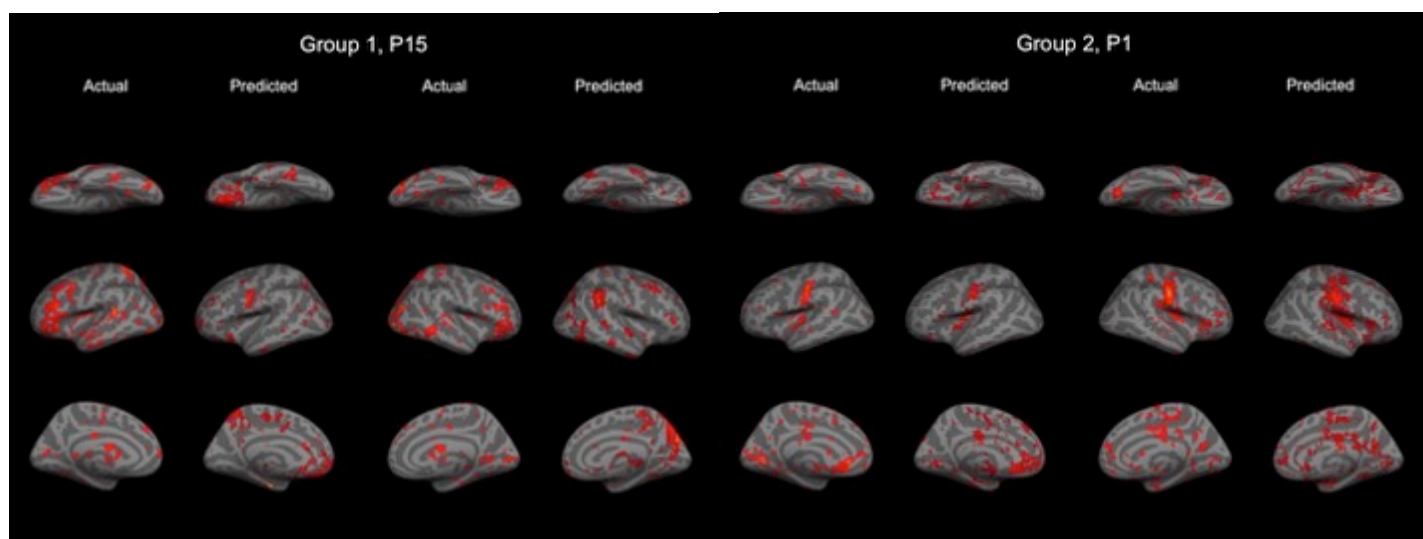
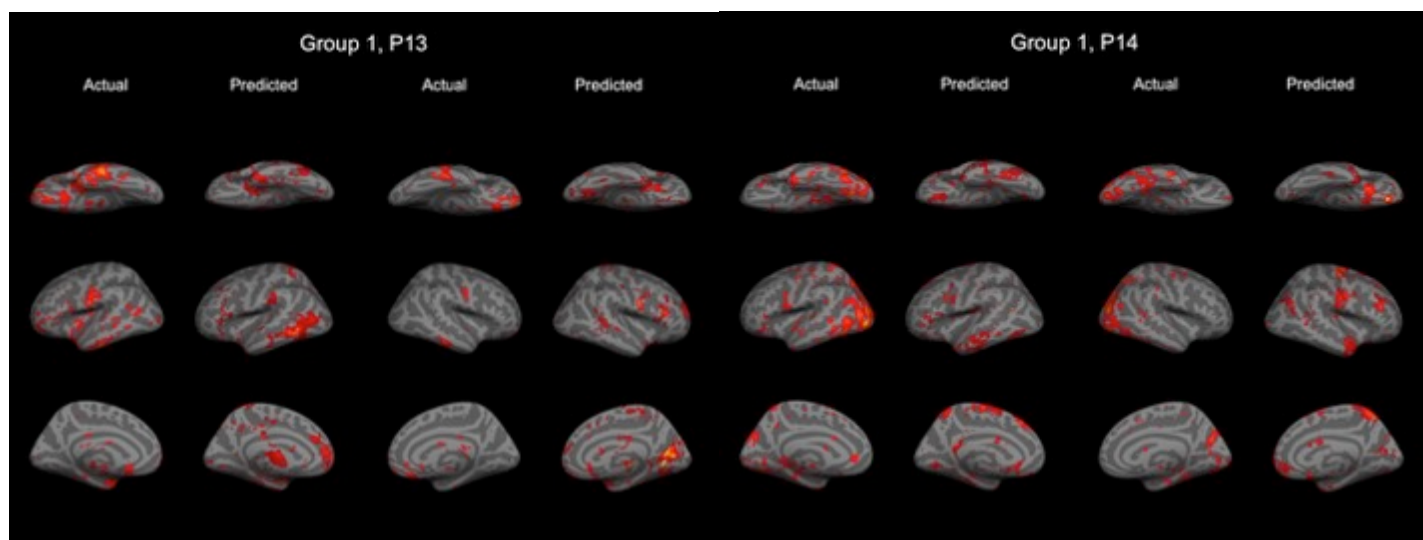


