

WHAT'S IN A WORD? AN FMRI INVESTIGATION OF SILENT SINGLE
WORD READING IN CHILDREN IN GRADES 2 AND 3

by

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Dalhousie University is located in Mi'kma'ki,
the ancestral and unceded territory of the Mi'kmaq.
We are all Treaty people.

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ABSTRACT

Amidst a large body of research investigating reading development, a lack of information remains concerning the brain regions engaged during word reading in developing readers. Thus, the present study aims to validate a passive word reading paradigm and identify the brain areas that are significantly active during single word reading, in second and third grade children. Five participants completed a word-screening task, behavioural assessments of reading, and a silent single word reading task during functional magnetic resonance imaging (fMRI). We demonstrated that during silent single word reading, children in grades 2 and 3 engaged the opercular and triangular parts of the left inferior frontal gyrus, the right superior temporal gyrus, and the left cerebellum. This result is valuable for increasing our understanding of skilled reading development, and future research may benefit from employing a similar experimental paradigm in a larger sample size, to increase clarity in the conclusions and literature.

LIST OF ABBREVIATIONS USED

fMRI	Functional Magnetic Resonance Imaging
PET	Positron Emission Tomography
BOLD	Blood-Oxygenation-Level-Dependent
MRI	Magnetic Resonance Imaging
WIAT-4	Wechsler Individual Achievement Test – Fourth Edition
TR	Repetition Time
BIDS	Brain Imaging Data Structure
MNI	Montreal Neurological Institute
DVARs	Spatial Standard Deviation of Successive Differences Images
AFNI	Analysis of Functional Neuroimages
EPI	Echo Planar Image
T1w	T1-weighted
INU	Intensity Non-Uniformity
CSF	Cerebrospinal Fluid
WM	White Matter
GM	Gray Matter
FD	Framewise Displacement

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CHAPTER 1: INTRODUCTION

1.1 DEVELOPING THE SKILL OF READING

During early development, a key focus of both teachers and children is the development of fluent reading skills, these being reading speed and accuracy (Peura et al., 2019). Primary school is a very important stage in literacy development, because children who do not develop adequate literacy skills by the end of third grade are at higher risk for reduced academic achievement (Snow & Mathews, 2016). By increasing our understanding of both the behavioural skills involved in reading development, and the neural correlates that underpin them, we may provide valuable insight that supports existing behavioural research of reading, and ultimately contributes to the development of improved teaching strategies to support developing readers.

1.2 SUBSKILLS OF READING

To understand the development of skilled reading, it is necessary to first understand the underlying skills involved in the acquisition of reading. Reading development is a complex and dynamic process, made up of a multitude of skills that change in their contribution to reading over the course of its development.

1.2.1 Phonological Skills

To begin the process of learning to read a child must develop phonological skills to recognize the segmental sounds that make up spoken words (Sandak et al., 2004).

There are different types of phonological processing abilities including *phonological memory*, engaged to encode and maintain information in a sound-based representation, *phonological access to lexical storage*, referring to the ability to retrieve phonological information from memory concerning words and word-parts, and *phonological*

awareness, the ability to recognize, discriminate, and manipulate individual sounds in words (Anthony & Francis, 2005). Phonological awareness is considered one of the most important early predictors of reading in normally developing children (Carroll et al., 2003). As children begin the process of learning the names of letters and their corresponding sounds, there is a dramatic influence on phonological awareness, and it is hypothesized that phonological information and representations become altered as letter-sound correspondences are developed (Anthony & Francis, 2005; Carroll et al., 2003).

1.2.2 Orthographic Knowledge

Orthography refers to the way in which words are spelled, and orthographic information encompasses the rules within a writing system (Apel et al., 2019). Thus, orthographic processing is the ability to acquire, remember, and use mental representations of written words and word segments, and apply the patterns and constraints of a given writing system (Apel, 2011). Orthographic skills develop as individuals acquire orthographic knowledge, which can be broken down into two main components. The first is general orthographic knowledge (or sublexical orthographic knowledge), which includes understanding the conventions used in a writing system such as the legal letter patterns in words, what position a letter may take in a word, and what letters can be combined to create a word (Apel et al., 2019; Conrad et al., 2013). Children begin to develop general orthographic knowledge at a very young age (Pollo et al., 2009). The second component of orthographic knowledge is word specific orthographic knowledge (or lexical orthographic knowledge), which refers to the stored mental representations of known words or word parts (Apel et al., 2019; Conrad et al., 2013). It

is this type of knowledge that can be used to quickly decode or recognize words, for fast and accurate reading (Ehri, 2005).

1.2.3 Semantic Knowledge

Semantic knowledge is the ability to access representations of the meaning of words (lexical-semantic knowledge) (Ehri, 2014; Mimeau et al., 2018; Perfetti, 2007), as well as the meaning-based relationships between words (broader semantic knowledge) (Ricketts et al., 2016). During early development, children undergo semantic learning, which is the process of learning the meanings for new written words (Mimeau et al., 2018). When developing readers are first exposed to a new word, they will begin to develop a representation of what that word means on the basis of a few interactions with the word (McGregor et al., 2002). Developing readers will store this representation in memory, and continue to update the representation of the word's meaning with each encounter, until they successfully develop a more stable representation of its meaning in lexical memory (Ehri, 2014; McGregor et al., 2002; Perfetti, 2007).

1.3 STAGE MODEL OF READING DEVELOPMENT

The ability to read fluently rests on the integration of phonologic, orthographic, and semantic information (Stites & Laszlo, 2017). Initially, while learning to read, children must rely on different aspects of these linguistic features to decipher and assign value to unfamiliar letters and words (Ehri, 2014). This is a complex process, and the contributions to reading skill from orthographic, phonologic, and semantic information change over the course of reading development. In an effort to better understand these contributions, models of the reading development trajectory have been created, breaking it down into a set of stages (Chall, 2013; Ehri, 1991). Each stage differs from one to the

next in qualitative ways. However, there is overlap of skills being used from one stage to another, throughout the continuous, dynamic course of reading development (Chall, 2013; Ehri, 2014). Thus, while ages and grades are presented along with developmental stages, these are only approximations. Children will proceed through the stages in a consistent sequence, however the pace at which they do so will vary from one individual to the next.

1.3.1 Pre-Reading Stage

The pre-reading stage is defined as occurring from birth to six years of age, this stage covers the greatest series of change of all the defined stages, beginning with oral language development (Chall, 2013). During this stage, pre-readers are learning that sounds in words can be segmented, broken down into parts and combined with other word parts, and individual sounds can be blended together to produce a whole word (Chall, 2013). These oral language skills are foundational to reading, and develop rapidly. By the age of six, the average child comprehends approximately 14,000 spoken whole words (Goswami, 2001), having effectively mapped the semantic information to the known pronunciation of the word in memory. During the pre-reading stage, children are also developing concepts about the features of writing. Towards the end of this stage, pre-readers typically know the general visual characteristics of text, can name most letters of the alphabet, write their names, and demonstrate an understanding that print has value for language and reading (Chall, 2013).

1.3.2 Initial Reading Stage

Children are in the initial reading stage between the ages of 6 and 7 (Chall, 2013). At this point in reading development, young readers are beginning to associate letters of the alphabet with their corresponding sounds, and begin to use this information to decode

unfamiliar written words (Steinman et al., 2006). During this stage, young readers are beginning to learn the rules that indicate how sounds will vary based on the larger structure of a word (e.g., the sound the letter ‘a’ makes in cap, versus cape) (Steinman et al., 2006). As children near the end of this stage of reading development they tend to rely on predicting written words based on the first and last letters of the word, or through context cues. Initial readers may use a decoding strategy for more familiar words, but have not yet mastered decoding unfamiliar words in text (Ehri, 2014).

1.3.3 Confirmation and Fluency Stage

Young readers are in the confirmation and fluency stage around the beginning of the second grade, between the ages of 7 and 8 years old. In this stage, children begin to use decoding skills effectively for both familiar and novel words, and develop more complex phonological skills (e.g., the ability to manipulate smaller phonological units) (Chall, 2013; Steinman et al., 2006). By gaining the ability to segment known word pronunciations into smaller units of sound, and eventually phonemes, beginning readers are able to map the spellings of words onto their pronunciations, which have already been associated with meaning in memory (Ehri, 2014).

The *Dual Route Model* for reading describes this process as the *indirect route* for reading (also known as the grapho-phonologic or lexical non-semantic route) (Ehri, 2014). When employing the indirect route for reading, readers map graphemes, the smallest unit in a writing system such as letters or a digraph (a pair of characters representing one sound), onto their individual phonemes. They can then blend these grapheme-phoneme correspondences until the pronunciation of a familiar word is

produced (Ehri, 2014). This process of decoding words is used for interacting with and learning new written words (Coltheart et al., 2001).

Towards the end of this stage, young readers have become efficient at using strategies to break down unfamiliar written words (Chall, 2013) and begin to use visual whole-word patterns to recognize highly familiar words (Chall, 2013; Steinman et al., 2006). Through efficient decoding, these readers actively create mappings between whole printed words, the associated pronunciation, and its meaning, in memory (Ehri, 2014). This leads to the development of a bank of *sight words* in memory (Ehri, 2014), which are developed when the sight of a word immediately prompts memory of its meaning and pronunciation (Jobard et al., 2003). Over the course of reading development, children are continuously developing sight words in memory. However, it is during this stage that efficient use of decoding strategies is able to accelerate the attainment of new sight words in memory and enable gains in reading fluency (Chall, 2013; Steinman et al., 2006).

1.3.4 Reading for Learning

Around the beginning of the third grade, between the ages of 8 and 9, developing readers have a continuously growing bank of sight words in memory. Reading sight words is described by the Dual Route Model as a *direct* (or lexicosemantic) route for reading (Ehri, 2014). This is a more efficient method for reading, as it is an automatic process that does not require breaking down or sounding out words (Ehri, 2014). As readers develop more sight words in memory, they are adding to a list of words for which they know the spelling, pronunciation, and meaning, which is also referred to as their *mental lexicon* (Coltheart, 2006). This allows for automatic visual word recognition, pronunciation, and understanding of words' meaning (Coltheart, 2006). Thus, readers are

increasing their reading fluency by more consistently relying on the direct route for reading (Chall, 2013; Ehri, 2014). This transition from reliance on the indirect route to a direct route for reading is a critical milestone in skilled reading development.

As sight word vocabulary and reading fluency increase, developing readers are able to become ‘unglued from print’ and no longer need to focus all their attention during reading towards decoding unknown words, and can instead focus on the meaning of the text they are reading (Steinman et al., 2006). It is for this reason that readers are said to be ‘reading for learning’, as they are no longer interacting with text exclusively to learn how to read, but can now extract information and knowledge from the text. Since it is between the second and third grade that children make this shift in reading skill towards more automatic and effortless word reading, this is an important development period to study in order to understand all the factors contributing to healthy reading development.

