2018-06-25

Early Language Abilities and the Underlying Neural Functional Reading Network in Preschoolers

Benischek, Alina Marie

UNIVERSITY OF CALGARY

Early Language Abilities and the Underlying Neural Functional Reading Network in Preschoolers

by

Alina Marie Benischek

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE

DEGREE OF MASTER OF SCIENCE

GRADUATE PROGRAM IN MEDICAL SCIENCE

CALGARY, ALBERTA

AUGUST, 2018

Abstract

Early childhood is a critical time for language development. Language impairments that go untreated in the early years can result in decreased academic achievement and future mental health concerns. Despite the importance of early language development, very little research has focused on the functional brain systems supporting language in typically developing young children. We investigated relationships between age, language abilities, and the brain's functional connectivity (FC) patterns seeded from brain areas associated with reading. The study included 50 healthy children aged 2.9-5.6 years (3.8 ± 0.6 years, 21f/29m) who completed a language assessment (NEPSY-II Phonological Processing and Speeded Naming) and underwent functional MRI (magnetic resonance imaging) scanning while watching a movie. Phonological Processing scores positively correlated with FC between the left angular gyrus and contralateral sensorimotor cortices, as well as between the right angular gyrus and the left supramarginal gyrus. Speeded Naming scores positively correlated with FC between the left inferior frontal gyrus, pars triangularis and the left fusiform gyrus, extending to the posterior region of the middle/inferior temporal gyrus and negatively correlated with the precuneus of the default mode network. Despite these variations in the FC patterns associated with speeded naming and phonological processing, both language measures positively correlated with FC between the ROI and the angular gyrus, supramarginal gyrus, and precentral gyrus. Age positively correlated with FC between regions within the ventral language pathway, including the inferior frontal gyrus and middle/inferior temporal gyrus and negatively correlated with FC between ipsilateral language regions and contralateral visual areas within the occipital cortex. The results demonstrate that better language abilities in young children are associated with stronger functional connections between brain regions within the language network identified in older children and adults who can perform more complex language processes.

Acknowledgements

Funding for this project was provided by grants awarded to my supervisor, Dr. Catherine Lebel, from the Canadian Institute of Health Research and the Alberta Children's Hospital Research Institute (ACHRI). My stipend was provided in part by the NSERC-CREATE I3T Graduate Scholarship and the 2015 and 2016 Queen Elizabeth II Graduate Scholarships.

Also, I would like to thank Elodie, Camilia and Ashleigh Frayne for collecting and organizing the majority of the data; Dr. Christiane Rohr and Dr. Xiangyu Long for your mentorship and teaching; as well as my committee members: Dr. Signe Bray, Dr. Deborah Dewey and Dr. Catherine Lebel for their constructive feedback and expert advice regarding the project methodology and results interpretation.

Table of Contents

Abstract ii
Acknowledgements iii
Table of Contents iv
List of Tables v
List of Figures vi
List of Symbols vii
1 INTRODUCTION 8
1.1 Behavioral Studies: Linguistic Development 10
1.2 Reading Impairments: Definitions, Prevalence, and Long-Term Outcomes 11
1.3 Language Assessments Appropriate for Studying Pre-Reading Language Abilities in Children 14
1.4 Functional Magnetic Resonance Imaging (fMRI) as a tool to study language 17
1.5 Functional Brain Networks involved in Language and Reading 21
1.6 Neural Mechanisms Underlying Speeded Naming and Phonological Processing. 25
1.7 Resting-State Functional Connectivity Studies: Associations with age and linguistic ability. 26
1.8 Objective. 29
1.9 Rationale 30
1.10 Research Aims (1 & 2) and Hypotheses. 31
2 METHODS 33
2.1 Participants 33
2.2 Data Acquisition: Procedure 34
2.3 Language Assessments 35
2.4 Behavioral Analysis 36
2.5 Functional Connectivity 37
2.5.1 Data Acquisition 37
2.5.2 Data Preprocessing. 37
2.5.3 Seed Regions of Interest 40
2.5.4 Functional MRI Analyses 42
3 RESULTS 44
3.1 Correlations between age, head motion, and language subtests measures. 44
3.2 Language Assessments. 44
3.3 Functional Connectivity Patterns within the Language Network 45
3.3.1 Relationship between Phonological Processing and the Language Network 47
3.3.2 Relationship between Speeded Naming and the Language Network 50
3.4 Functional Connectivity Correlates with Age 54
4 DISCUSSION 58
4.1 Functional Connectivity Correlates with Age and Language Skills 58
4.2 Functional Connectivity Patterns Associated with Age 59
4.3 Brain-Language Relationships 64
4.3.1 Relationship Between Phonological Processing and the Functional Language Network 65
4.3.2 Relationship Between Speeded Naming and the Functional Language Network 67
4.3.3 Similarities and Differences between Phonological Processing and Speeded Naming FC Patterns. 72
4.3.4 Lateralization & Intra and Interhemispheric Functional Connections of Language Network 75
4.4 Limitations 77
4.5 Future Directions 80
4.6 Conclusion. 82
4.7 References 85-98
Appendix A 99

List of Tables

83.3.1 Table 1. Phonological Processing Scores Correlate with Functional Connectivity. 48
3.3.2 Table 2. Speeded Naming Scores Correlate with Functional Connectivity 53
3.4 Table 3. Functional Connectivity Correlates with Age 57
A.1 Coordinates for Regions of Interest 99

List of Figures

2.4.3 Figure 1. Schematic Brain Including Regions of Interest 41
3.3 Figure 2. Group Average Seed-Derived Functional Connectivity Maps 46
3.3.1 Figure 3. Phonological Processing Correlates with Functional Connectivity Patterns. . . . 49
3.3.2 Figure 4. Speeded Naming Correlates with Functional Connectivity Patterns 51
3.4 Figure 5. Speeded Naming Correlates with Functional Connectivity Patterns 52
3.4 Figure 6. Age Correlates with ANG and STG Functional Connectivity Maps 55
3.4 Figure 7. Age Correlates with Inferior Frontal Gyrus Functional Connectivity Maps . . . 56

List of Symbols, Abbreviations and Nomenclature

Symbol	Definition
ADHD	Attention deficit hyperactivity disorder
AFNI	Analysis of functional neuroimages open-source software
ANG	Angular gyrus
BET	Brain extraction tool
BOLD signal	Blood-oxygen-level dependent signal
DVARS	RMS intensity difference of volume N to volume N+1
EPI	Echo-planar imaging
FC	Functional connectivity
FD	Frame displacement (average of rotation and translation parameter differences)
FEAT	General linear model-based fMRI analysis software for image preprocessing
FLAME	FMRIB's local analysis of mixed effects- for higher-level image analysis
FLIRT	FMRIB's linear image registration tool - linear inter- and intra-modal registration
fMRI	Functional MRI
FMRIB	FMRIB analysis research group, Oxford, United Kingdom
FOV	Field of view
FSL	FMRIB software library
FSLview	Interactive display tool for 3D and 4D data
FWHM	Full width at half maximum
GE 3T MR750w	General Electric 3 tesla MRI with a 70-cm patient bore
IFGtr	Inferior frontal gyrus, pars triangularis
MNI	Montreal Neurological Institute
MRI	Magnetic resonance imaging
NEPSY II	Second addition of the developmental neuropsychological assessment manual
PCC	Posterior cingulate cortex
RMS	Root mean squared
ROI	Region(s) of interest
rsFC	Resting state functional connectivity
SLI	Specific language impairment
SPSS	Statistical package for social science
STG	Superior temporal gyrus
T1	T1-weighted MRI image resulting from a specific MRI pulse sequence
T2*	T1-weighted MRI image resulting from a specific MRI pulse sequence
TE	Echo time
TR	Repetition time
U of C	University of Calgary
x y z	Cartesian coordinate system of the anatomical x, y, z planes

1 INTRODUCTION

1.1 Behavioral Studies: Linguistic Development

According to language theorists, early language development lays the foundation for more complex linguistic processes, such as reading (Ruben, 1999). The foundational language skills include: phonological awareness, phonological memory, and syntax. *Phonological awareness* refers to the specific ability to identify and manipulate speech sounds (phonemes) to build connections between sounds and print (i.e. the alphabet) (Lonigan et al., 2009). Phonemes are the smallest meaningful units of sound composed of specific syllables and sounds combinations that can be grouped together to form words. *Phonological memory* refers to the short-term storage of phonological information needed for word decoding and recall of text (Lonigan et al., 2009). These two cognitive processes are required for developing literacy and oral language skills and together comprise phonological processing. Finally, *syntax* defines the set of rules within a language used to form unique sentences and phrases. The fluency of oral and written language is dependent on the efficiency of these processes and their ability to function together to assist individuals in understanding and decoding language. Altogether, these basic language skills are utilized as tools to learn the meaning behind different speech sounds (Carota, Kriegeskorte, Nili, & Pulvermuller, 2017; Wagner & Torgesen, 1987).

According to the literature, the first two years of life are especially important for developing the fundamental phonological processing skills used to learn the more complex rules of language (Conti-Ramsden & Durkin, 2012; Ruben, 1999). This idea is supported by an earlier study that compared the language development trajectories between children born hard of hearing to children who acquired a hearing impairment in early childhood (Ling, 1989). According to Ling (1989), children who acquired a hearing impairment during the preschool years (around two years of age) demonstrated superior semantic and syntactic language skills in later childhood compared to children born with a hearing impairment. The author suggests that the early acquired phonological processing skills support the development of the semantic and syntactic aspects of language (Ling, 1989). More recent studies found evidence that suggests phonological awareness development begins in early infancy. According to these studies, children as young as two months of age can discriminate between different voices and are able to identify and attend to their caregiver'(s) voice (Conti-Ramsden & Durkin, 2012; Ruben, 1999). In addition, researchers found a strong resemblance between the intonation of an infant's pre-babbling canonical syllable sounds (well-formed consonant + vowel combinations), older infants babbling sounds (repetitions of syllables), and their caregiver's voice (Conti-Ramsden & Durkin, 2012; Ruben, 1999). These findings suggest that phonological awareness develops and strengthens with language exposure, particularly during infancy and early childhood.

As early as five months of age, children begin to demonstrate an understanding of the connection between speech sounds and their underlying meaning – an important skill for vocabulary building (Conti-Ramsden & Durkin, 2012). Sometime between 10 and 15 months of age, children utter their first word. After this point, children begin to build their vocabulary at a rate of approximately 10 words per month until the child has learned approximately 50 words, then rate of vocabulary building increases from 10-15 words to around 30 words per month (Conti-Ramsden & Durkin, 2012). This rate of vocabulary building remains elevated throughout the preschool years, until the child has learned approximately 14,000 words (around 6-years of age). During this early vocabulary building period, around two-years of age, children begin to show signs of grammatical knowledge by combining more than one word in short utterances, such as, "hurt head" or "more juice". By age five, most children can combine words and phrases together by applying the grammatical rules of their native language needed to create longer, more complex sentences and multiclause expressions. Before learning to read, around six years of age, children need to develop their fundamental phonological processing skills, grammatical speaking skills, and have built a vocabulary large enough to understand most of the words in the text (Conti-Ramsden & Durkin, 2012).

1.2 Reading Impairments: Definitions, Prevalence, Risk-factors, and Long-Term Outcomes

According to leaders in dyslexia research, reading difficulties are estimated to affect up to 20% of the North American population (Shaywitz et al., 2003). Developmental dyslexia, also called specific reading impairment, is a highly prevalent neurodevelopmental disorder that affects reading in 5 to 17.5% of children and 80% of children diagnosed with a learning disability in North America (Ferrer, Shaywitz, Holahan, Marchione, & Shaywitz, 2010; Ferrer, Shaywitz, Holahan, Marchione, Michaels, & Shaywitz, 2015; Shaywitz, Shaywitz, Fletcher, & Escobar, 1990). Developmental dyslexia is characterized by an unexpected difficulty in reading compared to peers of the same age and education level (Shaywitz & Shaywitz, 2005). Many language researchers argue that developmental dyslexia is caused by a core deficit in phonological awareness – the ability to recognize how different words are created from combining elemental units of sound (phonemes) in different ways – an essential ability given that reading requires that the reader map or link printed symbols to sound (Ferrer et al., 2010; Ferrer et al., 2015). While the severity of the phonological awareness impairment may be indirectly measured with speeded naming – a measure of the efficiency of serial word production (Ferrer et al., 2010; Ferrer et al., 2015; Vukovic & Siegel, 2006). According to researchers, phonological awareness is strongly linked to decoding and reading accuracy, while speeded naming is more strongly associated with reading speed and fluency (Norton et al., 2014; Vukovic & Siegel, 2006).

According to the *double deficit hypothesis of dyslexia*, individuals with deficits in both phonological awareness and speeded naming present with a more severe reading impairment compared to individuals with a specific deficit in phonological awareness (Norton et al., 2014; Vukovic & Siegel, 2006). Although the double deficit hypothesis is widely accepted among scientists, the degree of overlap between the underlying deficits of speeded naming and phonological awareness is still under debate. One theory is that developmental dyslexia is caused by an underlying deficit in phonological awareness, while speeded naming ability reflects the degree of the impairment. According to this theory, an individual with a serve impairment in phonological awareness will have carry over effects and perform poorly on speeded naming tasks, where an individual with a mild or moderate impairment in phonological awareness may score in the normal range for speeded naming. The counter argument, also known as the independent cognitive process theory, suggests that speeded naming and phonological awareness skills stem from primarily separate cognitive processes and utilize different brain areas, thus independently contribute to reading (Norton et al., 2014; Vukovic & Siegel, 2006). In line with the independent cognitive process theory, recent genetic-environmental studies examining the etiology of developmental dyslexia identified distinct cognitive variants, or subtypes of developmental dyslexia that were grouped based on their distinct genetic and environmental profiles (Fluss et al., 2008; Neef et al., 2017; Sun et al., 2017). More specifically, researchers were able to pair genes with cognitive deficits specific to phonological processing, speeded naming, and orthographic processing and characterize developmental dyslexia into distinct homogeneous reading-impaired subtypes based on different genotype-phenotype interactions (Neef et al., 2017; van Bergen, van der Leij, & de Jong, 2014; Willems et al., 2016). While, neuroimaging studies have identified differences in brain structure and function between typical and atypical readers (Neef et al., 2017; Sun et al., 2017). The primary environmental risk factors associated with reading challenges and have also been found to affect the severity of a reading impairment include, low socioeconomic status (SES) and little or poor-quality language and reading exposure in childhood. SES has been considered to influence language development because of the corresponding affects of low post-secondary maternal education, poor food quality, higher prevalence of chronic illness, mental illness, and violence within lower SES communities (Wu et al., 2003). While, the quality and amount of time caregiver(s) allocate to reading with their child is strongly associated with the child's vocabulary, grammar knowledge and reading skills (Fluss et al., 2008; Fluss et al., 2009; Gardner-Neblett & Iruka, 2015; Richels, Johnson, Walden, & Conture, 2013; Zubrick, Taylor, & Christensen, 2015). Researchers suggest that the genetic and environmental risk factors operate probabilistically to produce a variety of different reading-related cognitive impairments (Brian Byrne 2005; Willems, Jansma, Blomert, & Vaessen, 2016). Altogether, these findings provide support for the *multiple cognitive deficit model* of developmental dyslexia, which suggests that there are several underlying causes associated with a reading impairment (van Bergen et al., 2014; Vukovic & Siegel, 2006).

Similar to developmental dyslexia, individuals with other neurodevelopmental disorders, such as autism spectrum disorder (ASD) and specific language impairment (SLI) often struggle with reading (Leonard et al., 2002; Ricketts, Jones, Happe, & Charman, 2013). However, unlike developmental dyslexia, children with ASD often struggle with reading comprehension despite having intact decoding skills. Whereas, children with a SLI often have trouble comprehending and/or producing oral language despite their good health, intact hearing, normal intelligence, and are motivated to learn (Bishop & Edmundson, 1987; L. B. Leonard, 1998). Although SLI is sometimes associated with poor phonological processing skills, a phonological processing deficit is often more pronounced in persons with developmental dyslexia (Bishop, McDonald, Bird, & Hayiou-Thomas, 2009). Thus, information on the degree of the phonological processing deficit could be useful for identifying children who are high risk for developing a reading specific impairment.