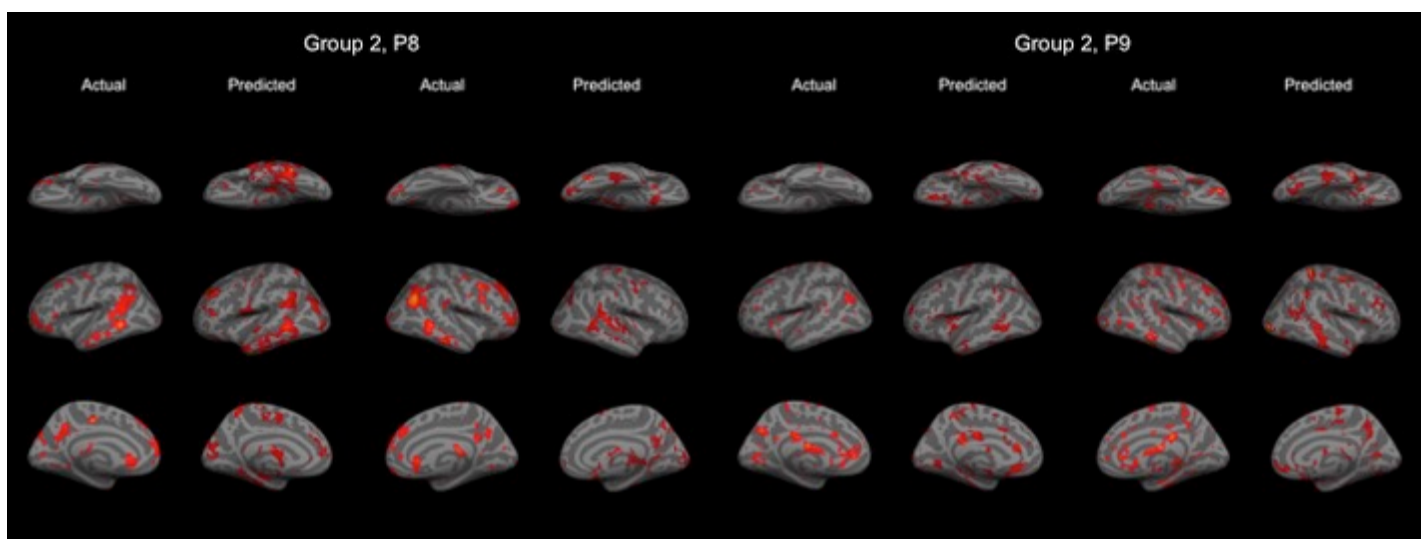
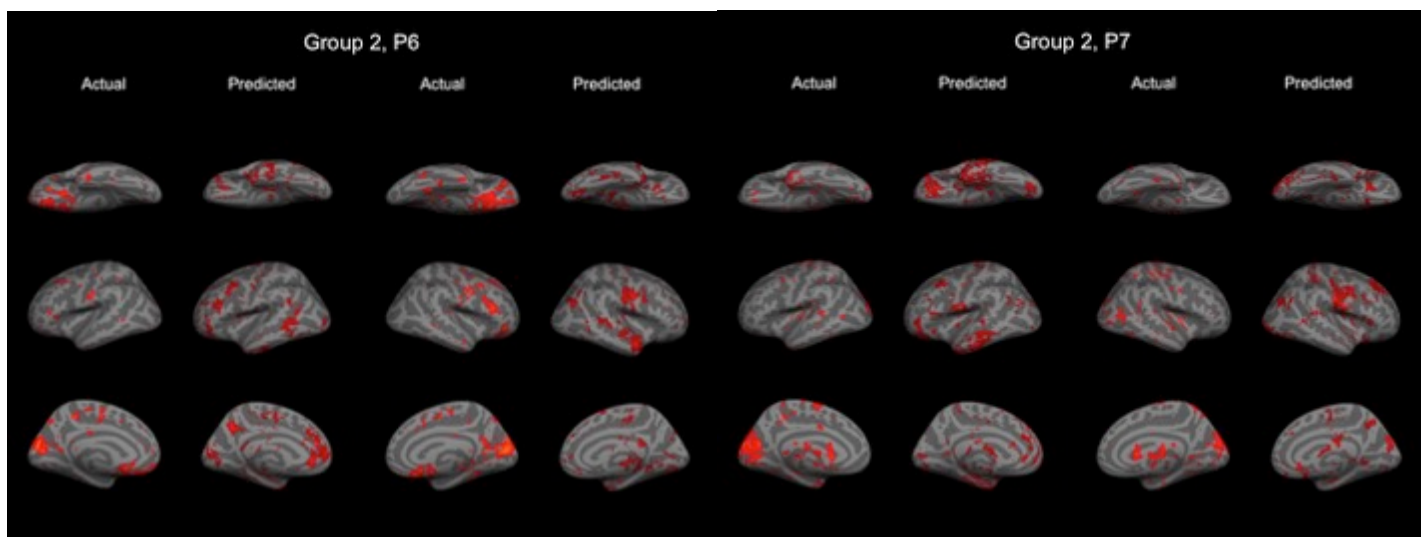