1.4 THE NEURAL BASES FOR READING

In addition to behavioural accounts of reading, neuroimaging studies have provided a detailed overview of the neural organization of reading. Generally, these studies involve functional magnetic resonance imaging (fMRI) and Positron Emission Tomography (PET). However, PET is used less frequently in recent studies, due to advantages in safety and experimental design flexibility provided by fMRI, which is non-invasive and does not involve exposure to radiation, making it a safe and effective way to study both adults and children (Anderson & Gore, 1997; Palmer et al., 2004).

1.4.1 Functional Magnetic Resonance Imaging

fMRI provides an indirect measure of brain activity, by measuring and quantifying the magnetic properties of oxygenated and deoxygenated blood in the brain (Palmer et al., 2004). This measurement provides information on the blood-oxygenation-level-dependent (BOLD) response, which describes local increases in blood oxygenation driven by increased neural activity in that area (Palmer et al., 2004). fMRI allows for the resolution of brain activity at the level of millimetres, by sampling activity in three-dimensional units (called voxels) that are typically on the order of 10-30 mm³. Each voxel is a discrete data value representing the cumulative activity of many neurons (Kriegeskorte et al., 2008). In skilled adult readers, fMRI investigations of reading have identified the temporoparietal cortex is sensitive to phonology; the left occipitotemporal cortex is sensitive to orthography; and the inferior frontal cortex exhibits selectivity for orthographic input (Glezer et al., 2016).

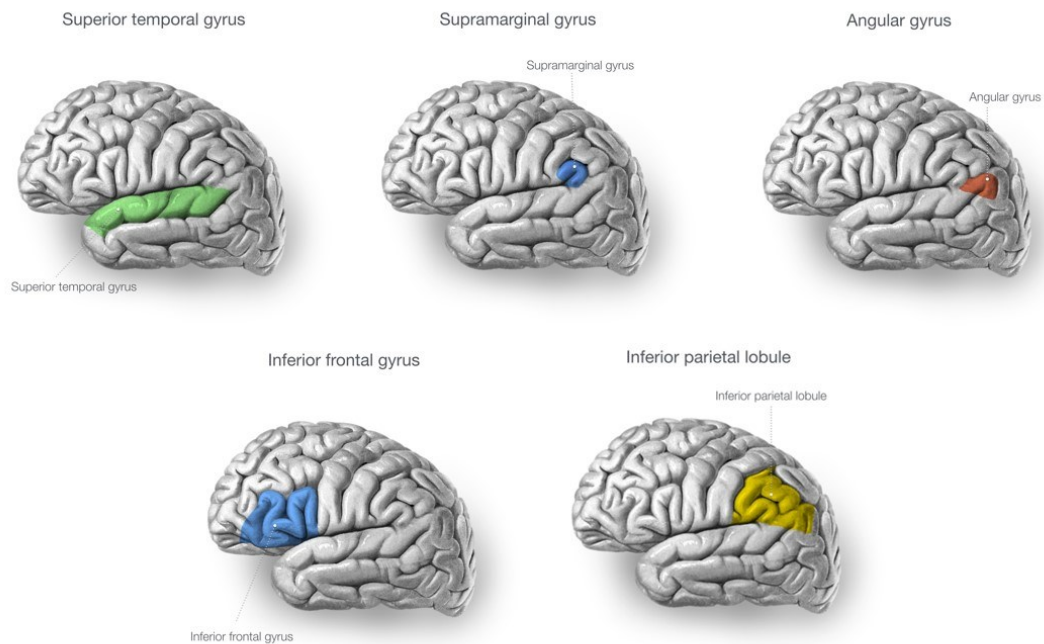
1.4.2 Subskills of Reading

Neuroimaging studies have successfully used fMRI to map the subskills of reading (phonologic, orthographic, and semantic processing) to associated brain regions. In order to associate brain regions with specific subskills of reading, tasks involved in these investigations are generated to specifically enhance or draw attention to one feature of word-level information. For example, the neural basis of phonological processing is most commonly investigated using rhyme-judgement tasks, pseudoword reading, and phoneme deletion tasks (Bitan et al., 2007). Through the application of these tasks, phonological processing has been associated with the left superior temporal gyrus in both children (Bitan et al., 2007; Mathur et al., 2020) and adults (Brennan et al., 2013).

Additionally, the supramarginal gyrus (Church et al., 2008), inferior frontal gyrus (Bitan et al., 2007; Burton, 2001; Glezer et al., 2016), angular gyrus (Glezer et al., 2016), and inferior parietal lobule (Bitan et al., 2007), have been associated with phonological processing, especially converting orthographic information to its phonologic representations. These brain areas can be visualized in Figure 1.

Figure 1

Visualization of the brain regions associated with phonological processing.



Note. These images were created by Frank Gaillard, and retrieved from Radiopaedia.org

With regard to orthographic processing, tasks used tend to include orthographic oddball paradigms (e.g., identifying when letters in a real word are replaced with a string of nonsense symbols or illogical letters, such as ‘abc’) or lexical decision tasks.

Orthographic processing has been associated with the left occipitotemporal area, and in particular the fusiform gyrus has been implicated in visual word form processing (Glezer

et al., 2016; Palmer et al., 2004). This brain region is considered to be finely tuned to whole words (Glezer et al., 2016; Martin et al., 2015) and is implicated in storage of orthographic information at both the individual letter and word level (Murphy et al., 2019), and is visualized in Figure 2. Additionally implicated in orthographic processing is the extrastriate cortex, which demonstrates left-lateralized activity in skilled readers (Cattinelli et al., 2013; Turkeltaub et al., 2002).

Figure 2

Visualization of the fusiform gyrus, a brain region associated with orthographic processing.



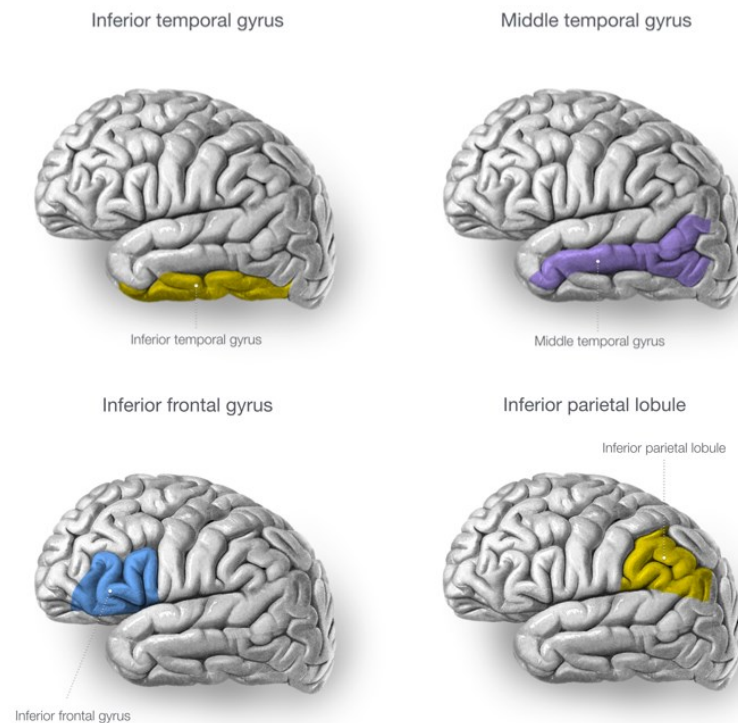
Note. This image was created by Frank Gaillard, and retrieved from Radiopaedia.org

Brain regions implicated in representing semantic information are investigated using semantic judgement tasks (e.g., is this word related in meaning to the word presented last), and include the inferior temporal, posterior middle temporal, and inferior frontal gyri (Blumenfeld et al., 2006; Jobard et al., 2003). During a semantic judgement

task, increasing age and reading skill were associated with increased activity in the left middle temporal gyrus and inferior parietal lobule, suggesting these areas are important for accessing semantic representations and forming semantic judgements in skilled reading (Chou et al., 2006). These brain areas can be visualized in Figure 3.

Figure 3

Visualization of the brain regions associated with semantic processing



Note. These images were created by Frank Gaillard, and retrieved from Radiopaedia.org

1.4.3 Single Word Reading

In an effort to investigate the neural bases of word reading more broadly, beyond the specific subskills of reading, a large number of neuroimaging studies have employed single word reading tasks. Single word reading is a popular task choice in neuroimaging research as it minimizes additional cognitive requirements (Palmer et al., 2004), is an

important predictor of text reading efficiency and accuracy (Hudson et al., 2012), and is malleable to different experimental designs. As this is a common task category in neuroimaging research, there are a number of meta-analyses that have been able to provide detailed overviews of the neural correlates of single word reading in skilled readers.

In skilled adult readers, meta-analyses of the literature have reliably identified the reading network of single word reading is made up of the brain regions that have been associated with the aforementioned subskills of reading. Across meta-analyses, the brain areas identified ubiquitously include those reported as engaged during phonologic processing (Cattinelli et al., 2013; Martin et al., 2015; Murphy et al., 2019; Palmer et al., 2004; Turkeltaub et al., 2002), orthographic processing (Cattinelli et al., 2013; Martin et al., 2015; Murphy et al., 2019; Palmer et al., 2004; Schlaggar & McCandliss, 2007; Turkeltaub et al., 2002), and semantic processing (Blumenfeld et al., 2006; Jobard et al., 2003).

1.5 MODELS OF THE READING NETWORK

Beyond simply identifying brain regions associated with sub-processes of skilled reading, some work has attempted to characterize how these regions integrate in networks, and model changes in these networks over reading development. Two main models have emerged in the literature, one referred to as the “classical” functional neuroanatomical model of reading (Pugh et al., 2000; Turkeltaub et al., 2002; Shaywitz et al., 2007), and recently a more “fluid” approach (Gaillard et al., 2003; Houdé et al., 2010; Martin et al., 2015). These models involve similar brain regions, but differ in how they characterize change over the course of reading development.