Although early detection and interventions for a reading impairment are important for good long-term outcomes, many children still receive insufficient training and support for their reading difficulties and might continue to struggle with word decoding and spelling in adulthood. Even children fortunate enough to receive early interventions for their reading challenges and learn to accurately decode words, read slower, and with greater mental effort than healthy controls with matched IQ scores (Ferrer et al., 2015). Since reading is an important skill for learning and communicating, individuals with a reading impairment might struggle in other areas, including memorization and other nonverbal social and academic skills that are typically learned through reading and interacting through written language (Conti-Ramsden & Durkin, 2007). For example, today most children and youth acquire their typing, spelling skills, and written social skills by communicating with their friends through different social media sites, online forums, and media posts. The recurring academic and social struggles and failures associated with a reading disability can place a child at risk of developing poor self-confidence, which is associated with greater social, emotional, and professional stress (Carawan, Nalavany, & Jenkins, 2016). Altogether, these academic, social, and psychological factors associated with a reading disability can result in less-favorable educational and developmental outcomes if not treated at an early age (Andres-Roqueta, Adrian, Clemente, & Villanueva, 2016; Barbu et al., 2015; Bishop & Edmundson, 1987; Conti-Ramsden & Durkin, 2007). Therefore, the development of earlier detection methods and interventions for children at risk or children diagnosed with a reading impairment could help to improve a child's mental health and overall quality of life.

1.3 Language Assessments Appropriate for Studying Pre-Reading Language Abilities in Children

Although developmental dyslexia cannot be formally diagnosed until the child begins learning to read, measures of phonological processing and speeded naming can be used to predict a child's future reading ability (Kirby, Parrila, & Pfeiffer, 2003; Olofsson, 2000) and identify potential future challenges (Puolakanaho A, 2007). As briefly described in Section 1.1, phonological processing encompasses phonological awareness and phonological memory to detect, identify, and manipulate word sounds long enough in our working memory to make a correct response (Wagner, & Torgesen, 1987). These two cognitive processes are required for developing normal literacy and oral language skills. While speeded naming tasks require coordination between several cognitive components to accurately identify a random series of visual symbols and produce the corresponding word (Moseley, Pulvermuller, & Shtyrov, 2013; Ries, Legou, Burle, Alario, & Malfait, 2015). More specifically, speeded naming measures the efficiency of lexical access (the process of converting visual symbols into phonological codes using stored orthographies), item identification (matching orthographic information with the correct semantic representation) before relaying the information to the sensorimotor system for word articulation (Logan, Schatschneider, & Wagner, 2011; Denckla & Rudel, 1974; Wagner & Torgesen, 1987; Wolf, Bally, & Morris, 1986). The moderately positive relationship between speeded naming and phonological processing scores is thought to reflect the overlap in the use of phonological processing to complete the tasks. While, the degree of overlap in the cognitive processing between these two language tasks is still under debate. Psychology studies found that speeded naming and phonological processing tasks provide independent information in regards to the cognitive processes required to process the language information, ultimately contributing to the variance in reading ability (Bowers & Swanson, 1991). For this reason, researchers strongly recommend that both speeded naming and phonological processing measures are used for evaluating a child's pre-reading language skills (Norton et al., 2014; van Bergen et al., 2014; Vukovic & Siegel, 2006).

Prior to inferring the predictability of the speeded naming and phonological processing measures to a child's future reading abilities, researchers need to take into account the child's previous linguistic experience, developmental stage, and the specific methods used to test these language skills. Recent studies found that the relationship between phonological processing and reading ability strengthens across early and mid-childhood (from 2 to 6 years of age) but becomes less significant as children become proficient decoders (Kirby, Parrila, & Pfeiffer, 2003). In contrast, speeded naming and reading ability continually strengthens across mid-childhood into late adolescence (Kirby, Parrila, & Pfeiffer, 2003). The difference in the timing between the two language measures is considered to reflect the child's developmental stage in their language learning. During the early and mid-childhood years, children are still in the process of acquiring and mastering their phonological awareness skills. Therefore, major delays or challenges in the development of phonological processing skills during this period may be indicative of a phonological processing cognitive deficit. Whereas, speeded naming—a measure of orthographic processing and efficient language production— cannot be accurately measured until the child has developed a solid foundation in their phonological processing skills. The timing of this developmental shift in the predictability of these two language measures depends on the orthographic depth of the language. Since English is highly inconsistent in its correspondence between word sounds (phonemes) to the spelling of these words (graphemes), English speaking children require more practice and instruction in word decoding compared to children who speak other alphabetic languages of lower orthographic depth, such as Spanish, German, and Dutch (Marinus, Nation, & de Jong, 2015). In English speaking children, the developmental shift in language processing occurs in mid-childhood (around grades 3-4) (Wolf, 2012). As a result, phonological processing ability may be better at predicting future reading ability in preschool-aged children, while speeded naming may help to identify children with more serious pre-reading language concerns (Miller, Vaughn, & Freund, 2014).

According to the literature, the relationship between speeded naming and reading fluency is greatest when the items (words, shapes, colours, symbols, etc.) used in the task are familiar and regularly used (Frijters et al., 2011; Meyer, Hart, & Felton., 1998; Sarborough et al., 1998). For this reason, the predictive relationship between reading fluency and speeded naming is greatest for young children (with little exposure and experience with numbers and letters) when the items presented in the task are alphanumeric (such as objects and colors) (Frijters et al., 2011; Meyer et al., 1998; Sarborough et al., 1998). In support of the stimuli familiarity hypothesis, two independent studies found a stronger positive relationship between the use of alphanumeric task stimuli in the speeded naming task and reading ability for older school-aged participants (aged 6-to-8 years) compared to the younger, preschool aged-children (3-5 years old) with less exposure to letters and numbers (Meyer et al. 1998, Wolf et al. 1986). For these reasons, non-alphanumeric task stimuli (such as colors and shapes) are preferred over alphanumeric task stimuli for preschool-aged children (Norton et al., 2014; van Bergen et al., 2014; Vukovic & Siegel, 2006).

In contrast to reading measures targeting reading comprehension and passage analysis, phonological processing and speeded naming measures are sensitive to the language skills associated with the reading process. As reading comprehension and passage analysis measures involve complex higher-level cognitive processes, these language abilities are strongly influenced by one's overall intelligence, subject knowledge, vocabulary size, and grammatical knowledge (Lonigan et al., 2009; Snowling & Hulme, 2011). Whereas, speeded naming and phonological processing measures are better at assessing and predicting reading processing abilities and associated learning disabilities (particularly, developmental dyslexia). Although not directly tested, specific cognitive abilities, including attention and working memory, are important for reading and analyzing written content.

1.4 Functional Magnetic Resonance Imaging (fMRI) as a Tool to Study Language

Functional magnetic resonance imaging (fMRI) is a powerful, non-invasive technique that indirectly measures the spontaneous modulation of neural activity at rest and in response to an external stimulus (Glover, 2011). Ogawa (1990), Kwong (1992) and colleagues first discovered and pioneered fMRI after discovering that hemoglobin has different magnetic properties in its oxygenated and deoxygenated states. Ogawa was the first to identify the magnetic resonance imaging (MRI) contrast signal associated with the concentration of blood deoxyhemoglobin, otherwise known as the *blood-oxygen-level-dependent (BOLD)* signal (Ogawa, Lee, Kay, & Tank, 1990). Functional MR imaging assumes that the magnitude of the hemodynamic response reflects the local changes in neural metabolism. As an increase in neural firing requires additional oxygen to meet the greater metabolic needs of the cells. The faster the metabolic rate, the more oxygen is delivered to the cells from the surrounding blood, the higher the concentration of deoxygenated hemoglobin in the local blood supply. In addition, an increased cellular metabolic rate is associated with an increased amount of energy by-products (particularly, CO2, NO, H+), which dilate the local blood vessels and cause an increase in oxygenated blood to the affected region by increasing blood volume and blood flow. However, the intensity of the BOLD signal is inversely proportional to the concentration of paramagnetic deoxyhemoglobin. Higher concentrations of deoxygenated blood is associated with a lower BOLD signal, which can be quantified over time, producing time courses for each voxel in the brain (Ogawa et al., 1990). Although fMRI scan time can vary across tasks and methods, it is common for resting state fMRI scans to acquire images every few seconds for 5 to 10 minutes. In the current study, we acquired fMRI images every two seconds for just over eight minutes (8.10 minutes).

Higher cognitive processes, such as reading, involve the dynamic interplay between various functional networks and systems (Maria de la Iglesia-Vaya, 2013; Tang, Tang, Tang, & Lewis-Peacock, 2017). Similarly, neurological and psychiatric disorders often involve deficits in widespread brain regions; these factors make fMRI a highly valuable multipurpose tool in cognitive neuroscience research (Greicius et al., 2008; Zhao et al., 2017). In fMRI, brain regions are said to be *functionally connected* when the measured BOLD signal in one region is correlated with that of another region. Functional connectivity (FC) strength is based on the correlational coefficient and depends on the degree of synchronization of the BOLD signal patterns between two separate brain areas (Biswal et al., 1995; Kelly et al., 2012). Whereas the degree of synchronization depends on the amount of overlap in the measured signal frequency and amplitude across a set timeframe averaged over a cluster of voxels anatomically representing a specific brain area. Regarding the interpretation of fMRI results, a positive correlational coefficient suggests that these distinct brain regions are functionally connected, or in direct communication (timecourse signals are in phase), whereas a negative correlation coefficient suggests that these two brain areas function in opposition (timecourse signals are opposite in phase). Both positive and negative correlations supply important information in regard to how brain networks function as a unit and communicate with other brain networks.

The FC patterns of the brain can be identified using either resting state or task-based brain activation methods (Gallagher, Tremblay, & Vannasing, 2016). However, task-based methods are limited in their scope to a specific task, whereas resting state FC (rsFC) studies examine how brain networks are intrinsically organized (Glover, 2011). According to the literature, the brain is organized into large-scale resting-state brain networks (RSNs) that function in concert when the stimuli is cognitively relevant, or in opposition, between brain networks that process cognitively opposing or irrelevant information for the task at hand (Fox & Raichle, 2007). Therefore, rsFC studies are useful for examining the FC relationship between distinct brain regions and their function within a specific brain network (Fox et al., 2005). For example, studies have consistently found a negative relationship between the language and the DMN (primary function is to regulate internal mental processes) and a positive relationship between regions of the functional language and attention networks (Fox et al., 2005;

Raichle et al., 2001). In addition, these rsFC brain maps can be correlated with a specific behavioral or cognitive measure to find the relationship between a factor of interest and the strength of the FC between distant brain areas (Glover, 2011).

Independent Component Analysis (ICA) and seed-based rsFC are the two most common methods used to investigate the brain's FC patterns within rsFC data. ICA is a data driven research method that is useful for identifying large-scale brain networks, whereas seed-based rsFC is a hypothesis driven method that examines FC patterns originating from preselected brain areas. Seed-based rsFC analysis works by first creating a region of interest (ROI), a collection of voxels placed within a preselected anatomical area, then correlating the average timecourse signal within the ROI with every other voxel in the brain to create group average FC maps. This seed-based rsFC analysis method is useful for understanding the functional relationship of a specific brain area with the rest of the brain and to gain a better understanding the role of each node within a functional brain network. For example, the seed-based rsFC method can be used to determine how different cognitive states, mental disorders, and health conditions impact brain function in males, females and individuals of different age groups (Power et al., 2011; Power, Fair, Schlaggar, & Petersen, 2010). The flexibility and adaptability of fMRI study designs makes rsFC analyses optimal for a variety of research, diagnostic and clinical treatment planning and evaluating purposes (Fox & Greicius, 2010; Glover, 2011). For these reasons, FC analyses can be used to help guide researchers in therapy program development and for refining treatment plans for different diseases and disorders, including reading disabilities.

Due to the need to remain still for the duration of the fMRI scan, little research has examined the FC patterns of children, and even fewer studies have investigated preschool aged children between two and six years of age who particularly struggle to remain still for long periods of time (Power, Mitra, Laumann, Snyder, Schlaggar, & Petersen, 2014). The primary reason for this limitation is head motion. Head motion artifacts are large-scale, spurious and systematic in nature. Associated with an increase in short-distance correlations and a reduction in long-distance correlations throughout the image (AfshinPour, Grady, & Strother, 2014; Power, Barnes, Snyder, Schlaggar, & Petersen, 2012; Power et al., 2014). Fortunately, new artifact post processing image correction methods and modified scanning procedures (such as passive motive watching) has enabled researchers to successfully study young children (Power et al., 2014). Although passive movie watching during fMRI imaging cannot be equated with rsFC (where the participants rest with their eyes either open or closed), recent FC adult studies have found comparable results (Vanderwal, Kelly, Eilbott, Mayes, & Castellanos, 2015). Despite these newly discovered methods and image quality improvements, the presence of an external stimulus during the MRI scan can still alter or dampen the FC strength (statistical significance) between the areas within the resting state networks. This dampening phenomenon occurs in-response to the presence of an external stimulus because the external processing brain networks function in opposition to the resting state networks involved in regulating one's internal mental processes (Fornito et al., 2013; Pamilo et al., 2012). In addition, an independent study found that movie watching altered of the frequency of the hemodynamic response across specific areas of the cortex (particularly, the primary auditory and visual cortex), accounting for the presence of the external stimulus (Kauppi, Jaaskelainen, Sams, & Tohka, 2010; Rohr et al., 2016). Overall, the potential negative impact caused by movie watching during the fMRI scan on the FC patterns are marginal in comparison to the effects of motion induced image artifacts. According to Fox and Grecius (2010), shorter resting state scans are preferred over longer within-scanner task-based studies for clinical and pediatric participant populations that find it difficult to remain still for extended periods of time. In task-based fMRI studies, around eighty percent of the acquired signal is discarded as noise after the images have undergone extensive averaging to produce average FC maps. Due to these limitations in scan time and postprocessing methods used to reduce the impact of motion artifacts, resting state scans typically have a higher signal-to-noise ratio than task-based studies, particularly when scanning high motion subjects: young children and clinical subjects

(Fox & Greicius, 2010). An additional benefit of the resting state fMRI study design is that it sidesteps the need to choose an 'ideal task' that would probe the network of interest, especially for children of different ages and educational backgrounds (Biswal et al., 1995; Kelly et al., 2012). In addition, rsFC studies are more reliably compared across research studies involving different age ranges and backgrounds as language tasks often vary in their method of delivery, content, and level of complexity.

Although fMRI is a useful tool with many advantages over the more invasive neuroimaging and neuroscience methods, we still do not have enough statistical power to draw strong conclusions based on individual subjects (Glover, 2011). Therefore, fMRI results are typically based-on group averages. This limitation is in part caused by the relatively low temporal resolution of the fMRI scan, which is dependent on the relatively slow responding (~ 1 second) hemodynamic response and general individual differences in brain structure and function. Despite these study limitations, group average FC maps still provide researchers with a solid understanding of the most prominent FC relationships.

1.5 Functional Brain Networks involved in Language and Reading

Neuroimaging research has provided scientists with a better understanding of the intricate relationship between language, reading, and the brain's functional and structural connections (Smits, Jiskoot, & Papma, 2014). In the mid-20th century, Geschwind (1965) first speculated that language and reading disorders arise from diminished structural connectivity between the brain's anterior and posterior functional systems after he observed that patients with damage to these white matter tracts had intact language comprehension but impaired and "disconnected" language production. Geschwind's structural connectivity theory was founded on the pioneering work of Pierre Paul Broca, who recognized that his patients with lesions to the left inferior frontal gyrus had trouble with language production, and spoke dysfluently, yet still maintained relatively good oral comprehension (known as Broca's aphasia) (Broca, 1861; Mohr et al., 1978). Around the same time, Karl Wernicke discovered that lesions to Wernicke's area (area within the left posterior superior temporal gyrus and temporal parietal junction) resulted in word finding and language comprehension difficulties. These patients often omitted key words or used words out of context but otherwise spoke using normal grammar, syntax, intonation, stress and rate (Heilman & Scholes, 1976). Since then, scientists have discovered that Wernicke and Broca's areas are involved in a variety of other language and reading cognitive processes (HorowitzKraus, Toro-Serey, & DiFrancesco, 2015; Vigneau et al., 2006; Zhong et al., 2014). More specifically, Broca's area is involved in language-associated executive functions, particularly syntactic language processing (Thothathiri, Kim, Trueswell, & Thompson-Schill, 2012), phonological processing, and semantic processing (Costafreda et al., 2006; Seghier et al., 2004). Whereas Wernicke's area has been associated with phonological processing, motor processing and reading fluency (Costanzo, Menghini, Caltagirone, Oliveri, & Vicari, 2013; Seghier et al., 2004). Although Broca and Wernicke's areas are important for reading (Thothathiri et al., 2012; Zhu et al., 2014), researchers now understand that reading is a complex skill that relies upon the functional integration of these traditional language areas, as well as, additional brain areas within the frontal, temporal, and parietal lobes (Zhu et al., 2014). These language regions work in concert and are organized into cortical-wide brain networks to perform complex linguistic operations, such as reading and writing (Koyama et al., 2010; Wu et al., 2013; Zhu et al., 2014). These FC reading brain regions are often referred to collectively as the functional reading network or the reading network for short.