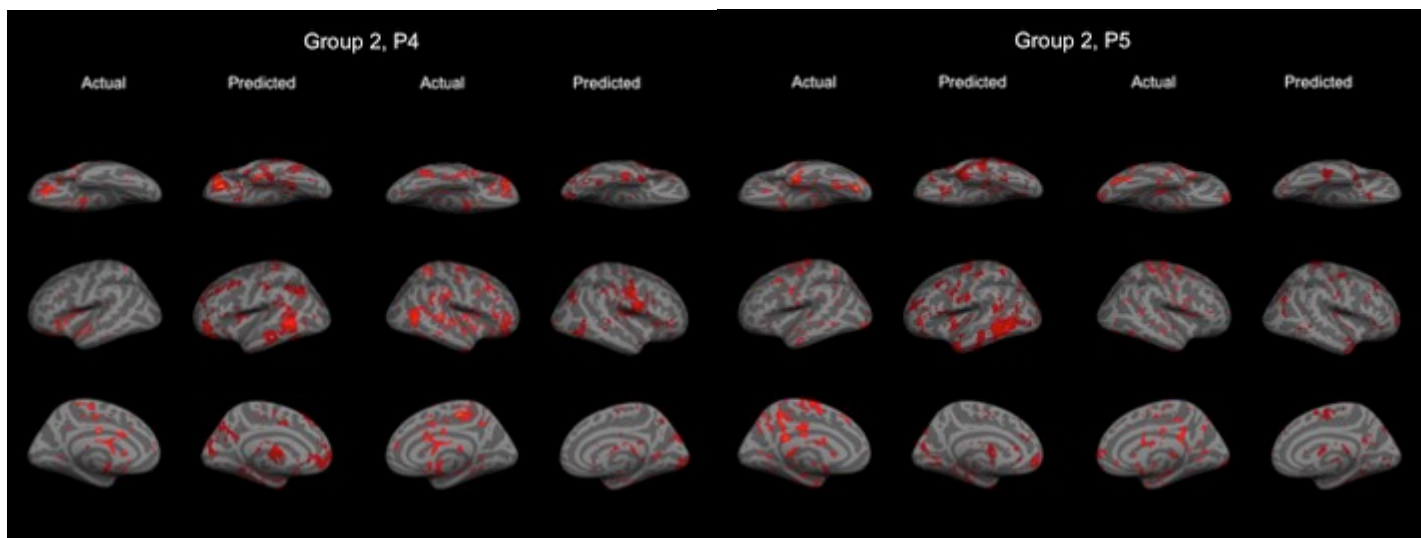


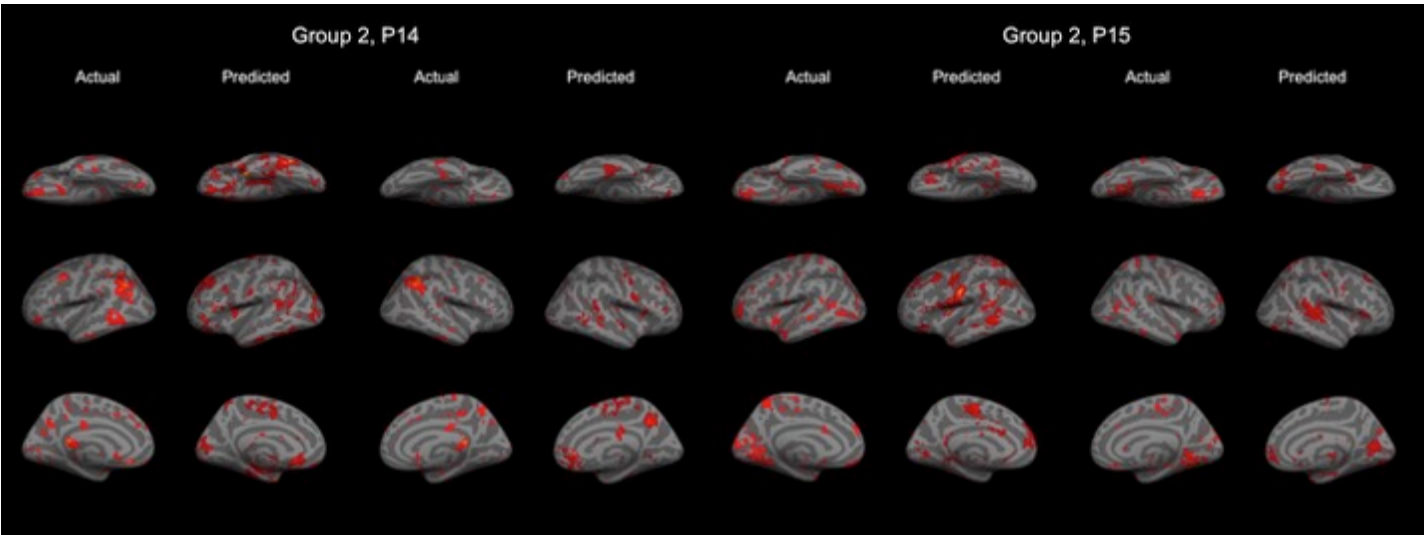