1.5.1 The Classical Functional Neuroanatomical Model

Early research of the neural correlates of reading proposed three distinct circuits for reading (Pugh et al., 2000). The first is the *dorsal* (temporo-parietal) circuit, which consists of the superior temporal gyrus and the inferior parietal lobule, made up of the angular and supramarginal gyri; brain regions associated with phonological processing and retrieval of semantic information (Bitan et al., 2007; Chou et al., 2006; Church et al., 2008; Glezer et al., 2016). The dorsal circuit is proposed to be essential for extracting relationships between orthography and phonology, decoding unfamiliar words, and integrating orthographic, phonologic, and semantic representations for novice readers during word reading (Turkeltaub et al., 2002; Pugh et al., 2000), and reading low frequency words during skilled reading (Pugh et al., 2000). In other words, the dorsal circuit is essential when the indirect route for reading is being applied, as these are the brain areas engaged when readers break down and sound out unfamiliar written words, and access the semantic representation through the resulting pronunciation. The second component in this model is the *ventral* (occipito-temporal) circuit, which consists of the lateral extrastriate area, left inferior temporal region, and the fusiform gyrus. The ventral circuit is proposed to be responsible for fluent word identification in skilled readers, and can be described as a fast, later developing circuit associated with increased reading fluency (Martin et al., 2015; Pugh et al., 2000). Thus, the ventral circuit is essential when the direct route for reading is being used, to enable fast and accurate processing of whole visual word-forms. The final proposed circuit is the *anterior* (inferior frontal) circuit, including the inferior frontal gyrus and precentral gyrus, and is involved during reading

aloud – in transforming written letter and word forms to speech output (Martin et al., 2015; Pugh et al., 2000).

The classical functional neuroanatomical model of reading posits these three circuits act independently, and the extent of the engagement of each circuit changes over the course of reading development. More specifically, beginning readers reliant on the indirect route for reading to break down and decode unfamiliar words demonstrate increased activity in dorsal circuit structures during reading, such as the posterior superior temporal gyrus (Pugh et al., 2000; Turkeltaub et al., 2002). This dorsal circuit activity is reduced as readers develop increased reading skill (Turkeltaub et al., 2002). As engagement of dorsal circuit structures declines, the classical functional neuroanatomical model supports a shift to reliance on structures of the ventral circuit (Pugh et al., 2000). This shift is endorsed by neuroimaging research that has demonstrated increasing activity in the left occipito-temporal cortex (a ventral circuit structure), associated with increasing age and reading skill (Shaywitz et al., 2007).

1.5.2 A More Fluid Model of the Reading Network

While data has provided support for the neural circuits described by the classical functional neuroanatomical model of reading, it has become evident the neural structures identified by the aforementioned model are not acting as independent circuits. Rather, these neural structures are engaged interactively by developing and skilled readers during the use of both indirect and direct reading strategies (Gaillard et al., 2003; Houdé et al., 2010; Martin et al., 2015).

Evidence indicates young readers do demonstrate greater engagement bilaterally of structures involved in phonological decoding, such as the posterior superior temporal

gyrus, supramarginal gyrus, and angular gyrus (Yamada et al., 2011). Novice readers recruit these structures to a greater extent when reading less familiar words, such that phonology based reading processes (e.g., decoding) are required (Church et al., 2008; Houdé et al., 2010; Martin et al., 2015). However, developing readers are not exclusively engaging brain areas associated with phonological processing and decoding during reading. The occipito-temporal and extrastriate cortex have been identified as bilaterally active during word reading in young readers (Martin et al., 2015; Schlaggar & McCandliss, 2007), with a shift to more left lateralized activity in skilled readers (Cattinelli et al., 2013; Turkeltaub et al., 2002). Additionally, developing readers demonstrate similar engagement of the fusiform gyrus during word reading as skilled adult readers (Houdé et al., 2010; Martin et al., 2015).

Therefore, with regards to differences between novice and skilled readers, the most recent literature does not suggest that certain brain regions belong to specific circuits, that are engaged independently. Rather, the structures involved in both novice and advanced phonologic and orthographic processing are engaged simultaneously during reading. Ultimately, children show increased bilateral activation early in reading development indicative of increased processing effort, that is reduced with increased reading fluency to result in a more left-lateralized and fine-tuned network during skilled reading.

1.5.3 Single Word Reading in Developing Readers

While there have been significant efforts to identify the reading network through development, there is a notable lack of research investigating the neural correlates of single word reading in developing readers. However, due to the well documented

similarities between the set of brain areas recruited for reading in adults and children, the results of meta-analyses of single word reading in adults prove useful to consider as a starting point to derive expectations for future analyses of investigations concerning developing readers.

One meta-analysis that supports this thinking provided a review of 19 studies involving single word reading tasks during functional MRI scanning in developing readers. This analysis identified significant clusters of activity in areas of the reading network such as the left inferior frontal gyrus (triangular and opercular parts), and the left superior temporal gyri (Martin et al., 2015). These areas have been reliably associated with phonological processing and orthographic to phonologic mapping (Bitan et al., 2007; Glezer et al., 2016). The meta-analysis also identified a significant cluster of activity in the ventral occipito-temporal cortex, associated with orthographic processing (Palmer et al., 2004; Martin et al., 2015; Murphy et al., 2019), and the middle temporal gyrus and parietal lobule, associated with semantic processing (Blumenfeld et al., 2006; Jobard et al., 2003). Additionally, this meta-analysis identified a significant cluster of activity in the left precentral gyrus, associated with transforming written word forms to verbal output (Martin et al., 2015; Pugh et al., 2000).

This meta-analysis identified brain regions that have been reliably associated with phonologic, orthographic, and semantic processing, similar to meta-analyses of skilled adult reading. However, it also identified additional clusters of significant activity in the bilateral supplementary motor area, and left posterior parietal cortex (superior parietal lobule) (Martin et al., 2015). This result has a less obvious interpretation, however the bilateral sensorimotor and left posterior parietal cortex have been described as forming a

frontal-parietal control network, which is engaged during challenging tasks to maintain goal-directed behaviour and task switching (Martin et al., 2015). This led the authors to conclude engagement of these structures may be due to the presence of complex single word reading tasks.

With regards to the tasks included in this meta-analysis, across studies there was significant variation in the experimental task design (Martin et al., 2015). Therefore, while the results of this meta-analysis are compelling due to the relation between significant clusters of activity and reading subskills, it is still challenging to confirm these clusters of activity are specifically relevant to individual word reading in developing readers. The different tasks included in this analysis each emphasize different features of word reading, and may be artificially inflating the engagement of certain structures beyond their true engagement during single word reading.

1.6 THE CURRENT STUDY

Behavioural investigations of reading have thoroughly investigated the developmental process of achieving fluent single word reading. The value of this work is emphasized by Perfetti & Hart (2002), who argue that reading is about the individual words, as word reading forms the basis for all higher levels of reading such as sentence and text-level comprehension. Furthermore, silent single word reading is considered to be the primary method of reading for proficient readers (van den Boer et al., 2014), and can elicit both indirect and direct strategies of word reading. However, in developing readers, neuroimaging techniques have not sufficiently investigated the neural basis of single word reading.

More specifically, the types of tasks included in the investigation of single word reading in developing readers significantly vary in their experimental task design. These tasks generally include single-word manipulations, rather than passive reading, such as rhyme-judgement, non-word reading, semantic judgement, one-back and lexical decision tasks (Martin et al., 2015). These types of tasks have been more formally created and used to investigate the brain areas associated with specific subskills of reading, due to their ability to emphasize different features of word reading (e.g., rhyme judgement to emphasize phonological processing, lexical decision to emphasize orthographic processing, etc.).

This variance in task selection is noteworthy, as the main objective of the present study is to pilot a passive word reading stimulus paradigm during functional MRI scanning. In prior investigations of word reading in developing readers, tasks have involved manipulating the target word to keep young readers engaged during word reading. However, in order to properly increase our understanding of the brain areas engaged by developing readers during passive single word reading, these previously employed tasks will not suffice. We have developed a silent single word reading task that can be performed by developing readers during functional imaging, with an animal identification task to maintain participant engagement. This task follows an event-related design, and allows for the analysis of the hemodynamic response to each individual word presented, without the need to include animal identification target items (the non-passive aspect of the task) in the data analysis.

If successful, this paradigm will be used to investigate neural activity during word reading and its association to reading skill longitudinally, in a sample of 90 developing

readers. Prior to launching this research investigation, it is important to confirm the stimulus paradigm and scanning parameters appropriately capture the reading network of the target subject population. Therefore, a secondary objective of the present investigation is to bolster our understanding of the neural correlates of reading at the word level, by identifying the brain regions that are significantly active during passive silent single word reading in a group of second and third grade children.

A main feature in theories of skilled word reading development is the successful transition from using decoding strategies when reading, to the more automatic processing of individual words reliant on a direct route for reading (Ehri, 2014). Therefore, in order to capture this process during single word reading at the neural level, children in grades 2 and 3 provide an optimal cohort of developing readers to draw on. At the beginning of grade 2, most children can effectively and easily decode unfamiliar written words, and by the end of the second grade children are transitioning to the direct route for reading (Nevo, et al., 2015). Thus, investigating the neural correlates of silent single word reading in readers that are effectively engaging both indirect and direct reading strategies may provide valuable insight into what is truly in a word, at the neural level.

In order to achieve these objectives, children in grades 2 and 3 were recruited to complete two study visits. In the first study visits, participants were asked to complete a lexical decision task screening their familiarity with a list of words, and then a series of behavioural assessments of reading and related skills. In the second study visit, participants each underwent an MRI scan during which they silently read a series of single, isolated words. This investigation was conducted in order to answer the following research question: are the brain areas significantly active during a silent single word

reading task in children in grades 2 and 3, those that have been associated with phonologic, orthographic, and semantic processing in prior literature?

1.6.1 Hypotheses

The stimulus paradigm in the current study was developed based on stimulus presentation paradigms that have achieved success in eliciting activity in the reading network. Therefore, I hypothesize this stimulus paradigm will be adequate to elicit reliable activity in the reading network defined for developing readers. Furthermore, given that single word reading tasks have reliably elicited significant activity in brain areas associated with phonologic, orthographic, and semantic processing in adult skilled readers (Cattinelli et al., 2013; Martin et al., 2015; Murphy et al., 2019; Palmer et al., 2004; Schlaggar & McCandliss, 2007; Turkeltaub et al., 2002), and this result was mostly replicated in a review of the literature for developing readers (Martin et al., 2015), I expect to replicate these findings here. More specifically, I hypothesize the silent single word reading task will result in increased activity during silent word reading as compared to baseline in the bilateral superior temporal gyrus, supramarginal gyrus, angular gyrus, occipito-temporal cortex, fusiform gyrus, extrastriate cortex, and the left inferior frontal gyrus.

CHAPTER 2: METHODS

2.1 PARTICIPANTS

Participants in this study were children from grade 2 ($n = 5$) and grade 3 ($n = 3$) who primarily speak English at home and are enrolled in either English or French immersion school programs. Participants were required to have normal (or corrected-to-normal) vision and normal hearing, as both hearing loss and impaired vision can impact reading ability negatively. Children were excluded from the study if they had been diagnosed with any developmental disorder, cognitive delay affecting language development, learning disability, neurological disorder, or known brain damage. Additionally, participants must meet all safety criteria for MRI scanning to be included, and children with a medical condition that could be made worse by stress associated with participation in MRI research were excluded from the study.