The reading network integrates the brain areas involved in processing and attending to language, visual, sensorimotor and auditory information (Dehaene et al., 2009). Most of the language regions reside along the dorsal and ventral language pathways. The dorsal language pathway functionally connects the posterior temporal/parietal cortex to the sensorimotor cortex (Saur et al., 2008) via the superior longitudinal fasciculus (SLF), where the left frontal and temporal-parietal language regions (involved in phonological processing) connect via the arcuate fasciculus (AF) (Dick & Tremblay, 2012; Vandermosten et al., 2012; Vigneau et al., 2006). Whereas the ventral language pathway connects the frontal, temporal, and occipital language areas via the uncinate fasciculus (UF), inferior longitudinal fasciculus (ILF), and inferior fronto-occipital fasciculus (IFOF) (Dick & Tremblay, 2012) for semantic (Saur et al., 2008) and orthographic processing (Jobard, Crivello, & Tzourio-Mazoyer, 2003; Vandermosten et al., 2012). However, scientists only found a moderate correlation between the structural and functional connectivity trajectories associated with language development. Many of the observed FC associated with language had no direct structural pathways, which suggests that these regions connect through indirect routes, such as smaller white matter tracts (Honey et al., 2009). According to two fMRI brain activation reading meta-analyses (Bolger et al., 2005; Houde et al., 2010), the primary hubs of the functional reading network include: the inferior frontal gyrus, middle temporal gyrus, precentral gyrus, postcentral gyrus, posterior superior temporal gyrus, fusiform gyrus, inferior occipital gyrus, angular gyrus and supramarginal gyrus. In addition, recent fMRI studies found that the cerebellum plays an active role in reading as well as fine motor control (Argyropoulos, 2015; Stoodley & Schmahmann, 2009). Whereas the left medial supplementary motor area and the thalamus have been found to play a role in reading, but primarily in children (Koyama et al., 2011). In addition, the posterior middle and inferior temporal gyrus have been found to activate in response to language and reading tasks in children, and positively associated with the child's age and reading-associated language skills (Weiss-Croft & Baldeweg, 2015b). Each of these language areas have been associated with more than one cognitive function involved in language processing and/or non-language function, which explains why researchers identified similar brain activation patterns across speeded naming, phonological processing, and orthographic processing tasks. Since phonological processing and speeded naming undergo major developmental milestones in early childhood, exploring the functional relationship between these language regions will help provide researchers with valuable insight into the biological factors predictive of future reading ability in young children.

In resting state fMRI analysis, the FC between the nodes of the language network positive correlate with each other (Bolger, Hornickel, Cone, Burman, & Booth, 2008; Seghier et al., 2004). In contrast, the brain regions known to decrease in activation during reading and language tasks, namely the precuneus and posterior cingulate cortex (PCC) of the default mode network (DMN), negatively functionally correlate with the regions of the language network in resting state fMRI studies (Fox et al., 2005; Raichle et al., 2001). In support of this idea, an independent study found a positive relationship between the coordinated oppositional activity between the posterior hubs of the DMN (precuneus and PCC) and the language network with an improvement in reading comprehension (Smallwood et al., 2013). These posterior regions of the DMN are thought to function in opposition to the language network and provide greater control to increase processing efficiency and support the synchronization of the language and attention networks (Smallwood et al., 2013). Since individuals are not actively attending an external stimulus during resting-state conditions, resting state FC analyses are useful for exploring the relationship between task-positive and task-negative brain areas (in both the left and right hemispheres), as well as additional language-related areas within the sensorimotor (Londei et al., 2010) and prefrontal cortices (Smallwood et al., 2013).

Efficient communication between the regions of the functional language network is needed to support higher order language processes, such as reading comprehension and literature analysis (Dehaene, 2009). Recent studies have identified distinct and specialized neural networks, nested inside the larger, more complex reading network to improve the efficiency of processing specific language information, such as phonological processing and orthographic processing (Blank, Kanwisher, &

Fedorenko, 2014; Weiss-Croft & Baldeweg, 2015b). Throughout childhood and adolescence, the cognitively relevant functional connections within and between the language network strengthen, while the cognitively irrelevant regions disintegrate and separate (Fair et al., 2007). The developmental transition towards building the long-range FC between the regions of the functional language network is associated with more proficient reading, improved reading comprehension, and reasoning within the text (Blank et al., 2014). While the maturity of these reading network(s) is associated with the myelination and integrity of the white matter tracts connecting the language regions (Greicius, Supekar, Menon, & Dougherty, 2009; Lebel & Beaulieu, 2009; Vydrova et al., 2015), as well as, the integration, strength, and efficiency of the FC between regions of the language network (Houde et al., 2010; Turkeltaub et al., 2002; Weiss-Croft & Baldeweg, 2015b). While reading impairments are often the result of a specific or a small number of highly specific cognitive deficits involved in language and/or sensory processing. These reading deficits are associated with poor synchronization and poor integration of one or more neural systems involved in reading, as well as structural abnormalities connecting the language regions (Friederici, 2006; Shaywitz et al., 1998). For these reasons, no single or absolute language or reading measure is sufficient to accurately identify all the potential underlying causes of a reading impairment (Norton, Beach, & Gabrieli, 2015). Therefore, a variety of reading and language measurements should be used to determine if a young child is at risk for developing a reading disability.

1.6 Neural Mechanisms Underlying Speeded Naming and Phonological Processing

As described in detail in section 1.5, reading impairments often arise from specific language-associated cognitive deficit(s), such as phonological awareness, speeded naming, and/or orthographic processing (Raichle et al., 2001; Sonuga-Barke et al., 2015; Wise et al., 2017). Neuroimaging studies have been used to identify the specific neural substrates associated with speeded naming and phonological processing, resided primarily within the frontal and temporal-occipital cortices' (Raschle et al., 2014; Vigneau et al., 2006; Yamada et al., 2011). Within the frontal lobe, the prefrontal cortex is associated with overcoming competition in word selection among semantically-related alternatives (a key ability for the speeded naming task) (Gabrieli, Poldrack, & Desmond, 1998; Ries et al., 2015); while the middle frontal gyrus is important for verbal working memory and manipulating the sounds within words (a key component of the phonological processing task) (Bolger et al., 2008). While a speeded naming study found a negative association between the degree of prefrontal cortex activation and the repetition frequency of the items presented when the trials randomly presented semantic alternatives during the speeded naming task (Ries et al., 2015). These study findings suggest that activation within the prefrontal cortex positively associates with task difficultly. Whereas an independent study found greater activation within the middle frontal gyrus for the rhyming task (a measure of phonological processing) compared to the spelling and semantic language tasks. These findings suggest there is a positive relationship between activation of the middle frontal gyrus and the degree of difficulty of the phonological processing component of the language task (Bolger et al., 2008). In comparison to speeded naming, phonological processing has been found to be more strongly associated with FC patterns between areas along the dorsal language pathway across the planum temporale, including the inferior frontal gyrus, superior temporal gyrus, angular gyrus and supramarginal gyrus (McCandliss & Noble, 2003; Norton et al., 2014; Schlaggar & McCandliss, 2007). However, a recent functional imaging study found that activation within the left angular gyrus increased for both reading and pseudo word reading tasks (a measure of phonological processing), which suggests that the angular gyrus is associated, but not specifically involved in phonological processing. The results showed that pseudo word reading (a measure of phonological processing) ability positively correlated with activation within the left angular gyrus, left inferior frontal gyrus, left superior temporal gyrus and left occipital gyrus (Hampson et al., 2006). In addition, Hampton and colleagues (2006) found that the FC strength between the left angular gyrus and Broca's area positively correlated with pseudo-word reading scores during resting state conditions (Hampson et al., 2006). While speeded naming was found to be more strongly associated with activation within the left posterior fusiform gyrus (alternatively called the visual word form area), which is important region for word recognition (Dehaene & Cohen, 2011), as well as the left ventral inferior frontal gyrus, which is important for combining phonetic and semantic information for efficient language processing (Costafreda et al., 2006).

Although language tasks target a specific language function, each of these language tasks require (at least partial) overlap with other cognitive and language functions (Carota et al., 2017; Londei et al., 2010; Moseley et al., 2013). The greatest degree of overlap in brain activation across the separate language tasks resides within the sensorimotor cortex, inferior frontal gyrus, and the posterior-temporal language areas needed for coordinating language information, as well as semantic and phonological processing (Carota et al., 2017; Londei et al., 2010; Moseley et al., 2013). In addition, many of the regions within the language network have been found to serve more than one cognitive function. For example, in addition to phonological processing, the angular gyrus has been found to play a major role in modulating and integrating the smaller neural language circuits for reading and passage analysis (Hartwigsen, Golombek, & Obleser, 2015; Rosselli et al., 2015). Whereas the post cingulate cortex and the precuneus of the DMN is involved in modulating the FC between supportive and oppositional functional brain networks (Fox et al., 2005; Kjaer TW, 2001; Raichle et al., 2001; Smallwood et al., 2013). These neuromodulation regions ensure that the specific but overlapping language processes operate efficiently.

1.7 Resting-State Functional Connectivity Studies: Associations with age and linguistic ability

Although certain language networks do not reach maturity until early adulthood, early childhood is a still period of profound neural-cognitive development. According to the current literature, the language network develops by first strengthening the local connections before the distant, complex cortical-wide connections get integrated into the functional network (Fair et al., 2007; Xiao et al., 2016). While, the rate of development of the language systems varies according to the cognitive demands necessary for that period of development. For example, the rudimentary sensory and motor networks are robust in children as young two years of age (Fransson, Aden, Blennow, & Lagercrantz, 2011), while the complex, large scale brain networks (including the reading networks) continue to develop throughout childhood and adolescence, sometimes reaching maturity in early adulthood (Zielinski, Gennatas, Zhou, & Seeley, 2010). The developmental transition from local to distant brain areas helps to explain the positive relationship between age, language, and the strength of the long-distant FC in the brain (Weiss-Croft & Baldeweg, 2015a).

Only a small number of fMRI studies have examined the dynamic relationship between language development and the developing brain. An fMRI study examining brain-language relationships in young children 3-to-5 years of age found that activation within the bilateral auditory cortex, left superior temporal lobe, left angular and supramarginal gyrus increased during a passive story listening task. The children's receptive vocabulary scores positively correlated with the increased activation within the left angular gyrus, left supramarginal gyrus, and bilateral thalamus (Sroka et al., 2015). These results suggest that the language network is undergoing major neurological changes that are associated with meeting major milestones in language development. Similarily, an independent longitudinal rsfMRI study found that the strength of the FC patterns between the left posterior superior temporal gyrus/superior temporal sulcus seeds and areas within the left middle frontal gyrus, left dorsomedial prefrontal cortex, bilateral angular gyrus, post cingulate cortex, and superior temporal gyrus/superior temporal sulcus increased in children from age five to age six (Xiao, Friederici, Margulies, & Brauer, 2015). However, when these two age groups were directly compared, the six-year old children demonstrated stronger FC between the left posterior superior temporal gyrus/sulcus seeds and the left angular gyrus and intrafrontal sulcus (Xiao et al., 2015). These studies show that both the intra and interhemispheric FC are developing in childhood, while the rsFC networks become slightly more left lateralized with increasing age and language ability. Altogether these studies demonstrate that early childhood is an important period in the development of the pre-reading language networks and that rsFC is an effective method for studying language development.

1.8 Study Objective:

The objective of my thesis is to explain the relationship between the FC patterns originating from reading-related brain areas, age, and language ability in preschool-aged children. We selected the angular gyrus, inferior frontal gyrus pars triangularis, and the superior temporal gyrus as our regions of interest (ROI) because they are involved in the early developmental stages of the reading network. By examining the relationship between the brain FC patterns, language, and age we can gain insight into how the brain matures and how these FC correlate with language ability. We selected language measures sensitive to reading ability and predictive of future reading abilities to help identify the early neurocorrelates predictive of future reading abilities in young children. In addition, we separated our language measures (phonological processing and speeded naming) into two statistical models to gain a better understanding of the specific language skills contributing to the separate cognitive components involved in reading and determine if our results are comparable to rsFC studies of older children and adults diagnosed with a reading disability.

1.9 Rationale:

Early childhood is an important period for language development, and language impairments left untreated in young children are often associated with future reading problems, poor academic performance, mental health concerns and reduced career prospects in adulthood (Berl et al., 2014; Wilson, Deri Armstrong, Furrie, & Walcot, 2009). Functional connectivity MRI is a powerful method for studying the neural basis of cognitive performance, especially for studies with a strong developmental component (Hampson et al., 2006; Koyama et al., 2011; Xiao et al., 2015). However, only a small number of studies have identified and explored language and reading FC networks using task-independent fMRI techniques, and even fewer studies have applied task-independent techniques on children (Xiao et al., 2015). Although studies have thoroughly investigated the relationship between language ability and disability with brain structure and function in school-aged children (Morken, Helland, Hugdahl, & Specht, 2014; Raschle, Chang, & Gaab, 2011; Sroka et al., 2015), very little research has examined the relationship between the FC patterns in preschool aged children. Recent adult studies suggest that the reading network is comprised of multiple brain circuits involved in language. Future research needs to focus on understanding the brain basis of language in early childhood and determine whether reading-associated language abilities are associated with changes in the brain's underlying FC patterns.

1.10 Research Aims (1 & 2) and Hypotheses

Aim 1: Determine whether there is a relationship between phonological processing, speeded naming, and FC patterns within the language network in 2-5-year-old children.

Aim 1 Hypotheses:

1a. We hypothesized that speeded naming and phonological processing ability would positively correlate with the strength of the FC between reading areas (ANG, STG, and IFGtr) and other brain areas involved in language processing, including the sensorimotor cortex. Also, we expect the Phonological Processing scores to positively correlate with the strength of the FC between our regions of interest (ROI) and other language areas within the posterior temporal-parietal cortex (including, the angular gyrus, supramarginal gyrus, superior temporal gyrus), as well as the middle frontal gyrus. In addition, we expected the Speeded Naming scores to positively correlate with FC between our ROI and the inferior prefrontal cortex and fusiform gyrus (Koyama et al., 2011; Stoodley & Schmahmann, 2009; Tomasi & Volkow, 2012; Weiss-Croft & Baldeweg, 2015b).

1b. We expected to find a negative relationship between language ability and the strength of the FC between our language ROI, additional adjacent language areas, the posterior regions of DMN (including, the precuneus and the PCC), as well as regions involved in more rudimentary language processes (such as primary auditory cortex for processing auditory information).

Aim 2: Determine if there is a relationship between age and the FC patterns of the language network in 2-5-year-old children.

Aim 2 Hypotheses:

2a. We hypothesized that age would positively correlate with the strength of the FC between our ROI and long-distant bilateral language areas within the frontal and temporal-parietal cortices around the temporal parietal junction and the middle and inferior temporal gyrus. In addition, we expect that age will positively correlate with FC between our ROI and frontal executive regions within the left inferior frontal gyrus (particularly the pars opercularis), left middle frontal gyrus, and left prefrontal cortex (Koyama et al., 2010; Koyama et al., 2011).

2b. We expected that age would negatively correlate with the strength of the FC between our ROI and spatially local brain areas associated with more basic language processing in the precuneus and PCC of the DMN, as well as, child specific language areas within the bilateral thalamus, non-language specific areas within the frontal and occipital lobes (Koyama et al., 2010; Koyama et al., 2011).

2 METHODS

2.1 Participants

Sixty-four healthy children between 2 and 6 years of age were recruited from Calgary as part of the larger APrON study, a pregnancy cohort study conducted in Alberta, Canada (Kaplan BJ et al., 2014). Participants with either excess head motion (see head motion assessment and regression), an accidental finding, or children who feel asleep during the scan were excluded from the analysis, resulting in 50 participants between 2 and 6 years of age (3.83 ± 0.61 years), including 21 females and 29 males (5 left-handed and 45 right-handed (90%). Eight participants were excluded for having excessive head motion, 5 participants feel asleep during the fMRI scan, and 1 additional participant was excluded because of an incidental finding. The majority of the subjects were Caucasian, with 1 participant being of Asian descent, and 6 participants being of mixed race. Seven of these participants reported having an immediate family member with a reading disability and two subjects reported secondary family member(s) with a language-based learning disability. All children were born at full term (>37 weeks), without any diagnosed neurocognitive or developmental disorders, spoke English as a primary language, had no contraindications to MRI scanning (i.e., metal implants), and had not yet received any formal reading instruction. To gain a better understand the socioeconomic status of our representative Canadian sample, we obtained information on the number of years of maternal post-secondary education (*M*= 5.5 ± 2.6 years). However, an additional five participants were excluded from the speeded naming portion of the analyses because they were unable to complete the entire subtest (reduced sample: *M* =3.81 ± 0.54 years of age, 21 females and 24 males; 4 left-handed and 41 right-handed (91.1%)). This study was approved by the conjoint health research ethics board at the University of Calgary. Informed consent was obtained from the participant's legal guardian(s), and verbal assent was obtained from the children.