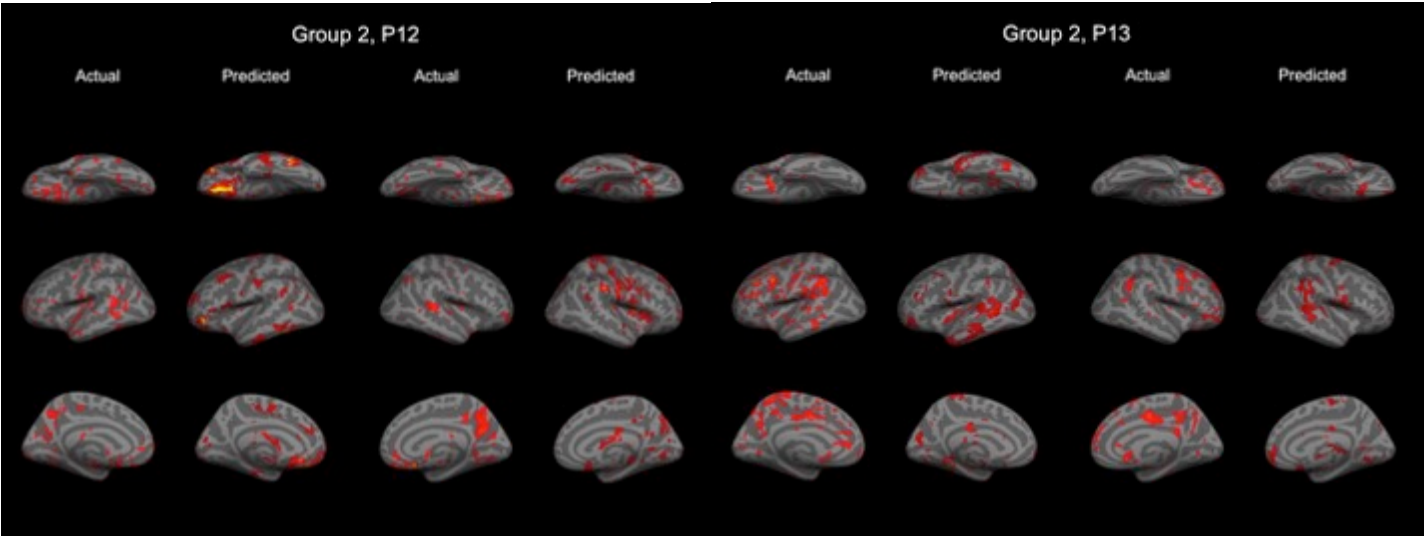
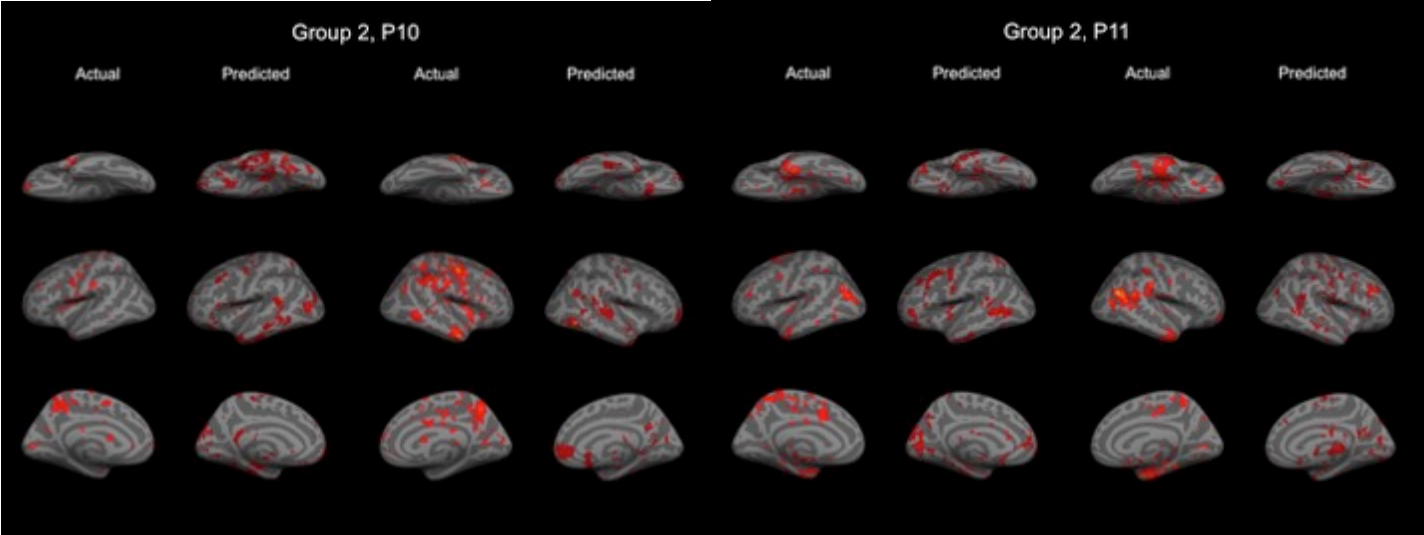
Exception Words > Pseudohomophones











Pseudohomophones > Exception Words