Data from 3 participants were excluded due to two participants choosing not to complete the MRI scanning procedure, and one reporting the target words had been presented upside down during functional scanning. The final sample of participants thus consisted of three participants in grade 2 (3 male) and two participants in grade 3 (1 male, 1 female).

Participants were recruited through the Neurocognitive Imaging Lab's established school and school board contacts, social media, community partners, and families that previously expressed interest in research participation. Upon recruitment into the study, a participant background information questionnaire and consent information were sent to the parent/guardian. Signed consent by the parent/guardian and verbal assent by the child

were obtained at the beginning of the first study visit, and continued child assent was obtained at the beginning of each subsequent study visit. Children received \$30.00 for participation, and the parent/guardian received \$20.00 compensation for accompanying the child, for each study visit. All procedures outlined received approval from the IWK Health Centre Research Ethics Board.

2.2 MATERIALS

2.2.1 Standardized Assessments

Participants were administered the complete Wechsler Individual Achievement Test-Fourth Edition (WIAT-4) (Wechsler, 2020). These data will not be presented as they are not relevant to the hypotheses of this study.

2.2.2 fMRI Task Stimuli

The list of stimulus words for the fMRI task were selected by first creating a list of nouns that were six characters in length or less, from reading outcome word lists for the first, second, and third grade, to be appropriate for second and third grade children. This word list was then fed into Python code that randomly samples 60 words and computes the orthographic, phonological, and semantic similarity for each pair of words. This code looped 1000 times to find a list of 60 words that had the greatest variance across orthographic, phonological, and semantic properties. Semantic similarity between words was measured using a latent semantic analysis (Landauer et al., 1998), orthographic similarity was measured using a bigram model (Fischer-Baum et al., 2017; Schoobaert & Grainger, 2004; Whitney, 2001), and phonological similarity was assessed using a measure of phonological distance (Hall et al., 2021).

Because each word was to be presented three times over the course of the experiment, the list of words was then randomized (using the *shuffle* function in the built-in Python module *Random*) three times, producing three separate lists with different ordering of the 60 words. Then, these three lists were combined (one below the other), and cut into 5 lists containing 36 words each. This produced 5 separate lists of stimulus words (one for each functional run). Additionally, for the target detection task (see below), a list of 28 animal words was created using common animals, and a set of 25 animal photos were downloaded from the stock photo provider Envato Elements (Envato, 2023).

2.3 PROCEDURE

Each participant completed two study visits: (1) a behavioural assessment of reading and related skills performed in the lab environment using standardized assessment measures, and (2) the MRI scanning conducted at the IWK Health Centre. The two visits occurred within one month of each other.

2.3.1 Prior to Arrival

Once a participants' parent/guardian contacted the lab to express interest in having their child participate in the study, a phone call was organized to confirm their eligibility based on defined screening criteria. Once deemed eligible for participation, the parent/guardian was provided electronic copies of the consent forms, a demographic questionnaire, and information about the study. Once they had reviewed the information, they were contacted again to determine if they were interested in participating and, if so, a first study visit was scheduled.

2.3.2 Study Visit 1

This study visit took place in a child-friendly lab space in the Life Sciences Centre, Dalhousie University, and took approximately 2.5 hours to complete. Upon arrival at the lab, signed informed consent by the parent/guardian and verbal assent by the child were obtained. After consent protocol was complete, the demographic questionnaire previously provided to the guardian was collected. Then, the participant was escorted to a child-friendly testing environment.

2.3.2.1 *Lexical Decision Task*

Once in the testing environment, the participant was screened for familiarity with the fMRI task stimulus words. This was assessed by having the participant complete a lexical decision task involving the random presentation of the stimulus words (60) intermixed with orthotactically legal pseudowords (60). The lexical decision task was presented to the participant on a laptop, using DirectRT version 2012 (Empirisoft, 2020) to present words and collect responses.

2.3.2.2 *WIAT-4*

After completion of the lexical decision task, the standardized assessments were administered in the same order for each participant, according to the published instructions in the WIAT-4 (Weschler, 2020). Administration of the full WIAT-4 was completed by a trained examiner, with an additional research assistant present in the room.

2.3.2.3 The Statue Game

Next, the participant's parent/guardian was invited into the testing room to join their child and the researchers. At this point in the study visit, the parent/guardian was provided with materials that provide answers to frequently asked questions concerning MRI scanning. These materials also included instructions for the 'Statue Game', which was demonstrated at this time, to prepare the participant to practice lying still at home leading up to their scheduled MRI scan. The demonstration of the Statue Game involved having the participant lie in a child play tunnel while the researcher timed them for 30 seconds. Once the participant was comfortable in the play tunnel, the researcher would tell them to lie as still as they could, and start the timer for 30 seconds. During this time, the researcher would provide verbal feedback to the participant if they moved and express the importance to the parent/guardian about aiming to reduce all movement during at home practice.

2.3.3 Study Visit 2

This study visit took place at the IWK Health Centre in Halifax, and took approximately 70 minutes, with around 41 minutes of that time spent in the MRI by the participant. Upon arrival, the plan for the study visit was explained to the participant and their guardian, providing an opportunity for the participant or guardian to ask questions. The participant's assent to continue being in the study was once again confirmed verbally. Next, the participant was given the opportunity to play the Statue Game for 30 seconds, or longer if they chose, in the mock MRI scanner in the waiting room. Then, the participant took part in a practice task demonstration, before being familiarized with the MRI scanner.

2.3.3.1 Practice Task

Each participant was provided the opportunity to practice the single word reading task they would perform in the MRI, on a laptop computer. This task demonstrated the types of words and types of animal photos the participant would see, during the MRI scan. The task encouraged the participant to press a button in response to the animal words and photos as they would during the real scan, and was presented using DirectRT.

2.3.3.2 MRI Scans

Once the participant was properly positioned in the MRI scanner by the technician and confirmed they were comfortable, the scout scans were obtained. Next participants completed the experimental task. During this task, participants were presented with the target stimulus words (e.g., STAR), animal words (e.g., PIG), and animal photos. Participants were instructed to press a button when they saw an animal word or photo.

The printed words were presented in white using the font KG Neatly Printed, on a medium grey background. Printed words were presented for 1500 ms each, followed by a blank screen for a 500 ms intertrial interval, a white fixation cross for 4500 ms, then another intertrial interval for 500 ms before the next word. When the animal photo was presented, it interrupted the fixation cross after it had been on the screen for 1000 ms. The animal photo stayed on the screen for 1000 ms, then the fixation cross reappeared for another 500 ms, before the screen went blank for the intertrial interval (500 ms). In each run, 36 stimulus words, 12 animal words, and 5 animal photos were presented. As well, evenly spaced throughout each run, five fixation crosses would remain on screen for 8000 ms, rather than 4500 ms. These “null events” were included to allow the fMRI BOLD

signal to return to baseline, allowing for better estimation of stimulus-evoked responses. There were five runs in total, and each was six minutes and 13 seconds long. Stimulus presentation and response collection were administered using DirectRT.

2.3.3.3 MRI Scanning Protocol

The MRI visit involved use of the 1.5 T MRI located at the IWK Health Centre. The scanner was operated by registered MRI Technologists employed by the IWK Health Centre. The MRI protocol included five functional runs, along with a T1-weighted anatomical scan and two T2-weighted anatomical scans, to allow for prevision in locating functional activation in relation to structural anatomy. This included the following:

T1-weighted anatomical scan: 3D-MP-RAGE sequence, TR= 2.729 s, TE = 3.9 ms, TI= 1.134 s, 1NEX, field of view = 22.4cm, 224 x 224 matrix resulting in 1mm³ voxel size. The scan took 3 minutes and 40 seconds to complete.

Functional MRI scans: Gradient-echo, echo-planar pulse sequence, TR = 1.8 s, TE = 23 ms, flip angle = 90 deg, field of view = 24cm, 64 x 64 matrix resulting in 3.75 x 3.75 mm in-plane voxel resolution with 34, 3.7 mm thick axial slices (no gap, interleaved slice acquisition). Each scan lasted 6 minutes and 5 seconds, comprising 197 acquisitions.

An additional echo-planar image was taken to obtain higher grey-white matter contrast in a T2-weighted image, to support registration between the functional data to the anatomical data. This scan was acquired with all the same parameters as the main functional scans, except it had a TR of 5.4 seconds and lasted 54 seconds, comprising 10 acquisitions. As well, an echo-planar image with a reverse phase encoding direction was collected with all the same parameters as the functional scans, except for the reverse

phase encoding direction. This image was collected to correct for magnetic field distortions and lasted 18 seconds, comprising 10 acquisitions.

First, the T2-weighted scan with an increased TR was collected (54 seconds), followed by the T2-weighted scan with reversed phase encoding direction (18 seconds). Next, two functional runs were completed (6 minutes and 13 seconds each), followed by the T1 weighted anatomical scan (3 minutes and 40 seconds). Then, the final three functional scans were collected. During all functional scans, participants performed the single word reading task, and during all anatomical scans cartoons were shown on the screen and the participant was instructed to relax and lie still.

2.4 DATA ANALYSIS

2.4.1 Behavioural Data Analysis

Using the log files saved by DirectRT, accuracy for real words and pseudowords on the lexical decision task, and accuracy for animal words and animal photos during the animal identification task were calculated for each participant. Total accuracy on the lexical decision task and animal identification task were also calculated for each participant, and mean accuracy and standard deviation on both tasks were calculated across participants in Python, using the built-in *describe* function.

2.4.2 Preprocessing

The following preprocessing method details come directly from *fMRIPrep* version 23.0.2 (Esteban et al., 2019; Esteban et al., 2018), which is based on *Nipype* version 1.8.6 (Gorgolewski et al., 2011; Gorgolewski et al., 2018). The text was automatically generated by *fMRIPrep* with the express intention that users should copy and paste this

text into their manuscripts *unchanged*. Note that *BIDS* refers to the brain imaging data structure standard for neuroimaging data, *FSL* is the name of a software library, *MNI* is the Montreal Neurological Institute, *DVAR_S* is defined as the spatial standard deviation of successive difference images (Smyser et al., 2011), and *AFNI* is a leading software developed for analysis and display of functional and anatomical MRI data (Cox & Hyde, 1997).

2.4.2.1 Preprocessing of B0 Inhomogeneity Maps

One field-map was available within the input BIDS structure for each subject. A B0-nonuniformity map (or field-map) was estimated based on two (or more) echo-planar imaging (EPI) references with *topup* FSL version 6.0.5.1 (Andersson et al., 2003).