2.2 Data Acquisition: Procedure

To prepare the children for MRI scanning, guardians were provided with information and resources prior to the first meeting. Guardian(s) were encouraged to talk to their child about the MRI scanning procedure using a child-friendly instructional video and story book published from our laboratory explaining the imaging procedure. In addition, we encouraged the guardian(s) to schedule a mock MRI training session for their child so they could practice lying still in a MR simulator prior to their first scan. The three subjects that underwent MR mock scan training, successfully completed the real MR scan.

Language assessments and MR imaging were scheduled within the same visit. Participants unable to successfully complete the language assessment on the same day due to fatigue or other concentration challenges repeated the assessment within two weeks of the initial scan. Language assessments were first administered to the participants by a trained research personal before the child underwent MR imaging while watching a movie of their choice through a projector and listening via noise reduction headphones. Both verbal consent from the child and written consent from the guardian(s) was obtained prior to the MR scan. To ensure the child fully understood and agreed to the MR scan, the MRI scanning procedure was explained to the child using child-sensitive language ("are you ready to get pictures taken of your brain within the noisy rocket ship? Ready to remain still like a statue?”).

2.3 Language Assessments

Participants underwent a Phonological Processing and Speeded Naming subtest from the standardized Developmental Neuropsychological Assessment (NEPSY-II) developed for children 3-16 years of age (Korkman et al., 2007). The standardized scoring methods are based on an investigative study conducted using over 1000 American children, aged 3-16 years and the specific language assessments were selected because of their association with reading ability (Korkman M, 2007). All participants successfully completed the Phonological Processing subtest, while only a subset of subjects completed the Speeded Naming subtest (N=45). The Phonological Processing subtest assesses phonemic awareness and short-term phonemic memory, whereas the Speeded Naming subtest measures the efficiency of lexical access and oral production of serially presented strings of well-recognized items (such as letters, colours or shapes). For the Phonological Processing subtest, the assessor reads four rhyming words aloud, then asks the child to point to the image associated with the cued phoneme. For example, if the child was presented with a picture of a dog, duck, and a door, then cued with the phoneme ‘uck’, the child would be correct to select the picture of the duck. This activity is strongly associated with reading, especially word decoding (Martinez Perez, Majerus, Mahot, & Poncelet, 2012; Martinez Perez, Majerus, & Poncelet, 2012). Whereas the Speeded Naming subtest measure is more strongly associated with reading fluency (Logan et al., 2011; Verhoeven, van Leeuwe, Irausquin, & Segers, 2016). Since the relationship between speeded naming and reading is strongest when the items presented are familiar and regularly used, the Speeded Naming subtest of the NEPSYII uses non-alphanumeric items (shapes and colors) (Frijters et al., 2011; Meyer et al., 1998; Sarborough et al., 1998). The speeded naming task was timed with a stopwatch and the scores for time and accuracy scores were combined and averaged across the two trials to create one composite Speeded Naming scaled score. These language assessments took approximately 10 minutes to complete.

To include participants under three years of age, we adapted the scaling of the language scores by extracting the effects of age from the raw language scores and applying linear regression to control for age. The standardized residual values were used in our analyses. As the Speeded Naming score is based on two latent variables (time to complete the task and the number of correct responses), we first applied factor analysis to quantify and combine these two averaged variables from the two trails (color and shape naming). Since the Speeded Naming variables were non-orthogonal, and strongly correlated $r= -.621$, $p<0.01$, we separated factors using the oblique rotation factor analysis method. From the factor analysis, we extracted two variables that accounted for 100% of the variance. Since factor 1 extracted most of the shared variance (specifically, 81.04% of the shared variance) between the two latent variables, we used these values to represent our composite Speeded Naming scores in our final analyses.

2.4 Behavioral Analysis

Pearson's bivariate correlations were computed to determine the relationship between age, sex, motion and language using SPSS (Chicago, IL). Independent samples t-tests were used to test for differences in age, average head motion, and language scores between males and females. We determined significance with a two-tailed probability value (p-value or p) of $p< 0.05$.

2.5 Functional Connectivity

2.5.1 Data Acquisition

MRI scanning was performed on a GE 3T MR750w (General Electric, Waukesha, WI) system using a 32-channel head coil at the Alberta Children's Hospital. Children were scanned awake watching a movie of their choice. Passive viewing functional MRI data were acquired with a gradient-echo echo-planar imaging (EPI) sequence (240 volumes, TR = 2000 ms, TE = 30 ms, flip angle = 60^{o}, 36 3.6 mm slices, voxel size = 3.6 x 3.6 mm isotropic; duration = ~8.10 minutes). Anatomical scans were acquired using a high-resolution T1-weighted 3D FSPGR BRAVO gradient echo sequence (4:12 minutes; TR = 8.228 ms; TE = 3.76 ms; TI = 540 ms; flip angle = 12^{o}; 210 slices; voxel size: 0.9 x 0.9 x 0.9 mm^{3}).

2.5.2 Data Preprocessing

Data preprocessing followed the pipeline described by Power and colleagues (2014) using functions from AFNI (Cox, 1996), FSL (Smith et al., 2004), and in lab developed functions from MATLAB. The pipeline consisted of skull stripping, interleaved slice-time correction, spatial smoothing (6 mm FWHM Gaussian kernel), motion correction, band-pass filtering (0.009 -0.08 Hz), image registration and normalization to the standard asymmetrical high-resolution 2mm^{3} pediatric template, optimized for children aged 33- 44 months (developed by the McGill McConnell Brain Imaging Center) (Fonov, 2009).

First, we skull stripped each subject's high-resolution T1 anatomical images, as well as the pediatric template by removing the non-brain tissue (skull, meninges, and fluid filled spaces between the skull and brain), from each subject's high-resolution T1 anatomical images using the FSL brain extraction tool (BET). After completing BET, any remaining non-brain tissue was manually removed in FSLview. The participant raw images were checked to ensure that registration was done correctly and brain masks (gray matter, white matter, cerebral spinal fluid, and whole-brain masks) did not reside outside the image field of view (FOV). Second, we applied interleaved slice-time correction, MCFLIRT linear motion estimation, and grand mean scaling of 1000 calculation for each participant's functional image to reduce the effects of noise and motion artifacts in the functional data. MCFLIRT uses trilinear interpolation methods to determine the identify transformation of all the functional volumes in the time-course (140 volumes in our study) to estimate motion in six directions (three translational (x, y, z) and three rotational (pitch, roll, and yaw); MCFLIRT accomplishes this by comparing the BOLD signal of each volume to the time lengths middle volume across each voxel in the FOV. Next, we calculated the framewise displacement (FD) from each subject's functional images using the FSL command, FSL Motion Outliers using a threshold of 0.3 mm. This function produces a matrix of zeros and ones, with each non-zero value representing an image volume with a FD or average rotational and translational parameter difference greater than the 0.3 mm set threshold between the volume and the reference volume.

Image registration and normalization involved anatomically warping each participant's low-resolution functional MR images to their own high-resolution T1-weighted image, then warping the resultant image to the standard asymmetrical high-resolution 2mm^3 pediatric template, optimized for children aged 33- 44 months (developed by the McGill McConnell Brain Imaging Center) (Fonov, 2009). These registration steps were taken to obtain a more anatomically accurate registration before warping each participant's data to the standardized pediatric template. We used linear regression to remove the pre-calculated head motion based on six rigid body realignment motion parameters (x, y, z, pitch, raw, roll) from MCFLIRT, as well as, other nuisance signals (including, average 4D signal by grand mean scaling, the global signal and signal within the white matter and CSF) (Jenkinson et al., 2012). Any remaining motion artifacts were detected by calculating the root-mean squared difference in the brain-wide BOLD signal intensity (DVARS) from one functional volume to the next. Next, we applied a band-pass filter of 0.009-0.08 Hz to filter out noise above or below the threshold range and focus on the low-frequency fluctuations (<0.1 Hz) involved in spontaneous FC. The final residual data underwent spatial smoothing using a Gaussian filter with 6 mm FWHM to increase the results signal-to-noise ratio.

Image quality was improved by regressing out head motion based on six rigid body realignment motion parameters (x, y, z, pitch, raw, roll) from FSL's MCFLIRT linear motion estimation tool, as well as signal from white matter, cerebral spinal fluid, and the global signal (Jenkinson et al., 2012). High motion corrupted volumes were identified by FSL MotionOutliers (Mean number of corrupted volumes=42.0 ± 28.15 SD; range 0-94 volumes or between 8 and 4 minutes, 52 seconds of usable data) then censored for volumes exceeding a frame-wise displacement 0.3 and 0.3% change in BOLD signal intensity (DVARS) (Jenkinson et al., 2012; Power et al., 2012; Power et al., 2014). Finally, functional image data with less than 4.5 minutes (>135 censored volumes) of usable uncensored data was excluded from analysis. Altogether, these motion corrections and noise reduction steps increased the signal-to-noise ratio of the functional imaging data.

2.5.3 Regions of Interest

To investigate how age and language skills reflect in the FC of the reading network, we selected three 6-mm radius regions of interests (ROI) that have been shown to activate during reading tasks (refer Appendix A for MNI and pediatric template coordinates) (Bolger et al., 2005; Houde et al., 2010; Rosselli et al., 2015; Stoodley & Schmahmann, 2009). We decided to focus our study to three main areas, including the posterior superior temporal gyrus (part of Wernicke's area), the inferior frontal gyrus, pars triangularis (IFGtr; central area of the inferior frontal gyrus, part of Broca's area), as well as the angular gyrus (ANG) because of its strong integrative role in linguistic (Callan, Callan, & Masaki, 2005) and semantic processing (A. R. Price, Bonner, Peelle, & Grossman, 2015). In addition, the angular gyrus has been found to correlate with reading performance and reading comprehension in both brain activation (Pugh KR1, 2000) and resting state studies (Hampson et al., 2006; Koyama et al., 2010). The extensive research evidence supporting the ANG's role in processing and regulating language information makes this region ideal for cross-study comparison (Rosselli et al., 2015). While, we selected the inferior frontal gyrus (IFG) and superior temporal gyrus (STG) to build upon the work of Koyama and colleagues (2011) by choosing the same coordinates for these specific regions (Koyama et al., 2011) (refer to Appendix A for coordinates). Koyama and colleagues (2011) selected these areas (as well as, nine additional reading regions) based on their spatial locations identified from child linguistic task (Houde et al., 2010) and adult word reading meta-analysis (Bolger et al., 2005). These regions were categorized into three groups: child-only, adult-only, or both (child and adult), depending on the distance between the average peak coordinates recorded in the child and adult meta-analyses. The average peak activation coordinates for the posterior STG were categorized as both (less than 15 mm apart in MNI adult brain template space), while the more spatially distant regions (greater than 15 mm apart) were categorized as either child or adult specific regions. We selected our ROI coordinates from the pars triangularis region within the IFG because only this area within the IFG was identified in the child meta-analysis (Houde et al., 2010). While the left ANG ROI coordinates were selected from the Harvard Oxford Cortical Structural Atlas (Rosselli et al., 2015; Stoodley & Schmahmann, 2009) within Brodmann area 39, to align with a previous resting state adult study (Hampson et al., 2006).

To better understand how the right hemisphere is involved in language development, we added ROI to the right hemisphere by flipping the left ROI coordinates (described above) into the right hemisphere in the non-symmetrical pediatric template space using the FSLview, then manually adjusted the ROI coordinates to anatomically match the left ROI onto the pediatric template (Fonov, 2009) in FSL view (Jenkinson et al., 2012). ROI were created in pediatric template space by expanding the preselected coordinates spherically outwards creating a 6-mm radius (refer to Appendix A for coordinates in MNI and pediatric template space).

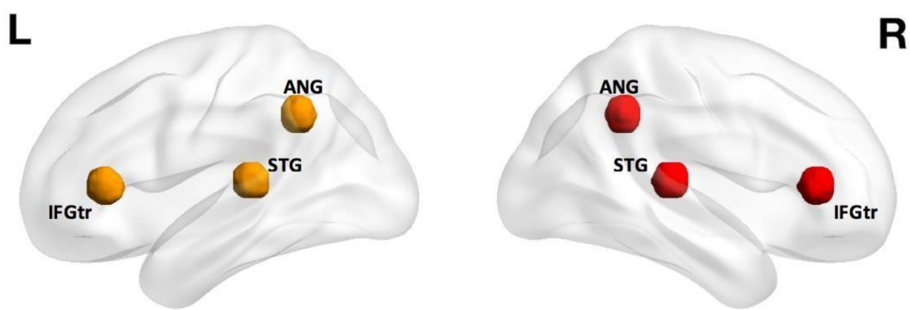

Figure 1. Schematic Brain Including Regions of Interest. Schematic demonstrates the placement of the left (yellow) and corresponding right (red) seed regions within the angular gyrus (ANG), superior temporal gyrus (STG), and inferior frontal gyrus, pars triangularis (IFGtr) for children (Houde et al., 2010) and adults (Bolger et al., 2005). The regions of interest were normalized to the 1mm T1-weighted MNI adult template for accurate placement on the adult BrainMesh ICBM152 smoothed surface template (Jenkinson et al., 2012; Xia, Wang, & He, 2013).

2.5.4 Functional MRI Analyses

To prepare for whole-brain seed-based FC analysis, the average time course for each ROI was extracted and correlated with every other voxel in the brain of each participant's 4D residual volume (excluding signal from the cerebral spinal fluid, white matter, and global mask signal). The resultant whole-brain FC correlation maps were then normalized to represent the Gaussian distributed values using Fisher's r-to-z transform ($z = .5[\ln(1+r) - \ln(1-r)]$) for cross-subject correlational analysis. Group-level statistical analysis was performed using the mixed-effects least-squares model implemented in FSL's Higher-level FEAT program (Smith et al., 2004).

First, we created a group average FC map from a model that included the group intercept, as well as age, sex, and the number of censored corrupted high motion volumes as a covariate of no-interest. Voxel-wise thresholding was set at z-score >2.3 and $p<0.01$ for the Gaussian cluster-wise correction. Second, we examined the relationships between the reading network and language ability by correlating the language subtest scores (Speeded Naming and Phonological Processing) with the group average seed-based FC maps, controlling for age, sex, and head motion (Aim 1). To control for statistical interactions between Speeded Naming and Phonological Processing (ContiRamsden & Durkin, 2012; Savage, Pillay, & Melidona, 2008), we input the language subtest scores into separate statistical models. Third, we correlated age with each of the seed-based average FC maps to examine the relationship between age and FC of the language network in in 2-5-year-old children, while controlling for sex and the z-scored number of corrupted high motion volumes (Aim 2). All Group level FC results were thresholded at Z-score > 2.3 using a Gaussian voxel-wise correction method and Holm's Bonferroni multiple comparison correction method was completed to maintain a family-wise error rate of 0.01 for the three comparisons (the number of seeds regions placed within each hemisphere; $p<0.0033$).

Finally, to ensure sex was appropriately incorporated into our statistical models, we ran the analysis a second time, excluding sex as a covariate and found comparable results (Arnett et al., 2017;

Burman, Bitan, & Booth, 2008; Largo, Molinari, Comenale Pinto, Weber, & Duc, 1986; Shaywitz et al., 2005). Comparing the results between the two models (sex added as a covariate (sex-included) vs. sex excluded as a covariate (sex-excluded)), the significant ($p<0.001$) clusters overlapped. However, the significant clusters ($p<0.001$) from the sex-excluded model were found to be larger than the sex-included model, extending into other language and non-language brain regions. To determine if the sex-excluded model derived significant clusters because of unwanted statistical variance, we followed-up our study with a group contrast. We compared FC maps between boys and girls, controlling for age, motion, and language scores (using separate models for Phonological Processing and Speeded Naming) and found significant differences between males and females ($p<0.01$, corrected for multiple comparisons). Therefore, we concluded that sex is an appropriate covariate in our statistical models. However, decided to exclude IQ as a covariate from our statistical models because previous neuroimaging studies found that including Full IQ scores led to overcorrected, anomalous and counterintuitive results (Dennis et al., 2009). The authors describe Full IQ to be a poor measure of intelligence for individuals with neurodevelopmental disabilities because the test was designed for neurotypical individuals who do not have a specific language or attention deficit that might undermine their ability to perform. For this reason, neurodevelopmental studies investigating brain-behavior relationships are particularity vulnerable to being overcorrected by adding unnecessary covariates that could bias the results (Dennis et al., 2009). Although the current study is examining typically developing children, our subjects are prereaders and have not been formally assessed for neurodevelopmental disabilities, therefore excluding IQ from our statistical models will keep our methods more consistent with other neurodevelopmental studies.

3 RESULTS

3.1 Correlations between age, head motion, and language ability

Age was found to be strongly positively correlated with Phonological Processing scores (raw scores: r= .646, p<0.01; scaled scores: r=.335, p=0.018) and Speeded Naming scores (raw scores: r=.691, p<0.01; scaled scores: r=.440, p=0.003). While head motion was not found to be significantly correlated with age (r= -.192, p = .181) or vary between males and females (F_{48} =1.79, p=.081).