2.4.2.2 Anatomical Data Processing

One T1-weighted (T1w) image was found within the input BIDS dataset per subject. The T1w image was corrected for intensity non-uniformity (INU) with *N4BiasFieldCorrection* (Tustison et al. 2010), distributed with ANTs version 2.3.3 (Avants et al., 2008), and used as the T1w-reference throughout the workflow. The T1w-reference was then skull-stripped with a *Nipype* implementation of the *antsBrainExtraction.sh* workflow (from ANTs), using OASIS30ANTs as the target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using FSL version 6.0.5.1 (Zhang et al., 2001). Brain surfaces were reconstructed using *recon-all* FreeSurfer version 7.3.2 (Dale et al., 1999), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of *Mindboggle* (Klein et al. 2017). Volume-

based spatial normalization to two standard spaces (MNIPediatricAsym:cohort-3, MNI152NLin2009cAsym) was performed through nonlinear registration with *antsRegistration* (ANTs version 2.3.3), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization and accessed with *TemplateFlow* version 23.0.0 (Ciric et al., 2022): MNI's unbiased standard MRI template for pediatric data from the 4.5 to 18.5 year age range [TemplateFlow ID: MNIPediatricAsym:cohort-3], ICBM 152 Nonlinear Asymmetrical template version 2009c [Fonov et al., 2009; TemplateFlow ID: MNI152NLin2009cAsym].

2.4.2.3 Functional Data Processing

For each of the 5 BOLD runs per subject, the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of *fMRIPrep*. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using *mcflirt* FSL version 6.0.5.1 (Jenkinson et al., 2002). The estimated field-map was then aligned with rigid-registration to the target EPI (echo-planar imaging) reference run. The field coefficients were mapped on to the reference EPI using the transform. BOLD runs were slice-time corrected to 0.874 s (0.5 of slice acquisition range 0-1.75 s) using *3dTshift* from AFNI (Cox & Hyde, 1997). The BOLD reference was then co-registered to the T1w reference using *bbregister* (FreeSurfer) which implements boundary-based registration (Greve & Fischl, 2009). Co-registration was configured with six degrees of freedom. Several confounding time-series were calculated based on the preprocessed BOLD: framewise

displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations following Power et al. (absolute sum of relative motions; 2014) and Jenkinson et al. (relative root mean square displacement between affines; 2002). FD and DVARS are calculated for each functional run, both using their implementations in *Nipype* (following the definitions by Power et al. (2014)). The three global signals are extracted within the CSF, the WM, and the whole-brain masks.

Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (CompCor; Behzadi et al., 2007). Principal components are estimated after high-pass filtering the preprocessed BOLD time-series (using a discrete cosine filter with 128s cut-off) for the two CompCor variants: temporal (tCompCor) and anatomical (aCompCor). tCompCor components are then calculated from the top 2% variable voxels within the brain mask. For aCompCor, three probabilistic masks (CSF, WM and combined CSF+WM) are generated in anatomical space. The implementation differs from that of Behzadi et al. (2007), in that instead of eroding the masks by 2 pixels on BOLD space, a mask of pixels that likely contain a volume fraction of GM is subtracted from the aCompCor masks. This mask is obtained by dilating a GM mask extracted from FreeSurfer's *aseg* segmentation, and it ensures components are not extracted from voxels containing a minimal fraction of GM. Finally, these masks are resampled into BOLD space and binarized by thresholding at 0.99 (as in the original implementation). Components are also calculated separately within the WM and CSF masks. For each CompCor decomposition, the k components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50% of variance across the nuisance mask (CSF, WM, combined, or temporal).

The remaining components are dropped from consideration. The head-motion estimates calculated in the correction step were also placed within the corresponding confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et al., 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardized DVARS were annotated as motion outliers. Additional nuisance timeseries are calculated by means of principal components analysis of the signal found within a thin band (crown) of voxels around the edge of the brain, as proposed by Patriat and colleagues (2017).

The BOLD time-series were resampled into several standard spaces, correspondingly generating the following spatially normalized, preprocessed BOLD runs: MNIPediatricAsym:cohort-3, MNI152NLin2009cAsym. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. All re-samplings can be performed with a single interpolation step by composing all the pertinent transformations (i.e., head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) re-samplings were performed using *antsApplyTransforms* (ANTs), configured with Lanczos interpolation (1964) to minimize the smoothing effects of other kernels. Non-gridded (surface) re-samplings were performed using FreeSurfer's *mri_vol2surf*.

2.4.3 Functional Data Analysis

All functional data analysis was performed in the MNI152 standard template space.

2.4.3.1 Subject Level Analysis

The results of the functional data preprocessing were first visually examined to assess data quality. Image registration was deemed acceptable for all participants. Motion correction was within acceptable parameters (framewise displacement $< 1/2$ voxel size) for all but one run for one participant; that run was excluded from statistical analysis.

A predicted time course for each stimulus condition (i.e., words, animal words, animal pictures, and button-press responses), across runs, for each subject, was created using *Nilearn* version 0.10.1 (Abraham et al., 2014), based on the timing events recorded in the log files saved by DirectRT during stimulus presentation. The predicted time course was built by concatenating the timing of each stimulus event across the five functional runs, for each stimulus type. The time course of each event type was then convolved with the standardized ‘glover’ function to model the hemodynamic response, forming a vector of the predicted BOLD response time course, for each stimulus type. A design matrix of regressors for each functional run was created by combining these predicted hemodynamic response functions for each condition within a set of cosine basis functions designed to model low-frequency signal drift (typically associated with respiration and cardiac artifacts), as well as seven motion correction time courses obtained during preprocessing (translation and rotation for each axis, plus overall framewise displacement), and a constant term. The design matrices for all runs were then concatenated together, as were the functional data for that participant, using the preprocessed data that had been transformed to the standard MNI152 space. The columns of this design matrix were then used as the regressors for a multiple regression analysis of

the functional data, at each voxel, using the *FirstLevelModel* function in *Nilearn*.

Contrasts were created for each stimulus type relative to baseline.

Due to the limited number of subjects, and low power of the group analysis, an additional exploratory analysis was performed at the subject level. Statistical (z score) maps for each subject were thresholded at $p \leq 0.05$ (uncorrected for multiple comparisons at the voxel level) with the additional constraints that clusters had to be at least 2 voxels in size, using *threshold_stats_img* in *Nilearn*. These images were then binarized and the results summed using *fslmaths*, to create an image in which the value at each voxel reflected the number of participants who showed supra-threshold signal change. Significant clusters of activity for the statistical (z) map for each subject level analysis were labeled using the automated anatomical labelling atlas 3 (Rolls et al., 2020), at the center of each cluster, such that the full cluster was in the labelled region.

2.4.3.2 Group Level Analysis

For each contrast of interest, the *SecondLevelModel* function in *Nilearn* was used to fit a general linear model to the effect size maps (regression coefficients) obtained for each participant in the subject-level analysis. For interpretation of the results, the resulting statistical (z) map for each contrasted was thresholded at $p \leq 0.01$ (uncorrected for multiple comparisons) with the additional constraints that clusters had to be at least 2 voxels in size, using *threshold_stats_img* in *Nilearn*. We performed an additional exploratory analysis at the group level, and created a statistical map following the same protocol, thresholded at $p \leq 0.05$. Significant clusters of activity for each group level analysis were labeled using the automated anatomical labelling atlas 3 (Rolls et al., 2020), at the center of each cluster, such that the full cluster was in the labelled region.

CHAPTER 3: RESULTS

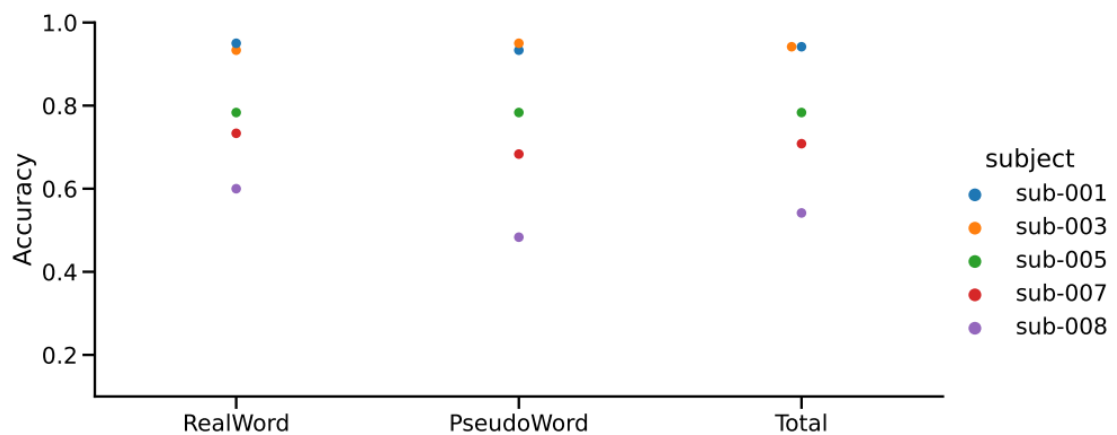
3.1 BEHAVIOURAL DATA

3.1.1 Lexical Decision Task

Participants' accuracy during the lexical decision task administered during study visit 1 is presented in Figure 4. Participants demonstrated higher accuracy for real words ($M = 0.800$, $SD = 0.146$) than for pseudowords ($M = 0.767$, $SD = 0.193$), although this difference in performance was quite small. Overall, participants demonstrated moderate to high accuracy on the lexical decision task across conditions ($M = 0.783$, $SD = 0.169$), with only one subject displaying a mean accuracy level below 70%.

Figure 4

Accuracy by Subject on the Lexical Decision Task



3.1.2 Animal Identification Task

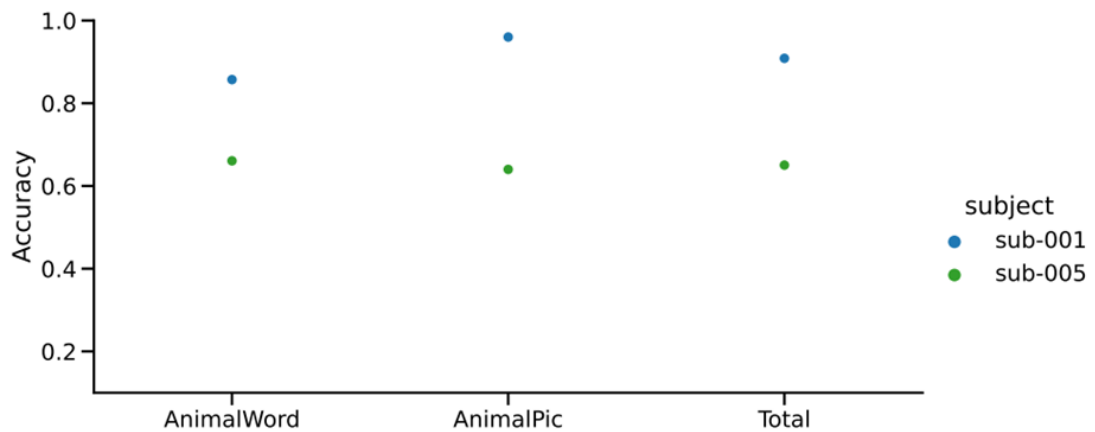
Due to a connection error between the MRI-safe handheld response buttons and the stimulus computer, accuracy data for three participants on the animal identification task during MRI scanning were not recorded. However, an auditory tone is played in the MRI control room when the buttons are pressed. Therefore, observational notes during

MRI scanning indicated that participants whose accuracy data was not recorded were still attending to the stimuli and performing the task with moderate to high accuracy during scanning.

Accuracy data for the two participants for which button responses were collected is presented in Figure 5. Accuracy for these participants was calculated for animal photo identification ($M = 0.800$, $SD = 0.226$), animal word identification ($M = 0.759$, $SD = 0.139$), and overall task accuracy ($M = 0.799$, $SD = 0.183$).

Figure 5

Accuracy by Subject on the Animal Identification Task.



Note. Data is only presented for subjects 001 and 005, as behavioural data was not recorded for all other participants during the task.

3.2 fMRI DATA

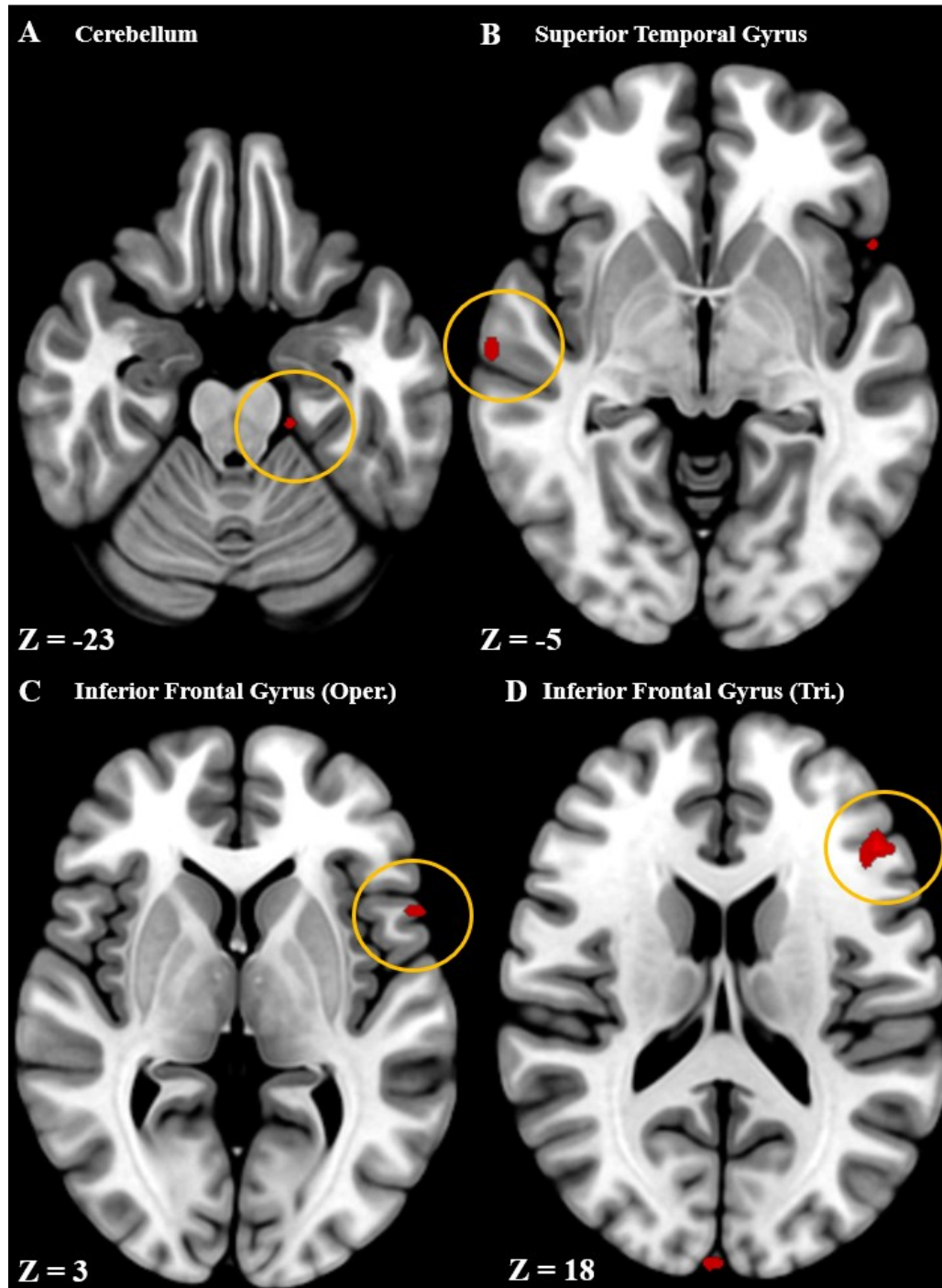
fMRI data analysis included the data from all five functional runs for each subject, with the exception of data from the fifth functional run for one subject. This data was excluded due to excessive movement by the subject during that scanning period.

3.2.1 Group Level Results ($p \leq 0.01$)

A statistical map of cluster-level z scores was created at the group level and thresholded at $p \leq 0.01$. Significant clusters of activity are visualized in Figure 6, and coordinates for each cluster are reported in Table 1. Activity was identified in the triangular and opercular parts of the left inferior frontal gyrus. Additionally, significant clusters of activity were identified in the left cerebellum, and the right superior temporal gyrus. Overall, clusters were quite small, with only the triangular part of the inferior frontal gyrus exceeding two voxels.

Figure 6

Significant clusters of activation at the group level of analysis ($p \leq 0.01$), displayed in the axial plane.



Note. Significant clusters of activity in the (A) left cerebellum, (B) right superior temporal gyrus, (C) left inferior frontal gyrus (opercular part), (D) left inferior frontal gyrus (triangular part).

Table 1*Significant clusters of activation identified at the group level of analysis ($p \leq 0.01$)*

Cluster ID	X	Y	Z	Peak Statistic	Cluster Size (mm ³)	Cluster Label
A	-18	-28	-23	2.78	104	Left cerebellum, lobule 4/5
B	65	-13	-5	2.71	104	Right superior temporal gyrus
C	-55	14	3	2.41	104	Left inferior frontal gyrus, opercular part
D	-52	29	18	3.43	728	Left inferior frontal gyrus, triangular part

Note. Cluster ID corresponds to cluster labelling in Figure 6. Coordinates are reported in millimetres for significant clusters of activation that have corresponding anatomical labels in the automated anatomical labelling atlas 3 (Rolls et al., 2020), on the MNI152NLin2009cAsym standardized template.

3.2.2 Group Level Results ($p \leq 0.05$)

Due to the low number of significant clusters of activity identified at our original statistical threshold ($p \leq 0.01$), a second exploratory analysis of the group-level data was performed. A statistical map of cluster-level z scores was created at the group level and thresholded at $p \leq 0.05$, and the coordinates for significant clusters of activity are reported in Table 2. Activity was identified in the triangular and opercular parts of the left inferior frontal gyrus, the left and right superior temporal gyri, and the left inferior temporal gyrus. Additionally, two significant clusters of activity were identified in the left

cerebellum, as well as two clusters in the right cerebellum, and one in the left postcentral gyrus.

Table 2***Significant clusters of activation identified at the group level of analysis ($p < 0.05$).***

X	Y	Z	Peak Statistic	Cluster Size (mm ³)	Cluster Label
-52	29	18	3.43	3277	Left inferior frontal gyrus, triangular part
-52	18	-8	3.23	3017	Left temporal pole, superior temporal gyrus
-52	-69	-34	2.78	1977	Crus 1 of the left cerebellum
-18	-28	-23	2.78	676	Left cerebellum, lobule 4/5
-63	-13	33	2.61	676	Left postcentral gyrus
65	-13	-5	2.71	364	Right superior temporal gyrus
5	-83	-38	2.35	364	Crus 2 of the right cerebellum
-48	-62	-8	2.20	260	Left inferior temporal gyrus
-52	10	29	1.99	260	Left inferior frontal gyrus, opercular part
5	-88	-23	1.91	312	Crus 1 of the right cerebellum

Note. Coordinates are reported in millimetres for significant clusters of activation that have corresponding anatomical labels in the automated anatomical labelling atlas 3 (Rolls et al., 2020), on the MNI152NLin2009cAsym standardized template.

3.2.3 Subject Level Results

Because of the low number of participants, we additionally investigated results at the group level using an alternative approach, aimed at quantifying how many participants showed supra-threshold activity at each voxel. Statistical z -maps for each subject, across functional runs, were created at the cluster-level and thresholded at $p \leq$

0.05. The z-maps were then binarized and combined across subjects. This allowed for the identification of clusters of significant activation that were consistent across subjects. Images were thresholded at a minimum overlap of 2 subjects. However, all clusters above this threshold demonstrated overlap from 3 or more subjects, and these results are reported in Table 3. With regards to the regions of interest hypothesized, regions of overlapping significant clusters were observed in the left inferior frontal gyrus, left superior temporal gyrus, left inferior parietal gyrus, right middle temporal gyrus, and right inferior occipital gyrus. Additionally, overlap of significant clusters was observed in the right insula, left superior parietal gyrus, left posterior cingulum, left precuneus, and left cerebellum.

Table 3*Significant clusters of activation identified at the subject level of analysis.*

X	Y	Z	Cluster Label
-47	-72	-20	Crus 1 of the left cerebellum
31	25	-1.7	Right insula
35	-87	-1.7	Right inferior occipital gyrus
-41	29	6	Left inferior frontal gyrus
40	-65	10	Right middle temporal gyrus
-51	-30	13	Left superior temporal gyrus
-10	-47	17	Left posterior cingulum
-3	-61	17	Left precuneus
-40	-27	43	Left inferior parietal gyrus
-29	-58	51	Left superior parietal gyrus

Note. Coordinates are reported in millimetres for significant clusters of activation that have corresponding anatomical labels in the automated anatomical labelling atlas 3 (Rolls et al., 2020), on the MNI152NLin2009cAsym standardized template.

CHAPTER 4: DISCUSSION

While there is extensive research on the neural correlates of single word reading in adult skilled readers, much less work has been published for developing readers – in particular, using a simple reading task as opposed to tasks that draw attention to specific features of words (e.g., phonology) that could bias the resulting patterns of activation. The present study aimed to validate a research protocol for a larger longitudinal study, while at the same time adding to the current body of literature concerning the brain areas engaged by second and third grade children during single word reading. Participants first completed a lexical decision task to screen for their knowledge of the stimulus words used in the fMRI study, behavioural assessments of reading skill, and then a silent single word reading task during fMRI scanning. Functional imaging data was combined across five runs for each subject, and was analyzed at the group level to identify significant clusters of brain activity during silent single word reading. In addition, two exploratory analyses were performed: a group-level analysis with a less conservative statistical threshold, and a subject-level exploratory analysis to further investigate brain areas that showed consistent activity across developing readers.