3.2 Language assessments

Language scores were in the below average (6-10th percentiles) to average (>75th percentile) range for both the Speeded Naming (M= 11.82 ± 3.27, *range* = 5-19) and Phonological Processing (M= 11.28 ± 2.63, *range* = 6-16) measures. Our mean scores are slightly above the expected population mean of 10 ± 3 (Korkman M, 2007). The two language assessment scores were found to be weakly positively correlated r= 0.24, p= 0.02 (weak correlation is a coefficient r with an absolute value between .20 and .39). We found no significant difference between the male and female participants scaled language scores (Phonological Processing scores t_{48}= .176, p= .86; Speeded Naming scores t_{43}= -1.35, p= 0.18).

3.3 Functional Connectivity Patterns within the Language Network

Group average FC maps of the left and right ANG, STG, and IFGtr seeds are shown in Figure 2 (refer to Figure 1 for schematic diagram of ROI placement). Consistent with adult and child imaging studies, we observed positive FC between the ROI and adjacent and contralateral brain areas, as well as more distant brain areas in other brain lobes (refer to Figure 1). Where we found widespread negative FC across the occipital and frontal-parietal cortices. More specifically, we found that the ANG ROI demonstrated positive FC across the frontal lobes and the middle/inferior temporal gyrus, while negative correlations were found across the occipital, inferior medial-frontal and sensorimotor cortices. The STG ROI demonstrated positive FC across the superior temporal gyrus, extending towards the edge of the middle temporal gyrus, as well as, the medial parietal lobe and the precentral and postcentral gyrus, while negatively correlated with the bilateral frontal pole, precuneus and the occipital cortex. Finally, we found the IFGtr ROI to be positively FC between areas across the temporal-parietal and middle/inferior temporal gyrus but negatively FC with regions across the inferior temporal, superior central parietal, and the lateral/middle occipital cortex.

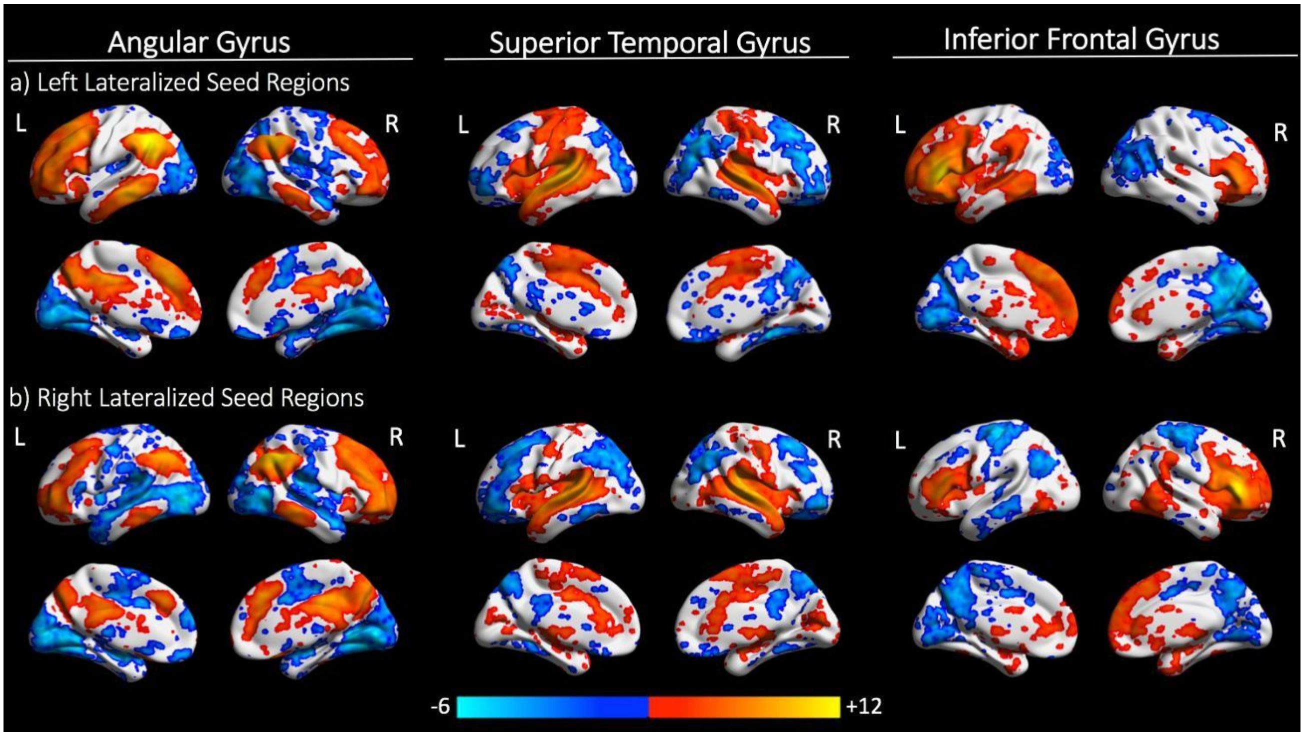

Figure 2. Group average FC maps of the a) *left* and b) *right* ANG, STG and IFGtr seeds, after controlling for age, sex, and motion. The scale bar represents the group average z-scores derived from the FC maps (p<0.01, multiple comparison corrected). The results were normalized to the 1mm T1-weighted MNI adult template prior to mapping the results onto the adult BrainMesh ICBM152 smoothed surface template (Jenkinson et al., 2012; Xia et al., 2013).

3.3.1 Relationship between Phonological Processing and the Language Network

Phonological Processing scores positively correlated with the FC originating from both the left and right ANG ROI. More specifically, scores on the Phonological Processing subtest positively correlated with the FC between the *left* ANG ROI and the right sensorimotor cortex, particularly the middle precentral gyrus and postcentral gyrus, extending outwards the right anterior region of the supramarginal gyrus. In addition, Phonological Processing subtest scores were positively correlated with the negative FC between the *left* ANG ROI and the right lateral occipital cortex, nestled between dorsal and ventral regions of the lateral occipital cortex, overlapping the posterior edge of the temporo-occipital area of the middle temporal gyrus (Figure 3a). While we found the FC between the *right* ANG ROI and the right supramarginal gyrus to be positively correlated with Phonological Processing ability (Figure 3b).

Sign of Association	Seed	Hemisphere	Connectivity	Voxels	p-Value	Z-Max	x	y	z
Positive									
	L ANG	R	Lateral Occipital Cortex, anterior part Lateral Occipital Cortex, posterior part Middle Temporal Gyrus, temporo-occipital part	728	0.0452	4.4	44	-68	12
	L ANG	R	Precentral Gyrus, Postcentral Gyrus Supramarginal Gyrus, anterior division	1643	8.03E-05*	3.91	50	-20	51
	R ANG	R	Supramarginal Gyrus, anterior division	1005	0.00304*	3.98	41	-40	16

Table 1. Functional connectivity is associated with phonological processing. Regions of interest (STG= superior temporal gyrus, posterior division; ANG= angular gyrus; IFGtr= inferior frontal gyrus, pars triangularis) were selected from word reading and linguistic task brain activation meta-analyses for children (Houde et al., 2010) and adults (Bolger et al., 2005). The average time course of each seed (6mm radius) was extracted and correlated with each voxel in the brain. Linear regression was used to find the association between the FC patterns and Phonological Processing scores. The order of the presented functionally connected regions was arranged from largest to smallest (top to bottom) percent overlap with the brain regions underlying the significant clusters. Coordinates are in MNI space. All results are significant at the 0.05 alpha value; *Significant p<0.05, family-wise after applying Bonferroni multiple comparison correction (p-Value <0.0033) for the three seed regions.

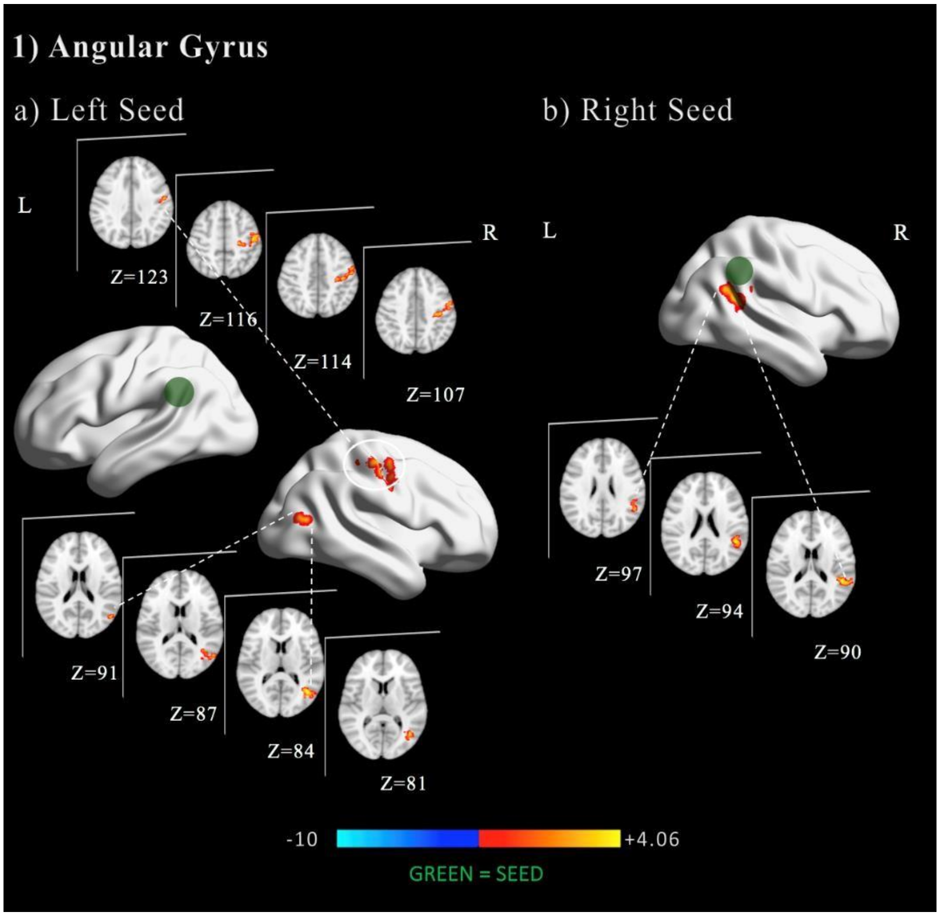

Figure 3. Phonological Processing scores correlated with the ANG seed-derived FC maps after controlling for age, sex, and head motion. Phonological Processing scores *positively* correlated (yellow-red clusters) with the strength of the FC between the a) *left* ANG and the right pre/postcentral gyrus, right supramarginal gyrus, right lateral occipital cortex and right middle temporal gyrus, as well as, between the b) *right* ANG and right supramarginal gyrus. The scale bar demonstrates the group average z-scores representing the relationship between the Phonological Processing scores and the strength of the FC between correlated areas ($p<0.05$). Significant clusters were normalized to the 1mm T1-weighted MNI adult template for accurate placement on the adult BrainMesh ICBM152 smoothed surface brain model (Jenkinson et al., 2012; Xia et al., 2013).

3.3.2 Relationship between Speeded Naming and the Language Network

Speeded naming scores positively correlated with FC between the IFGtr seed regions and areas activated during sight reading, word articulation, and linguistic processing (refer to Table 2. for connectivity details). More specifically, speeded naming ability was positively correlated with the strength of the FC between the *left* IFGtr and the posterior left middle/inferior temporal gyrus, left fusiform gyrus (Figure 4a) (connection often involved in sight reading) (Dehaene & Cohen, 2011), left frontal operculum, left insular cortex, right supramarginal gyrus, right parietal operculum and the right angular gyrus (Figure 4a). Secondly, Speeded Naming scores positively correlated with the strength of the FC between the *right* IFGtr and the left precentral gyrus, extending from the precentral gyrus to the posterior region of the middle frontal gyrus, as well as, and the bilateral medial dorsal and left ventral posterior regions of the thalamus (Figure 4b). Thirdly, speeded naming ability positively correlated with the strength of the FC between the *right* STG and the left supramarginal gyrus and left angular gyrus for complex language processing, while negatively correlated with the negative FC correlation between the *right* STG and the left precuneus and left occipital cortex (Figure 5a). Lastly, Speeded Naming scores were negatively correlated with the strength of the negative FC correlation between the *right* ANG and the right superior occipital pole for visual processing (Figure 5b).

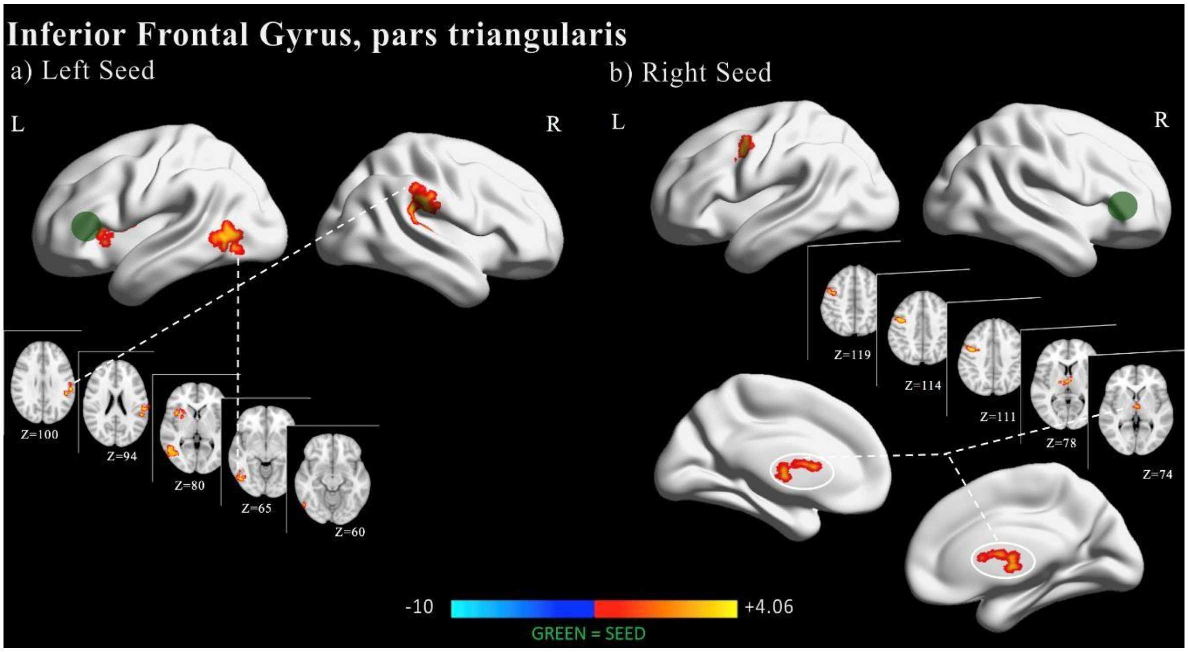

Figure 4. Speeded naming scores positively correlated with the FC between the a) *left* IFGtr seed-region and the left posterior middle/inferior temporal lobe and the right temporal-parietal junction, as well as between the b) *right* ANG seed and the bilateral thalamus and contralateral sensory-motor cortices (yellow-red clusters). The scale bar represents the group average z-scores derived from the relationship between the Speeded Naming scores and the strength of the FC between correlated areas ($p<0.05$, family-wise Bonferroni multiple comparison corrected for the three seed regions). The results were normalized to the 1mm T1-weighted MNI adult template for accurate placement on the adult BrainMesh ICBM152 smoothed surface model template (Jenkinson et al., 2012; Xia et al., 2013).