4.1 CONFIRMING THE PARADIGM AT THE BEHAVIOURAL LEVEL

4.1.1 Lexical Decision Task

Data from the lexical decision task allows us to assess the suitability of the stimulus words selected, for children in grades 2 and 3. If participants performed with low accuracy on this task, it would indicate the stimulus words may be too challenging for children in this age range. Our results indicate that participants in this study had good knowledge of the stimulus words presented. All participants displayed accuracy levels

well above chance performance (50%) for real words, with the lowest performing participant still achieving an accuracy score of 60%.

While our primary interest was in determining how many of the real words participants recognized, it is important to consider the potential weaknesses of using a lexical decision task to do this. Specifically, if children adopt a liberal response bias in which they assume each word they do not recognize is a real word, and respond accordingly, they will likely achieve quite high accuracy on the real words. Contrastingly, this would result in quite low accuracy on the pseudowords, as these unfamiliar words would be incorrectly characterized as real words as well. Considering accuracy for each word condition (real and non-real) separately, as well as overall task accuracy, provides some opportunity to confirm participants' true performance. However, for participants who do achieve high accuracy on real words and low accuracy on pseudowords, it becomes challenging to identify how well they actually recognized the real words.

In the present data, accuracy for both real and pseudowords appears to be relatively consistent within each subject, suggesting participants demonstrated true recognition of the real words and correct rejection of the pseudowords for which they responded correctly. However, in the future longitudinal investigation, increased analysis of the lexical decision data may be required beyond basic accuracy measures. One such option would be to take a signal detection theory approach. Signal detection theory breaks down response types into four categories: hits (correct identification), false alarms (incorrect identification/'yes' response), misses (incorrect rejection), and true negatives (correct rejection) (Stanislaw & Todorov, 1999). This break down of response types allows for two measures to be calculated, the hit rate (probability of correctly responding

‘yes’ to ‘yes’ trials) and the false alarm rate (probability of incorrectly responding ‘yes’ to ‘no’ trials). This method of breaking down response types allows for the categorization of each subjects’ response bias in the face of uncertainty, being liberal (always says ‘yes’) or conservative (always says ‘no’) (Stanislaw & Todorov, 1999). If we categorize participants response bias, it provides additional insight into whether participants who obtain high accuracy on real words are achieving so because they correctly recognize the words, or because they have a liberal response bias and tend to indicate the answer is ‘yes, it is a real word’ when they are uncertain.

4.1.2 Animal Identification Task

Considering accuracy data of participants during the animal identification task allows us to identify if participants are attending to the stimulus words during scanning, and if the task can be easily performed by children in grades 2 and 3. Participating in an MRI scan can be a distracting and potentially overwhelming experience for a child. Thus, it is important to confirm that in such a distracting environment participants still read the stimulus words being presented, and complete the task correctly.

Unfortunately, due to the connection error reported between the MRI-safe handheld response buttons and the stimulus computer, accuracy data for the majority of participants on the animal identification task was not recorded. However, the auditory tone indicating a button-press response and the observational notes of researchers do suggest that all participants were performing the task correctly the majority of the time. Furthermore, the accuracy data that was successfully collected indicates reasonable task performance on both the animal word and photo identification. However, for one of two participants for which we do have accuracy data, the results indicate they only identified

animal words and photos less than 70% of the time. The low accuracy for animal photos suggests the participant may have been distracted during the functional scanning, and low accuracy for animal words suggests the participant may not have been reading the words or did not recognize the animal words.

In the present study, the target animal words used during functional scanning were not included in the lexical decision task. However, the low accuracy observed here for one participant on animal word identification indicates it may be valuable to include these animal words in the word screening task. Being able to identify how many of the animal words participants know prior to scanning could better inform our selection of animal words, and also provide some additional insight when looking at in-scanner animal word identification accuracy. More specifically, if a participant demonstrates good recognition of the animal words prior to scanning, but poor accuracy on those words during scanning, this could indicate the participant was not reading the stimulus words during the task.

4.2 GROUP LEVEL ANALYSIS

Group-level statistical analysis revealed significant clusters of activity consistent with our hypotheses in the triangular and opercular parts of the left inferior frontal gyrus, and the right superior temporal gyrus. This analysis also revealed a significant cluster of activity in the left cerebellum, which was not consistent with our hypotheses.

Furthermore, we expected to identify a much greater number of clusters of significant activity at the group level. There were a number of brain areas that we predicted would demonstrate significant clusters of activity (i.e., the bilateral supramarginal and angular gyri, occipito-temporal cortex, fusiform gyrus, extrastriate cortex, and inferior parietal lobule), in which significant activity was not observed. It is worth noting this lack of

activity may not be due to a lack of predicted brain areas being active during word reading in developing readers, but rather due to a lack of sensitivity in our results.

4.2.1 The Inferior Frontal Gyrus

The significant activity observed in the left inferior frontal gyrus, in both the opercular and triangular parts, is consistent with our hypotheses and with existing literature. The left inferior frontal gyrus has been consistently associated with phonologic and semantic processing, and has demonstrated engagement in skilled adult single word reading (Bitan et al., 2007; Burton, 2001; Glezer et al., 2016; Martin et al., 2015). More specifically, the opercular and triangular portions of the left inferior frontal gyrus have been attributed to phonological processing of visual word forms, and mapping of orthographic to phonologic information during word reading (Burton, 2001; Martin et al., 2015). Consideration of the role of the inferior frontal gyrus through development has identified this brain area displays activation during the early stages of reading acquisition (Church et al., 2008), with increases in its engagement associated with increased reading skill in developing readers (Bitan et al., 2007). This is due to the proposed role for the inferior frontal gyrus in skilled phonological segmentation used during efficient decoding strategies (Burton, 2001), which aligns well with the behavioural expectations of word reading processes and reading skill in second and third grade developing readers.

4.2.2 The Superior Temporal Gyrus

In the present study we also identified a significant cluster of activity in the right superior temporal gyrus, which was in line with our hypotheses and prior literature. This region was defined in our hypotheses due to its observed increased activation in developing readers, who recruit this region to a greater extent when reliant on phonology

based reading processes (Church et al., 2008; Houdé et al., 2010; Martin et al., 2015). However, we hypothesized bilateral engagement of the superior temporal gyrus, but observed activation only in the right superior temporal gyrus during word reading. This result is slightly less intuitive, as previous research has reported this brain area as being bilaterally active in young readers, with a shift to left lateralization with increasing reading skill (Yamada et al., 2011). Therefore, observing activity only in the right hemisphere structure seems less obvious than observing bilateral or left-lateralized activity. Ultimately, the lack of bilateral (or left-hemispheric) engagement of the superior temporal gyrus is likely not be due to a lack of its activity during word reading in developing readers, but rather due to the lack of sensitivity in our results suggested above.

4.2.3 The Cerebellum

The significant activity observed in the cerebellum was not in line with our hypotheses. However, it does correspond with existing literature of word reading. The left cerebellum, specifically lobules IV and V, have been implicated in passive language processing and silent reading in skilled adult readers (Martin et al., 2015; Stoodley & Stein, 2013; Turkeltaub et al., 2002). Furthermore, this brain region has been associated with skill automaticity during reading, with its engagement emerging alongside increasing automaticity and skill during reading development (Stoodley & Stein, 2013).

A meta-analysis of single word reading identified a significant cluster of activity in the left cerebellum in studies of skilled adult readers, but not in those of developing readers (Martin et al., 2015). The authors suggested the lack of converging evidence for engagement of the cerebellum in developing readers was due to its role in skill automaticity, suggesting developing readers may have not yet achieved this level of

reading skill. In the present study, the significant cluster of activity observed in the left cerebellum may indicate developing readers in the second and third grade have achieved levels of automaticity in reading. However, arguably more likely is that the words presented were familiar enough to the participants, and in this simple reading context where they did not need to perform a task, these words were being read fluently. In previous studies, such as those included in the meta-analysis reported, tasks required manipulations of the words or had working memory components (Martin et al., 2015). This would be much more challenging for developing readers and likely reduce the ability for fluent reading and word recognition. Thus, this result suggests that during passive word reading, developing readers are engaging the cerebellum.

4.2.4 Exploratory Group Level Analysis ($p \leq 0.05$)

Due to the limited number of significant clusters of activity observed in the group-level analysis, we performed an exploratory group-level analysis with a less conservative statistical threshold. This analysis yielded clusters of activity that were much larger, and in brain areas consistent with our hypotheses. These included significant clusters of activity in the opercular and triangular parts of the left inferior frontal gyrus and bilateral activity in the superior temporal gyrus, brain areas associated with phonology-based reading in developing readers (Bitan et al., 2007; Burton, 2001; Church et al., 2008; Martin et al., 2015). As well, this analysis yielded two significant clusters of activity in the left cerebellum, and two in the right cerebellum, and a significant cluster of activity in the left postcentral gyrus.

This exploratory group level analysis provides some additional support that the stimulus paradigm is eliciting activity in the reading network of developing readers, as we

predicted. Furthermore, this analysis may indicate that with increased statistical power, the scanning protocol and stimulus paradigm could be adequately sensitive to observe statistically significant clusters of activity in the hypothesized brain regions at the group-level of analysis.

4.3 SUBJECT LEVEL ANALYSIS

Additionally, we performed an exploratory subject-level analysis to identify clusters of activation that were consistent across a majority of subjects, but that may not have reached significance at the group level. This analysis yielded results that were more consistent with our predictions. More specifically, considering our hypotheses, at the subject level our results demonstrate significant activity from three or more subjects in the left inferior frontal gyrus, left superior temporal gyrus, and left inferior parietal gyrus, all brain areas associated with phonological processing. This analysis also yielded significant clusters of overlapping activity in the right inferior occipital gyrus, associated with orthographic processing. As well as in the right middle temporal gyrus and left inferior parietal gyrus, brain areas associated with semantic processing. Additionally, while the left cerebellum was not included in our hypotheses, it did demonstrate significant converging activity at this level of analysis as well.

However, we also identified convergence of activity in clusters we did not hypothesize observing. The presence of clusters of significant activity in the right insula, left superior parietal gyrus, left posterior cingulum, and left precuneus is challenging to interpret. Due to the limited sample size of the investigation, and the exploratory nature of this subject level analysis, further investigation would be required to draw any conclusions around the activity in these clusters.

These subject level results provide some evidence to suggest that across subjects there was convergence of activity in the hypothesized brain areas. However, none of the hypothesized brain areas were identified as active in every participant. This individual variability is not atypical in fMRI studies, although given the small sample size the absence of significant activity in these clusters in one or two participants (nearly half the sample) helps us understand the absence of these areas in the group-level analysis results. This exploratory subject-level group analysis provides support that while activity is present in the hypothesized brain areas, in such a small sample, the existing data is not robust enough to withstand the individual variability that is present in functional imaging data.

4.4 LIMITATIONS

4.4.1 Sample Size

The most prevalent limitation in this investigation is the sample size. An investigation of statistical power in fMRI analysis suggests a sample size of 80 or more is required for fMRI investigations to provide replicable results through cluster-level analysis (Turner et al., 2018). In the present study, only 5 participants completed MRI scanning successfully and were included in the statistical analysis. Thus, it is quite likely that due to the small sample size of this investigation there were brain regions engaged by the single word reading task that did not reach significance in group-level analyses.

While we clearly lack sufficient statistical power in the present study, it does not necessarily mean the results of the current analysis are entirely misleading: Murphy & Garavan (2004) demonstrated that in small sample sizes the observed clusters that reach significance are generally replicated in larger sample sizes. In fMRI research, false

positive results are not the main concern of low sample size investigations, but rather false negatives (Murphy & Garavan, 2004). Therefore, in fMRI investigations with smaller sample sizes, there is a much greater possibility of missing brain regions that were engaged by the task, than identifying activity in regions that would not be expected to replicate.

It is also worth noting here that while it is not best practice to have such small sample sizes in fMRI research, it is reasonable to do so for an initial validation of the experimental protocol. MRI research is extremely expensive and involves time consuming data collection and analysis. Therefore, it is somewhat expected that during validation of a study one would not invest too many resources in the efforts of achieving a significantly large sample. Due to the investment required of MRI research, these low sample sizes exist not only for study validation, but also in the published literature. Yeung (2018) performed a meta-analysis of 338 published fMRI studies involving human subjects and reported the median sample size across studies was only 33, and the lowest reported sample size was 7 participants.

4.4.2 Animal Identification Task Results

In addition to our small sample size reducing the sensitivity of our results, the accuracy data from the animal identification task does not conclusively suggest that participants were consistently attending to the stimulus words. First and foremost, it is challenging to qualitatively identify how accurately participants actually performed and responded to the animal words and photos based off of observational records alone. While we know they were performing the task correctly the majority of the time, the ability to interpret this information stops there. In considering the subjects for whom we do have

accuracy data, it suggests that at least one participant missed a surprising proportion of the target items. A lack of responses to target animal words and photos may indicate that the participant was distracted during the task. If participants were distracted, reduced attention to the words being presented would likely lead to weaker engagement of brain regions involved in word reading, then would be predicted if they were fully on task.

4.4.3 Event-Related Design

An additional limitation of this analysis may have been that the stimulus paradigm employs a slow event-related design, such that there is a minimum of six seconds between every stimulus word presentation. This style of stimulus presentation was selected due to the nature of the larger, longitudinal investigation that will be performed. During this investigation, the goal is to recover the hemodynamic response for each individual word presented, so that we can characterize the differences between words, which would not be possible if the hemodynamic response to successive stimuli overlapped.

However, when multiple closely spaced stimuli of the same category are presented, the hemodynamic response is typically weaker than what would actually be predicted, due to adaptation of the response (Burock et al., 1998; Newman, 2018). Furthermore, it has been argued that presenting stimuli using an event-related design with less than 15 seconds between each stimulus leads to a significant decrease in the statistical power (Burock et al., 1998; Dale, 1999). Generally, if presenting multiple stimuli of the same category, an option to increase the hemodynamic response would be to employ a blocked design. This involves reducing the time between each stimulus, such that their individual hemodynamic responses overlap and summate, and analyzing this

summed response. However, the trade-off of this approach is that it is then not possible to recover the hemodynamic response to each individual stimulus presented, and thus would not benefit the investigation at hand.

While changing the interstimulus interval to be longer could result in increased statistical power, it also comes with the requirement to increase scanning time or reduce the number of stimuli presented – neither of which are compelling choices. An alternative method to increase the hemodynamic response during a slow event-related design, and overcome the observed signal loss, is to jitter the stimulus presentation. Jittering the stimulus presentation involves presenting the stimuli with varying interstimulus intervals. In doing so, this creates greater variance in the hemodynamic response recorded, with longer intertrial intervals allowing the hemodynamic response to return closer to baseline, and shorter intervals allowing for summation of the signal (Barock et al., 1998; Dale, 1999; Newman, 2018), ultimately increasing the signal that can be recovered in response to each individual stimulus.

4.4.4 1.5 T MRI Field Strength vs. 3 T

Finally, this investigation was performed using an MRI scanner with a magnetic field strength of 1.5 Tesla (T), which is a fixed property of the scanner. This scanner was selected due to its location at a children's hospital, and thus the MRI Technologists who work with this scanner are very familiar and capable of achieving the best scanning results when working with children. As well, the scanner and surrounding environment are decorated in a child-friendly way. However, 1.5 T is considered a relatively weak magnetic field strength for fMRI research, as contrast-to-noise ratio (which reflects the ability to detect a reliable task-related change in BOLD signal) increases exponentially

with magnetic field strength. For example, Krasnow and colleagues (2003) found task-related clusters of activity that reached statistical significance in 3 T data, but did not reach significance at 1.5 T, within the same individuals performing the same tasks. Furthermore, the researchers identified numerous sets of voxels that were significantly more active at 3 T than 1.5 T. Based on the results of our analysis, and this support from the literature, it is possible the reduced signal quality of the 1.5 T scanner, compounded with a small sample size and our chosen timing between word presentations, all contributed to a reduced sensitivity to observe significant signal change within the full reading network that was predicted based on the literature.

4.5 FUTURE DIRECTIONS

The most immediate implication of this work is that it provides a detailed analysis of the passive single word reading stimulus paradigm developed, and the resulting elicited reading network. Based on the results of this analysis, and the limitations identified, there are a number of recommendations that can be made to enhance the performance of this stimulus paradigm and scanning protocol for the longitudinal investigation.

The first recommendation I propose is to add the animal words presented during scanning to the word-knowledge screening, lexical decision task, that is performed during the first study visit. When participants perform with low accuracy on identification of animal words during scanning, it would be beneficial to be able to consider whether this was due to them not reading the stimulus words or due to them not recognizing the animal words presented. Furthermore, if numerous participants do not demonstrate correct recognition of specific animal words, this data would provide information that would

allow us to adjust the list of animal words to be more appropriate for the participant population age group.

In considering the animal identification task, it may also be of benefit to consider providing feedback to participants during scanning on their performance. After each functional run, we repeat the instructions to participants who appear to be performing the task incorrectly. However, during the task, participants receive no feedback on how frequently they are correctly identifying the animal words and photos. Immediate feedback after each animal word and photo, indicating whether or not participants' responded correctly, may enhance participants' motivation to continue attending to the stimuli, and ultimately increase their engagement in word reading during scanning.

My next recommendation concerning the stimulus paradigm is to model different stimulus timing options, that involve jittered stimulus presentation. Jittering stimulus presentation allows for increased variance in the hemodynamic response to each stimulus presented, without significantly increasing the length of the paradigm or decreasing the number of stimulus words presented. There is computer software, such as *optseq* version 2 (Dale, 1999), that can be used to create optimized functional imaging designs within a certain maximum time frame and number of stimulus presentations. This will create interstimulus interval timing for the entire stimulus presentation, that is optimized for recovery of the maximal hemodynamic response for each stimulus presented. Therefore, it would be of benefit to create an optimized, jittered, stimulus presentation and use this timing sequence for 5 subjects, to compare the results of its performance to the results of the current stimulus timing.

My final recommendation would be to investigate the performance of this stimulus paradigm in a 3T MRI scanner. Lack of sensitivity in the present analysis may not be entirely due to the use of a 1.5 T scanner, as other potential limitations have been identified. However, prior to launching such a large investigation that will involve a significant investment of both resources and time, it would be worthwhile to compare the performance of the two scanners. This could be done by running 5 participants in the 3T MRI scanner, and performing the same data analysis as was performed here, and directly comparing the sensitivity of the two. If the difference in performance is only small, it would be worthwhile to continue using the 1.5 T scanner, as it is in such a child-friendly environment. However, if the difference in performance is substantial, the scanner used could be a beneficial switch to make in the protocol.

4.6 CONCLUSIONS

This analysis did not yield results that were as sensitive to engagement of all brain areas in the reading network as we would have hoped. However, it does indicate that the paradigm we have created to prepare children for the MRI is extremely successful. We created videos that provide information about the MRI for parents and children to watch at home, a statue game to practice lying still, and even provide parents with audio files of the MRI noises to desensitize participants to the loud noises prior to scanning. With all of this effort, we only lost two participants due to an inability to complete the scanning protocol. Furthermore, using these training materials, for all the participants that completed the scanning protocol, all but one run passed motion correction requirements during preprocessing. This indicates that all the materials that have been created to prepare children for scanning are quite effective.

Furthermore, in such a small sample of 5 participants, our analyses do provide positive indications that our scanning protocol elicits activity in expected areas. We did identify significant clusters of activity at the group level that were in line with our hypotheses. Furthermore, exploratory analyses at the group-level demonstrated greater clusters of activity in hypothesized brain areas, and at the subject-level demonstrated consistent activity across three or more subjects in numerous hypothesized brain areas.

However, while the results are promising, the small sample size of this investigation was a limiting factor. At the group level, we did not observe significant clusters of activity in a number of brain areas that were predicted based on prior literature, suggesting a lack of sensitivity in our data. Additionally, the exploratory analyses identified activity across multiple participants in brain areas that were not predicted a priori, and thus have the potential of being false positives. False negatives and positives are a common issue in smaller sample size investigations, and are likely both present in the current analysis. However, as sample size increases, there is a decreasing likelihood of observing false negatives (Murphy & Garavan, 2004) and false positives (Turner et al., 2018). Thus, with a greater number of data sets included in the analysis, conclusions can be drawn with greater confidence that the significant clusters of activity observed are truly representative of task-related activity.

Therefore, if the recommendations for increasing sensitivity of our scanning protocol are evaluated, with an increased sample size and minor adjustments this paradigm should be extremely successful at investigating the neural correlates of passive word reading in developing readers. Given the present results in such a small sample size, I am optimistic that once the full study has been optimized, it will be able to contribute

quite meaningfully to our understanding of the neural correlates of passive single word reading in developing readers. Thus, in conclusion, this analysis provides promising evidence this paradigm has the potential to successfully identify what is in a word, at the neural level, in developing readers.

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