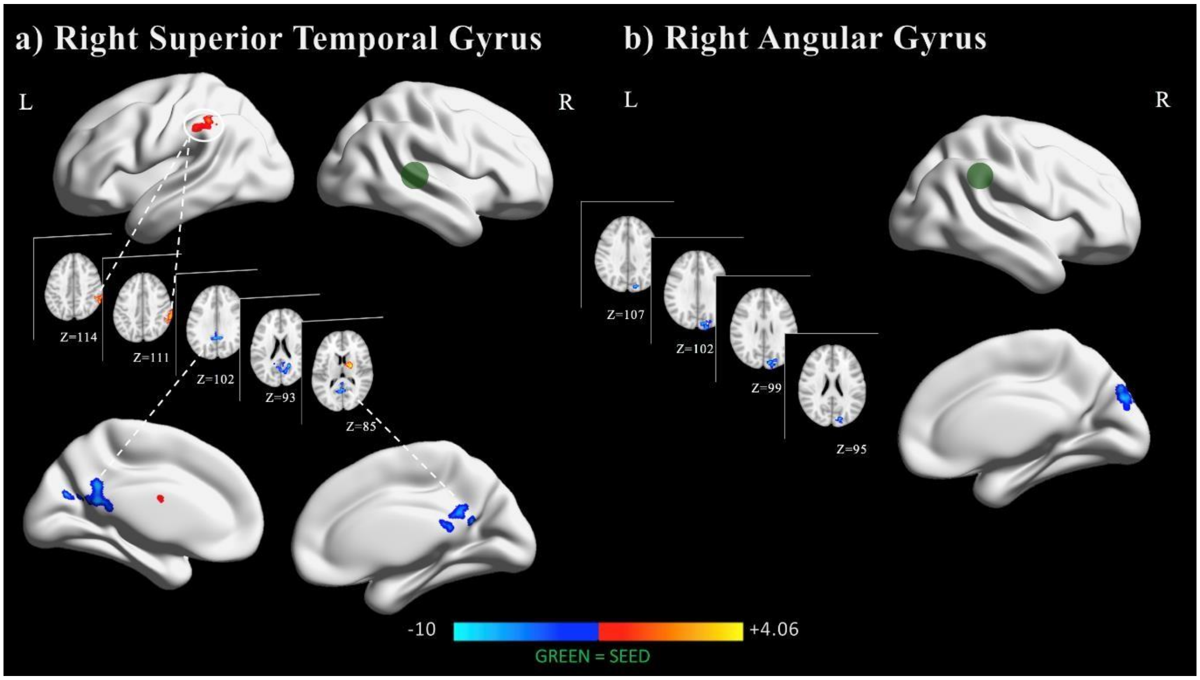

Figure 5. Speeded Naming scores positively correlated with FC between the a) *right* STG seed and the left angular gyrus (yellow-red clusters) and negatively correlated with the bilateral precuneus extending out to the medial visual cortex (blue clusters), as well as between the b) *right* ANG seed and the ipsilateral visual cortex (blue clusters). The scale bar represents the group average z-scores derived from the relationship between the Speeded Naming scores and the strength of the FC between correlated areas ($p<0.05$, family-wise Bonferroni multiple comparison corrected for the three seed regions). The results were normalized to the 1mm T1-weighted MNI adult template for accurate placement on the adult BrainMesh ICBM152 smoothed surface model template (Jenkinson et al., 2012; Xia et al., 2013).

Sign of Association	Seed	Hemisphere	Connectivity	Voxels	p-Value	Z-Max	x	y	z
Positive									
	L IFGtr	L	Middle Temporal Gyrus, temporo-occipital Inferior Temporal Gyrus, temporo-occipital Fusiform Gyrus, temporo-occipital	1805	2.41E-05*	3.66	-51	-53	0
	L IFGtr	R	Supramarginal Gyrus, Parietal Operculum Planum Temporale, Angular Gyrus	1520	0.000142*	4.37	61	-31	27
	L IFGtr	L	Frontal Operculum Cortex Insular Cortex	1075	0.0029	4.06	-27	19	8
	R IFGtr	L	Precentral Gyrus	994	0.000925*	4.12	-41	1	48
	R IFGtr	L/R	Left Medial Dorsal Thalamus Left Ventral Posterior Medial/Lateral Thalamus Right Medial Dorsal Thalamus	802	0.00522	3.93	-4	-11	7
Negative	R STG	L	Supramarginal Gyrus Angular Gyrus	697	0.0194	3.94	-67	-41	40
	R ANG	R	Superior Occipital Pole	707	0.0103	4.44	17	-88	25
	R STG	L	Precuneus Cortex Cuneal Cortex Supracalcarine Cortex	1963	1.01E-06*	4.25	-20	-58	22

Table 2. Functional connectivity is associated with speeded naming ability. Regions of interest (STG= superior temporal gyrus, posterior division; ANG= angular gyrus; IFGtr= inferior frontal gyrus, pars triangularis) were selected from word reading and linguistic task brain activation meta-analyses for children (Houde et al., 2010) and adults (Bolger et al., 2005). The average time course of each seed (6mm radius) was extracted and correlated with each voxel in the brain. Linear regression was used on the connectivity maps to find the association between the brain's FC patterns and the Speeded Naming scores. The order of the presented functionally connected regions was arranged from largest to smallest (top to bottom) percent overlap with the brain regions underlying the significant cluster. Coordinates are in MNI space. All results are significant at the 0.05 alpha value; *Significant at the 0.01 alpha value after applying Bonferroni multiple comparison correction (p-Value <0.0033) for the three seed regions.

3.4 Functional Connectivity Correlates with Age

Age positively correlated with FC between several cross-cortical brain areas involved in linguistic processing. More specifically, age positively correlated with FC between the *left* ANG and the right inferior fronto-parietal cortex (including Broca's areas), as well as the right superior lateral occipital cortex, while negatively correlated with the right inferior occipital pole (for processing visual information) and the left central middle temporal gyrus (which is important for executive language functioning) (Figure 6.1a). Whereas the right ANG FC maps demonstrated a positive relationship between age and the strength of the FC between the *right* ANG and the left pre/postcentral gyrus but negatively correlated with Crus I of the right cerebellum (Figure 6.1b). In addition, we found that age positively correlated with the FC patterns between the STG (both left and right seeds) and the contralateral temporal-parietal language areas (Figure 6.2a and 6.2b). More specifically, age positively correlated with the FC between the *left* STG and the right angular gyrus and the right supramarginal gyrus, as well as the right posterior inferior temporal gyrus, extending out towards the temporo-occipital fusiform gyrus. While FC patterns of the *right* STG average FC maps were found to positively correlate with the FC strength between the *right* STG and the left pre/postcentral gyrus. Finally, we found a positive relationship between age and the FC strength between the *left* IFGtr and the right middle frontal gyrus, and a negative relationship between the *left* IFGtr and the occipital pole (right superior occipital and the left lateral occipital pole) (Figure 7).

2013).

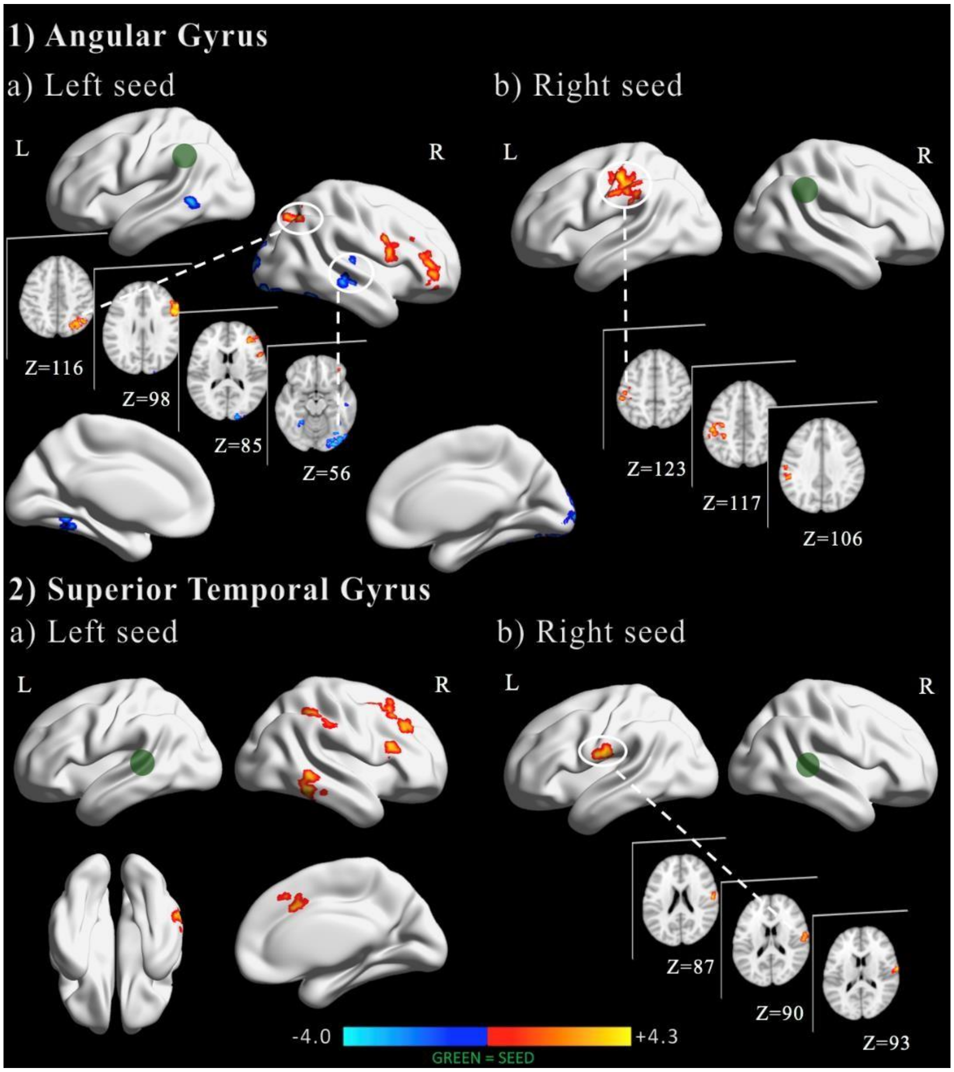

Figure 6. Age correlated with the FC originating from the ANG and STG seed-regions after correcting for sex and head motion. Age positively correlated with FC patterns between the 1a) *left* ANG seed and contralateral inferior frontal-parietal and occipital language processing regions (yellow-red clusters) and negatively correlated with the inferior visual cortex (blue clusters), as well as, between the 1b) *right* ANG seed and the left sensorimotor cortex. Age positively correlated with FC patterns between the 2a) *left* STG seed and contralateral posterior temporal and sensorimotor association language areas, as well as, between the 2b) *right* STG seed and the inferior left sensorimotor cortex. The scale bar represents the group average z-scores derived from the relationship between the Speeded Naming scores and the strength of the FC patterns with the ROI ($p<0.05$, family-wise Bonferroni multiple comparison corrected for the three seed regions). The results were normalized to the 1mm T1-weighted MNI adult template for accurate placement on the adult BrainMesh ICBM152 smoothed surface model template (Jenkinson et al., 2012; Xia et al., 2013).

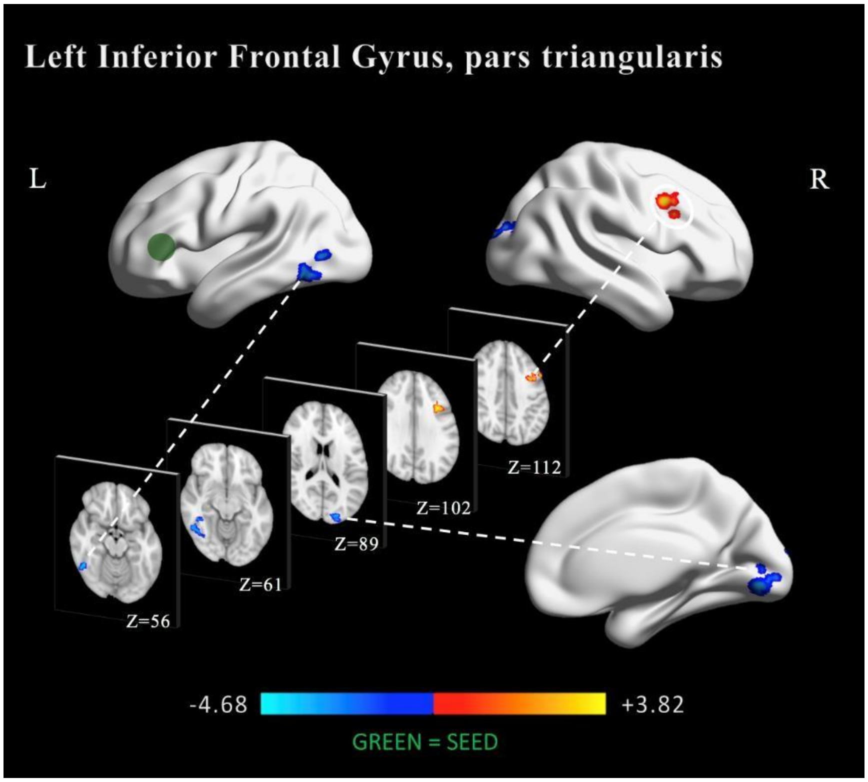

Figure 7. Age correlated with FC between the IFGtr ROI and areas within the right frontal-motor and posterior inferior temporal-occipital cortices after correcting for sex and head motion. Age positively correlated with FC patterns between the *left* IFGtr seed and the right middle frontal gyrus (yellow-red clusters) and negatively correlates with the visual cortex (blue clusters). The scale bar represents the group average z-scores derived from the relationship between the Speeded Naming scores and the strength of the FC patterns with the ROI ($p<0.05$, family-wise Bonferroni multiple comparison corrected for the three seed regions). The results were normalized to the 1mm T1-weighted MNI adult template for accurate placement on the adult BrainMesh ICBM152 smoothed surface model template (Jenkinson et al., 2012; Xia et al., 2013).

Sign of Association	Seed	Hemisphere	Connectivity	Voxels	p-Value	Z-Max	x	y	z
Positive									
	L ANG	R	Inferior Frontal Gyrus, Pars Opercularis Precentral Gyrus	1518	7.71E-05*	4.34	61	19	26
	L ANG	R	Frontal Pole Inferior Frontal Gyrus, pars triangularis	1514	7.93E-05*	3.92	48	45	4
	L ANG	R	Superior Lateral Occipital Cortex	1168	0.000897*	4.03	35	-72	57
	L ANG	L	Cerebellum Crus VIIb & II	890	0.00753*	3.83	-34	-71	-53
	R ANG	L	Postcentral Gyrus Precentral Gyrus	1510	0.000169*	4.33	-51	-22	48
	L IFGtr	R	Middle Frontal Gyrus	863	0.0155	3.91	35	16	31
	L STG	R	Middle Frontal Gyrus	1514	3.06E-05*	3.63	41	1	60
	L STG	R	Inferior Temporal Gyrus, temporooccipital Fusiform Gyrus	1125	0.000575*	4.19	62	-45	-16
	L STG	R	Angular Gyrus Supramarginal Gyrus	963	0.00215*	4.13	59	-48	52
	R STG	L	Postcentral Gyrus Precentral Gyrus	609	0.0372	4.24	-70	-10	14
Negative									
	L ANG	L	Middle Temporal Gyrus, posterior division Inferior Temporal Gyrus, temporo-occipital region	1060	0.00201*	4.09	-34	-55	-4
	L ANG	R	Occipital Pole	1029	0.00254*	3.98	18	-100	20
	L ANG	R	Inferior Occipital Pole	710	0.0333	4.1	31	-93	-17
	R ANG	R	Cerebellum Crus I	746	0.0373	3.83	34	-71	-23
	L IFGtr	R	Fusiform Gyrus, occipital part Medial Occipital Pole	1519	0.000167*	4.97	22	-84	0

Table 3. Functional connectivity is associated with age. Regions of interest (STG= superior temporal gyrus; ANG= angular gyrus; IFGtr= inferior frontal gyrus, pars triangularis) were selected from word reading and linguistic task brain activation meta-analyses for children (Houde et al., 2010) and adults (Bolger et al., 2005). The average time course of each seed (6mm radius) was extracted and correlated with each voxel in the brain. Linear regression was used on the connectivity maps to find the association between seed-based FC patterns and age. The order of the presented functionally connected regions was arranged from largest to smallest (top to bottom) percent overlap with the brain regions underlying the significant cluster. Coordinates are in MNI space. All results are significant at the 0.05 alpha value; *Significant at the 0.01 alpha value after applying Bonferroni multiple comparison correction (p-Value <0.0033) for the three seed regions.

4 DISCUSSION

4. 1 Functional Connectivity Correlates with Age and Language Ability in Preschoolers

Reading is a complex task requiring a multitude of cognitive functions derived from FC networks associated with language, executive functions and sensorimotor skills. Early childhood is a period of rapid brain development where children acquire the fundamental language skills required for reading. The purpose of this study was to gain a more solid understanding of how specific reading-related language skills relate to brain function in young children. To accomplish this, we examined the relationship between age, language ability, and the FC patterns of the brain's intrinsic reading networks. We selected speeded naming and phonological processing because these language skills are associated with reading ability and are commonly used among a battery of cognitive assessments to make a formal diagnosis of dyslexia (Jap, Borleffs, & Maassen, 2017; Korkman, Kirk, & Kemp, 2007). To our knowledge, we are the first to examine the relationship between the brain's intrinsic FC and reading diagnostic measures (phonological processing and speeded naming) in preschool aged children.

As hypothesized, we found that age positively correlated with the strength of the long-distant FC patterns between brain areas associated with reading in older-children and adults. This includes regions along the dorsal language pathway (involved in mapping sound information onto the motor network for verbal articulation), as well as regions found along the ventral language pathway (involved in corresponding language sounds to their specific meaning) in both verbal and written language (Saur et al., 2008; Hickok & Poeppel, 2004; Scott et al., 2000). After we controlled for age, language ability positively correlated with the FC patterns between brain areas associated with the language measure of interest (either speeded naming or phonological processing). These findings suggest that the strength of the FC patterns between the language regions are associated with language ability but strengthen with increasing age. Our findings are congruent with models of neurodevelopment that suggest that the language network becomes increasingly robust across childhood as the long-distant language regions become further integrated into the language network (Dosenbach et al., 2010; Fair et al., 2009; Fair et al., 2007; Menon, 2013; Power et al., 2010).

4.2 Functional Connectivity Patterns Associated with Age

As hypothesized and briefly introduced, we found that age positively correlated with the strength of the FC patterns across the regions of the language network (within the frontal, temporal, and parietal lobes), while negatively correlated with FC patterns between adjacent and contralateral regions within the visual cortex (refer to Table 3, Figure 6 and 7 for details). Our findings support previous neurodevelopmental studies that found the more distant FC of the language network integrate and strengthen once the more local FC have developed (Fair et al., 2007; Rowlands et al., 2016). This developmental pattern may reflect increased myelination in the language associated white matter tracts, allowing for more efficient communication between brain regions (Pol, 2010). These neurodevelopmental milestones need to be established before children can undergo more complex, higher-level cognitive processes such as reading (Ferretti, Mazzotti, & Brizzolara, 2008; Franceschini, Gori, Ruffino, Pedrolli, & Facoetti, 2012).

As previously hypothesized, age positively correlated with the FC strength between regions of the language network previously identified in older-children and adults. This includes regions within the dorsal and ventral language pathways that connect the posterior temporal/parietal language areas to the inferior frontal lobe for language processing and verbal expression (Saur et al., 2008; Hickok and Poeppel, 2004; Scott et al., 2000). The dorsal stream is involved in phonological processing and mapping sounds onto the motor pathway for verbal articulation via the arcuate fasciculus and the superior longitudinal fasciculus. While the ventral stream is associated with recognizing the meaning behind language sounds for both verbal and written language via the uncinate fasciculus and the inferior fronto-occipital fasciculus (Saur et al., 2008; Hickok and Poeppel, 2004; Scott et al., 2000). These language streams have been further divided into two sections connecting the posterior and anterior language areas (Brauer et al., 2013). The primary dorsal pathway (D1) terminates in the premotor cortex and is considered to be important for auditory-motor integration for early language learning (Friederici et al., 2011), while the secondary dorsal pathway (D2) terminates in the inferior frontal gyrus and is associated with more complex linguistic processes (Friederici et al., 2006; Brauer et al., 2011). In our analysis, we show that age positively correlated with the strength of the FC patterns between both the left STG, left/right ANG seed regions and the left frontal-parietal areas of the dorsal and ventral language processing streams. More specifically, we found that age positively correlated with the FC strength between the *left* ANG and the superior lateral occipital cortex, inferior frontal gyrus, and precentral gyrus of the D1 and D2 pathways. In addition, we found that age positively correlated with the FC strength between the *right* ROI (ANG and STG) and the left pre/postcentral gyrus of the D1 pathway for mapping language information onto the motor system. These findings are in-line with a structural neurodevelopmental MRI study that found evidence of the primary and secondary dorsal pathway tracts connecting the posterior temporal/parietal lobe to the inferior/middle frontal gyrus in 5-8-year-old children, whereas only the D1 pathway was identified in the infant group (Brauer et al., 2013).

These findings suggest that the development of the functional language network follows a similar trajectory as previously identified in structural imaging studies.

In contrast to adult studies, a tractography study examining 2-to-5 year-old children did not find phonological processing ability to positively correlate with the integrity of the ventral and dorsal route tracts. Instead, phonological processing ability positively correlated with fractional anisotropy (a measure of the structural integrity of the white matter) in the bilateral inferior fronto-occipital fasciculus of the ventral tracts (Walton et al., 2016). These findings suggest that the ventral and dorsal tracts are still developing in 2-to-5-year-old children. We also expected to find a positive relationship between age and the strength of the FC patterns between our ROI and the *bilateral* inferior/middle temporal gyrus. However, we found age positively correlated with the FC between our ROI and the inferior/middle temporal gyrus localized to the same hemisphere. More specifically, we found that age positively correlated with the FC strength between the left STG and the *contralateral* inferior temporal gyrus and fusiform gyrus, while negatively correlated with the FC strength between the left ANG and the *ipsilateral* middle/inferior temporal gyrus. Although we cannot equate structural and functional connectivity, our findings support previous structural imaging studies that suggest the language pathways are still immature in preschool-aged children.

In line with our original hypothesis, age positively correlated with the FC between several brain areas across the language network that are both independent and dependent of language ability. In support of these findings the we found a positive relationship between age and the raw language scores. These results are in line with previous fMRI studies that found the development of the language network to be coupled with improvements in both reading fluency and reading comprehension (Brauer, Anwander, Perani, & Friederici, 2013; Croft & Baldeweg, 2015; Ferguson, Nielsen, & Anderson, 2014). More specifically, we found that age positively correlated with the FC strength between the *left* STG ROI and the inferior temporal gyrus (region primarily associated with language development), as well as between the ANG, IFGtr, STG and the inferior frontal gyrus, middle frontal gyrus, supramarginal gyrus and angular gyrus (language regions associated with both age and language performance) (Weiss-Croft & Baldeweg, 2015a). These findings are congruent with the results of the child meta-analysis that found a positive correlation between age and the degree of activation within the inferior frontal gyrus and middle/inferior temporal gyrus during semantic language tasks, regardless of task performance (Weiss-Croft & Baldeweg, 2015a). In addition, previous studies have found a positive relationship between the magnitude of activation within the inferior frontal gyrus and the middle/inferior temporal gyrus with the FC strength between the regions of the language network and reading automaticity (Weiss-Croft & Baldeweg, 2015a). While, in the current study, FC patterns between the inferior frontal gyrus and the middle/inferior temporal gyrus both positively associated with age and speeded naming ability, suggesting that the involvement and integration of these brain regions are associated with both speeded naming and the development of the language network. In contrast, the left cerebellum— brain area considered to play a role in working memory, visual short-term memory, and attention—positively correlated with age but not with language ability (Table 1 & 2) (Berninger, Richards, & Abbott, 2017; Koyama, Stein, Stoodley, & Hansen, 2011; Nguyen et al., 2017). Our findings suggest that increased FC strength between the left ANG and the left cerebellum (Crus VIIb & II) might be more strongly tied with brain maturation than language performance in preschool-aged children. In contrast, a meta-analysis examining the brain activation patterns associated with language in children found that the middle frontal gyrus positively correlated with both age and language performance (Weiss-Croft & Baldeweg, 2015a). These findings help explain the relationship between attention span, working memory capacity and language ability. Therefore, we are not surprised to find that age positively correlated with the FC patterns between language and executive function between areas to support other cognitive processes, such as reading (Koyama, Stein, et al., 2011; Nguyen et al., 2017; Plaza & Cohen, 2007; Rohr et al., 2017). In addition, the FC patterns between the language and executive function areas help explain the high comorbidity rates between developmental dyslexia and ADHD (Plaza & Cohen, 2007). Therefore, our findings support previous studies that suggest the language network follows a strong developmental pattern that can be moderated by language performance (Barquero, Davis, & Cutting, 2014; Davis et al., 2011; Simos et al., 2007). In addition, these findings suggest that both age and language ability positively associate with the degree of functional integration of the more distant brain regions (Brauer, Anwander, Perani, & Friederici, 2013; Croft & Baldeweg, 2015; Ferguson, Nielsen, & Anderson, 2014). These results were expected, as efficient communication between several brain areas is needed to support the more complex cognitive functions, such as reading (Ferretti, Mazzotti, & Brizzolara, 2008; Franceschini, Gori, Ruffino, Pedrolli, & Facoetti, 2012).

As expected, we found that age and speeded naming ability negatively correlated with the FC patterns between our ROI and short-distant ipsilateral and contralateral language regions within the occipital pole for visual processing (Figure 6a and Figure 7). We found that younger preschool-aged children display stronger FC between ipsilateral language regions and contralateral visual areas compared to older children. This finding is inline with previous studies that found greater FC between ipsilateral, short-distant language regions, and rudimentary sensory processing areas in younger children compared to older children and adults (Fair et al., 2007; Weiss-Croft & Baldeweg, 2015b). In contrast to our original hypothesis, age was not found to negatively correlate with the FC patterns between our ROI and the precuneus and PCC of the DMN (brain regions previously found to segregate from the language network and strengthen within the DMN with increasing age and language skill improvement in school-aged children and adolescents) (Fair et al., 2007). This developmental pattern is thought to be associated with more efficient language functioning as the brain develops by strengthening the functionally relevant brain connections, while weakening connections with the less cognitively irrelevant areas (Fair et al., 2007). In contrast to the correlational patterns with age, speeded naming ability negatively correlated with the strength of the FC between the right STG and the left precuneus. These findings suggest that the separation between of the functional language network and DMN regions may begin in early childhood but is more strongly associated with speeded naming (a measure of efficient language processing) than age within the preschool period.

4.3 Brain-Language Relationships

After controlling for age, language ability positively correlated with the FC patterns of the language network associated with the cognitive skill in question. We found speeded naming and phonological processing ability to be associated with distinct FC patterns within the language network, which suggests that the speeded naming and phonological processing subtests utilize separate language functions (Korpilahti, Valkama, & Jansson-Verkasalo, 2016; Norton et al., 2014; Pennington et al., 2012; Vukovic & Siegel, 2006; Willems, Jansma, Blomert, & Vaessen, 2016). Adult brain activation fMRI studies found that speeded naming tasks induced similar brain activation patterns to orthographic language tasks, particularly within the inferior prefrontal cortex, fusiform gyrus, and inferior frontal gyrus. While phonological processing increased activation within the middle frontal gyrus, inferior frontal gyrus, sensorimotor cortex and posterior temporal-parietal areas (previously associated with phonological awareness and semantics). The greatest overlap in the brain activation maps between the speeded naming and phonological processing tasks were found in the inferior frontal gyrus and sensorimotor cortices, which is important for sound-to-motor mapping, verbal articulation, and semantic processing (Brian Byrne 2005; Korpilahti, Valkama, & Jansson Verkasalo, 2016; Norton et al., 2014; Pennington et al., 2012; Savage, Pillay, & Melidona, 2008; Vukovic & Siegel, 2006; Willems, Jansma, Blomert, & Vaessen, 2016). In the current study, we decided to separate the two language measures to gain a clearer understanding of the FC patterns associated with speeded naming and phonological processing in prereaders. First, we describe our findings regarding the relationship between language ability and the brain's intrinsic FC patterns. Second, we discuss the similarities and differences in the FC patterns associated with speeded naming and phonological processing ability.

4.3.1 Relationship between Phonological Processing and the Functional Language Network

After we corrected for age-related effects, we found a positive relationship between phonological processing ability and the FC strength between the left and right ANG ROI and posterior language regions within the right middle temporal gyrus, supramarginal gyrus, and the primary sensorimotor cortices (precentral and postcentral gyrus). These brain areas are important for language perception and semantic representation and integration of language information (supramarginal gyrus) (Bulut, Hung, Tzeng, & Wu, 2017; Gonzalez-Garrido, Alejandro Barrios, Gomez-Velazquez, & Zarabozo-Hurtado, 2017; Mattheiss, Alexander, & Graves, 2017), while the primary and secondary sensorimotor cortex is involved in mapping semantically-associated phonological information onto the motor pathways for speech articulation (Bolger, Hornickel, Cone, Burman, & Booth, 2008; Heim, Opitz, Muller, & Friederici, 2003). More specifically, phonological processing ability positively correlated with the strength of the FC between the *left* ANG and the right sensorimotor cortex, including the precentral gyrus, postcentral gyrus and superior parietal lobule (refer to Table1& 3 and Figure 3 & 5). While the angular gyrus is important for processing semantic information and orchestrating the functional processes of the language network to improve processing efficiency (Seghier, 2013).

Although, age and phonological processing ability were found to positively correlated with the FC patterns between the ANG and the primary sensorimotor cortices (precentral and postcentral gyrus), the significant clusters were found in opposite hemispheres. Age positively correlated with FC between the *right* ANG and the *left* precentral and postcentral gyrus, while phonological processing ability positively correlated with FC between the *left* ANG and the *right* precentral and postcentral gyrus (Figure 3a and Figure 6b). These results suggest that the strength of FC patterns between the ANG and the sensorimotor cortex increase with age and phonological processing performance; while the left angular gyrus and the *right* superior sensorimotor cortex is more strongly tied to phonological processing ability in young children. However, when seeded from the *right* hemisphere, Phonological Processing scores positively correlated with the FC strength between the *right* ANG and the *right* anterior supramarginal gyrus. These findings suggest that the FC between the left ANG and right sensorimotor cortex is strongly positively associated with phonological processing ability in preschool aged children, while the FC patterns between the right ANG and the left sensorimotor cortices is more strongly tied to age. In contrast to speeded naming, the significant cluster within the sensorimotor cortex associated with phonological processing encompassed a larger surface area than the cluster associated with speeded naming. This finding suggests that the sensorimotor cortex might play a larger role in phonological processing that diverges from speeded naming ability (Horwitz, Rumsey, & Donohue, 1998). Altogether, our findings support the dorsal stream hypothesis of phonological processing, which suggests that FC patterns between the posterior temporal-parietal language and sensorimotor cortices are important for phonological processing (D1 pathway) (Saur et al., 2008; Vandermosten et al., 2012; Vigneau et al., 2006). Altogether, these results provide support for the sensitive period of language development theory, which suggests that children make significant gains in phonological processing skills within the first five years of life (Conti-Ramsden & Durkin, 2012).

4.3.2 Relationship between Speeded Naming and the Functional Language Network

Speeded naming measures the efficiency of language processing across the visual, auditory and motor systems. These processes involve the coordination between the visual and orthographic systems to interpret the written symbols for semantic representation and the sensorimotor cortex to produce the corresponding words (Meyer et al., 1998). In the current study, we found a positive relationship between the Speeded Naming scores and the FC strength between Broca's area (left IFGtr) and the posterior region of the left middle/inferior temporal gyrus, left fusiform gyrus, right angular gyrus, and right supramarginal gyrus (Figure 4a). The left posterior fusiform gyrus (also called the word form area) has been previously found to be involved in visual recognition of written language (Dehaene & Cohen, 2011; Devlin et al., 2006), which is important for identifying letter patterns and recognizing words as whole units (rather than letter by letter) for sight reading (Bolger et al., 2008; Messer & Dockrell, 2011; O'Brien, Wolf, Miller, Lovett, & Morris, 2011). Whereas the inferior frontal gyrus has been associated with combining phonetic and semantic information for language production (Meyer MS, 1998). Our findings help explain the relationship between orthographic processing and speeded naming. A previous fluency-based reading intervention study found that children with improvements in orthographic processing performed better on the rapid letter naming tasks, but on the spelling tasks (O'Brien et al., 2011). Altogether, these findings suggest that speeded naming heavily relies on orthographic processing to identify the correct symbol (word, object or shape), while spelling is more strongly associated with phonological processing to select the appropriate letters that match the specific word sounds (Conti-Ramsden & Durkin, 2012). An independent longitudinal FC study found an increase in activation of the fusiform gyrus during reading for children with developmental dyslexia that underwent an intensive speed reading program, independent of their initial reading ability (Horowitz-Kraus, DiFrancesco, Kay, Wang, & Holland, 2015; Horowitz-Kraus, Toro-Serey, & DiFrancesco, 2015). This suggests that the FC strength between the fusiform gyrus and the other areas of the language network increase with age and practice with orthographic processing, such as letter or object recognition. Since we know that speeded naming is associated with reading fluency (Savage et al., 2008; Stanovich & Siegel, 1994), and fluent reading depends on proficient orthographic processing (Bolger et al., 2008; Messer & Dockrell, 2011; O'Brien et al., 2011), we suggest that the FC strength between the IFGtr and fusiform gyrus in pre-readers might help predict future reading ability in young children.

According to previous fMRI task-based studies, orthographic and phonological processing assessments utilize separate functional networks and provide independent information regarding reading skills (Bolger et al., 2008). Previous research has linked speeded naming and orthographic processing with the FC strength between the fusiform gyrus, inferior frontal gyrus, and other regions within the functional language network (Bolger et al., 2008). These findings suggest that speeded naming and phonological processing tasks activate predominately independent neural networks. As a result, speeded naming measures may provide researchers with independent information from phonological processing regarding the predictability and specificity of future reading ability in preschool-aged children. While the relationship between speeded naming ability and FC strength between the left IFGtr and the left fusiform gyrus might provide researchers with greater insight into how the development of the language network(s) in typically developing young children diverges from impaired readers. These results explain why individuals with developmental dyslexia often demonstrate lower activation patterns in the fusiform gyrus compared to typical readers during reading tasks (Dehaene & Cohen, 2011). These findings suggest that children with inferior speeded naming skills may present with different reading-associated challenges (even if within a normal range for reading) compared to children with inferior phonological processing skills. In addition, our findings support the double deficit hypothesis of developmental dyslexia, which suggests that phonological processing and speeded naming contribute independent information regarding severity and the underlying cause of the reading impairment.

We found that speeded naming ability positively correlated with the FC strength between our ROI and the frontal operculum/insular cortex (specifically between the left IFGtr and the left ventral frontal operculum and insular cortex) (Figure 4a). According to previous lesion and neuroimaging studies, the left insular cortex is involved in meditating the motor aspects of speech production for articulatory planning and control (Chang, Lee, & Metcalfe, 2017). An independent brain activation fMRI study found that the insula is divided into separate regions, each of these regions are associated with a different cognitive function involved in speech and language processing (Chang et al., 2017). The authors found greater frontal lobe activation within the ventral insula in response to expressive language tasks compared to the speech perception tasks; these findings suggest that the left insular cortex is more strongly associated with speeded naming than phonological processing ability (Chang et al., 2017). Based on previous findings, the significant clusters we identified in the frontal lobe (including the inferior frontal gyrus, fontal operculum, and insular cortex) might reflect the major top-down cognitive control processes needed for the speeded naming task, particularly in young children who are still undergoing major language developmental milestones (Basso, Spanhauer, Arnold, & Deplazes, 2014; Gabrieli, Poldrack, & Desmond, 1998; Hussey, Ward, Christianson, & Kramer, 2015; Ries, Karzmark, Navarrete, Knight, & Dronkers, 2015).

In agreement with our initial hypothesis, speeded naming ability positively correlated with the FC strength between the right IFGtr and the bilateral medial dorsal thalamus (Figure 4b). Although the thalamus is not well-recognized in the literature as a language region, two neuroimaging study reported increased activation of the bilateral thalamus in response to reading tasks in children, but not in adults (Koyama, Di Martino, et al., 2011). The authors suggest that the bilateral thalamus is a child-specific language area involved in speeded naming (Koyama, Di Martino, et al., 2011). Similarly, we did not find a significant relationship between our ROI and the thalamus when we correlated our findings with age. However, a longitudinal fMRI study found activation within the left thalamus increased from age 5 to age 11 for word generation tasks (Szaflarski et al., 2006). While an independent adult brain activation study found a positive relationship between activation within the medial and ventral thalamus and coordination between the cognitive and motoric aspects of language production (Johnson & Ojemann, 2000). Altogether, these findings suggest that the thalamus might be associated with greater efficiency in language production in preschool-aged children.

Since previous longitudinal FC studies found evidence that suggests the language and default mode networks separate and independently strengthen with increasing age and language skill advancement, we expected to find a negative relationship between our language ROI and the DMN (Fair et al., 2007). Similarly, previous brain activation studies found a negative relationship between speeded naming ability and activation within the precuneus/PCC and visual cortex. For example, one study found that language skill and reading comprehension negatively correlated with the degree of activation within the precuneus and PCC during reading tasks (Fox et al., 2005; Fransson, 2005; Mar, 2011; Smallwood et al., 2013). Whereas, task-based adult brain activation studies found that the location and degree of activation change within the precuneus and PCC changed with the different language and reading tasks (Fox et al., 2005; Fransson, 2005; Klawiter, 2013; Mar, 2011; Smallwood et al., 2013). However, rsFC MRI adult studies found the FC strength between the *posterior* precuneus/PCC and the primary visual cortex to be more strongly associated with visual and orthographic processing, compared to phonological language processing (Klawiter, 2013; Zhang S, 2012). For example, one study found that the activation within the precuneus/PCC decreased more for a spelling task than for the rhyming task (involving phonological processing skills) (Bolger et al., 2008). Bolger and colleagues (2008) interpreted the differences in the language-specific activation patterns within the precuneus and PCC to correspond to a difference in the language associated cognitive processes for the spelling and rhyming tasks. Rhyming involves phonological awareness and working memory, while spelling involves a larger range of language processes including, phonological processing, orthographic processing, and semantic knowledge. In line with previous findings and our hypothesis, we found a negative relationship between speeded naming ability and the strength of the negative relationship between our ROI (ANG and STG) and the posterior parietal-occipital regions of the occipital cortex and DMN. More specifically, Speeded Naming scores negatively correlated with the strength of the negative FC patterns between the right STG and areas within the left precuneus and cuneal cortex, as well as between the right ANG and the right superior occipital pole (Figure 5a and 5b). In contrast, we did not find a relationship between phonological processing ability and FC patterns between the regions of the language network and the posterior hubs of the DMN. Altogether, these findings suggest that the negative relationship between the precuneus/visual cortex and our language ROI are more strongly associated with speeded naming than phonological processing in preschool aged children. In addition, our findings support previous studies that suggest the posterior precuneus/PCC hub of the DMN plays a dynamic role in reading and language (Klawiter, 2013; Seghier, 2013).

Interestingly, we did not find a relationship between age and the FC patterns between regions of the language network and DMN. Only after we controlled for age did we observe that the FC patterns between the STG and precuneus/PCC significantly correlated with the Speeded Naming scores (Table 2). This finding suggests that the FC patterns between regions our ROI (ANG, IFGtr, and STG) and the DMN are more tightly linked to language performance than brain maturation in young children. As a result, the FC strength between the intrinsic STG and the precuneus/PCC hub may provide greater insight into how the early speeded naming skills relate to future reading ability. In conclusion, we demonstrate that speeded naming ability in young children is associated with the strength of the FC between regions involved in orthographic processing and coordinating language information.

4.3.3 Similarities and Differences between Phonological Processing and Speeded Naming

We provide support for the double deficit hypothesis of developmental dyslexia that suggests phonological processing and speeded naming measures contribute independent information regarding the severity and underlying cause of a specific reading impairment (Vandermosten et al., 2016). This finding is in line with previous neuroimaging studies that identified both distinct and overlapping brain activation patterns during speeded naming and phonological processing tasks, with the majority of the overlap in activation around the temporal parietal junction and sensorimotor cortex (Bolger et al., 2008; Lidzba, Schwilling, Grodd, Krageloh-Mann, & Wilke, 2011; Lonigan et al., 2009; Norton et al., 2014; Pennington et al., 2012; Raschle, Stering, Meissner, & Gaab, 2014). The overlap in brain activation maps between the two language tasks is thought to reflect the overlap in cognitive demands, specifically item identification and phoneme recognition (Bolger et al., 2008; Lidzba, Schwilling, Grodd, Krageloh-Mann, & Wilke, 2011; Lonigan et al., 2009; Norton et al., 2014; Pennington et al., 2012; Raschle, Stering, Meissner, & Gaab, 2014). Although we found similar FC patterns between correlations with Phonological Processing and Speeded Naming scores (refer to Table 1 and Table 2), the significant clusters resided in opposite hemispheres and encompassed a different amount of spatial area. For example, we found that speeded naming and phonological processing ability positively correlated with the FC patterns between the ROI and the primary sensorimotor cortices (precentral and postcentral gyrus), while the significant clusters associated with phonological processing encompassed a much larger area and was found in the *right* pre/postcentral gyrus, in contrast with the *left* sensorimotor cortex that was found to be associated with speeded naming (Figure 3a and Figure 4b). More specifically, Phonological Processing scores positively correlated with the FC strength between the *left* ANG and the *right* pre/postcentral gyrus (primary (D1) dorsal language pathway), while Speeded Naming scores positively correlated with the FC strength between the *right* IFGtr and the *left* precentral gyrus (part of the secondary (D2) language pathway). These findings suggest that the sensorimotor cortex might be more directly associated with phonological processing than speeded naming in preschool-aged children. In addition, these results support the dorsal stream of language processing theory that suggests the sensorimotor cortex plays a key role in phonological processing (Saur et al., 2008; Vandermosten et al., 2012; Vigneau et al., 2006).

We identified several discrepancies in the FC patterns when correlated with either speeded naming or phonological processing. Speeded Naming scores positively correlated with the FC strength between brain regions critical for orthographic and language-motor processing, including the left and right inferior frontal gyrus (Broca's area), the left posterior inferior temporal gyrus, left fusiform gyrus, and left insular cortex, whereas Phonological Processing scores positively correlated with the FC strength between the angular gyrus and the supramarginal gyrus, precentral gyrus and postcentral gyrus (important regions for semantic and phonological processing). These observed discrepancies found in the FC correlational patterns between the two language measures suggest that speeded naming information might be primarily processed along the ventral language pathway, whereas phonological information might be primarily processed along the dorsal language pathway. However, based on previous findings conducted on older-children and adults, we suspect that the FC patterns between Broca's area and the posterior temporal-parietal language regions will increase with age and phonological processing ability once the child has began learning to read (Heim et al., 2003). As a result, our findings suggest that the FC patterns between the anterior and posterior language areas involved in phonological processing are immature in preschool-aged children.

In the current study, we found that the angular gyrus plays a critical role in the development of phonological processing in preschool-aged children. We found that both the left and right ANG seed-derived FC maps were significantly correlated with phonological processing ability but not with speeded naming. Phonological Processing scores positively correlated with the strength of the FC between the *right* ANG and the right supramarginal gyrus, while the *left* ANG positively correlated with and the right lateral occipital cortex, posterior right middle temporal gyrus, right supramarginal gyrus, and the right sensorimotor cortex. These findings suggest that the ANG plays an important role in phonological processing that might diverge from speeded naming (Horwitz, Rumsey, & Donohue, 1998). Previous studies report that the angular gyrus plays an important role in modulating and directing brain function to improve the efficiency of language processing, while the primary and secondary sensorimotor areas are critical for semantic processing and speech articulation (Hickok, 2012a, 2012b; Seghier, 2013). Anatomically speaking, the angular gyrus is well situated to perform this type of integration, as it is closely positioned near the end of the major white matter tracts beside the classic language areas and the sensorimotor cortex within the inferior-frontal and superior-temporal cortices (Seltzer & Pandya, 1978; Pandya & Seltzer, 1982; Yeterian & Pandya, 1985; Mesulam & Mesulam, 2000; Bonner et al., 2013).

In conclusion, our findings suggest that speeded naming and phonological processing contribute both overlapping and independent information in regard to reading predictability in preschool-aged children (refer to Table 1 & 2 for details). However, we cannot conclude that our findings are specific to our language measures because we utilized a resting-state FC correlational cross-sectional design. Therefore, it is possible to find similar findings if we correlated our results with other language measures, such as orthographic processing or vocabulary scores. In fact, previous studies have reported similar FC patterns associated with other related language skills, such as vocabulary size (Lonigan et al., 2009; Sroka et al., 2015), reading comprehension (Lidzba et al., 2011; Price, Moore, Humphreys, & Wise, 1997; Seghier et al., 2004; Vigneau et al., 2006), spelling and word decoding (Bolger et al., 2008; Savage et al., 2008). Despite the limitation in our interpretative power, we are confident that our results are accurate and reliable as our findings reflect previous FC language studies conducted with adults and older-children.

4.3.4 Lateralization of the Functional Language Network

Although language processing is usually considered to be left lateralized, brain activation studies found that certain language tasks can induce bilateral or right hemispheric brain activation (Lidzba et al., 2011). For example, one brain activation fMRI study found a positive relationship between reading comprehension and bilateral activation of the sensorimotor cortices (Lidzba et al., 2011). In addition, Lidzba and colleagues (2011) found that the verbal IQ scores positively correlated with activation in the right posterior temporal-parietal language areas during a brain activation during a reading task. The authors suggest that superior reading comprehension and higher verbal intelligence requires efficient processing across a large range of brain areas, involving the right hemisphere to access memory stores, make inferences, and shift attention to relevant information (Lidzba et al., 2011). According to previous resting-state fMRI studies, the functional language network transitions from a highly distributed, bilateral network to a slightly left lateralized, specific interconnected functional network (Brauer et al., 2013). The FC patterns between the regions of the language network have been found to increase with age (Weiss-Croft & Baldeweg, 2015a) and language skill advancement (Koyama, Di Martino, et al., 2011; Sroka et al., 2015). In the current study, both age and language ability positively correlated with the long-distant and cross-cortical FC patterns between the language areas but negatively correlated with shorter and more lateralized FC patterns (refer to Tables 1, 2 and 3 for details). Our findings show that stronger, long-distant FC between language regions positively correlate with both phonological processing and speeded naming ability (Horowitz-Kraus, DiFrancesco, et al., 2015; Norton et al., 2014; Tomasi & Volkow, 2012) and support our original hypothesis stating that the language measures will be positively correlated with the more anatomically distantly brain areas associated with language and reading. These findings suggest that children with superior language scores may have stronger FC between the longer-distant language regions needed for more efficient and complex language processes. In contrast, we found age and Speeded Naming scores negatively correlated with the strength of the FC between language regions within the same hemisphere. This observation suggests that children with inferior language skills might process language information more locally and at a slower rate because their language network might still be underdeveloped or inefficiently developed (Koyama, Di Martino, et al., 2011; Sroka et al., 2015).

More recent studies suggest that the lateralization of the language network(s) should be viewed as a continuous variable, involving both intra and interhemispheric functional connectivity patterns. It is important to consider that lateralization of the FC networks can be influenced by a variety of different factors, including study methodology (resting state vs. task-condition), the specific language measure/task used, participant factors (e.g., age and previous language exposure) and statistical thresholds (Seghier, 2008). In the current study, we examined the relationship between the intrinsic FC patterns of the language and reading networks while the child passively watched a movie (Lee et al., 2012; Tomasi & Volkow, 2012). Fortunately, previous adult FC studies found similar results between passive movie watching and traditional resting state conditions (Vanderwal, Kelly, Eilbott, Mayes, & Castellanos, 2015). Therefore, we are confident that our findings can be interpreted in terms of traditional resting state conditions. While the strength of the FC patterns between the spatially distinct language regions helps provide insight into the efficiency of language processing (Koyama et al., 2010). Our results are comparable to previous resting state FC studies conducted on adults, suggesting that the efficiency of language processing increases with both age and language ability in preschool aged children (Koyama et al., 2010). In addition, our results support previous studies that found a positive relationship between the strength and distance of the FC patterns between the language regions with phonological processing and speeded naming ability (Horowitz-Kraus, DiFrancesco, et al., 2015; Norton et al., 2014; Tomasi & Volkow, 2012), suggesting that children with superior language scores have stronger FC between distant language regions. In contrast, we observed a negative relationship between age, language ability and the strength of the FC between more local brain areas, predominately localized to the same hemisphere. This observation suggests that children with inferior language skills have an underdeveloped, more basic language network (Koyama, Di Martino, et al., 2011; Sroka et al., 2015).

4.4 Limitations

Although we found strong correlations between reading-associated language skills (phonological processing and speeded naming) and the strength and complexity of the intrinsic FC of the language network in young prereaders, we cannot assume that these FC are specific to the language skill in question. To more accurately predict future reading ability in preschool-aged children, future studies need to use a longitudinal study design and follow young prereaders through the stages of language and reading development. In addition, environmental factors, such as socioeconomic status (SES), caregivers' education level, and the time parents invested in their child's learning may contribute to the variation in our participants' early language abilities. Previous language development studies found a positive relationship between the caregiver's vocabulary, complexity of language usage, and the amount of time caregivers spend speaking and reading to their child with their child's written and oral communication skills. Therefore, major variations between the participants linguistic environment is a potential confounding factor (Fluss et al., 2008; Karahmadi, Shakibayee, Amirian, Bagherian-Sararoudi, & Maracy, 2014). Although we did not specifically control for language exposure, we did collect demographic data on the number of years of maternal post-secondary education, which we used as a proxy for SES (Gardner-Neblett & Iruka, 2015; Horowitz-Kraus, DiFrancesco, et al., 2015; McKean et al., 2017; Richels, Johnson, Walden, & Conture, 2013; Zubrick, Taylor, & Christensen, 2015). We found little variation between subjects on the number of years of maternal education (mean of 5.5 ± 2.6 years of postsecondary education), which suggest that the children experienced little variability in the quality and amount of language exposure. Previous language exposure if important factor to consider because a child with lower amount and lower quality language exposure may underperform until they have been provided with the opportunity to catch up to their peers with formal education (HorowitzKraus, DiFrancesco, et al., 2015; Horowitz-Kraus, Toro-Serey, et al., 2015; Mermelshtine, 2017; van Bergen, van der Leij, & de Jong, 2014). We also cannot equate reading and written language with verbal language. Although our language measures are predictive of future reading abilities, children with attention difficulties or other learning challenges might also perform poorly on our language assessments. Thus, it is possible that poor performance on the language measures might also be associated with non-reading factors, such as ADHD.

Functional imaging research is limited by the technical constraints of the MR scanner. Current MRI scanners cannot adjust to changes in participant position or correct the effects of motion within the scanner, which ultimately results in motion image artifacts. Head motion artifacts are spurious and systematic in nature, thus have the potential to alter the FC patterns. In line with the well-recognized functional imaging methods by Power and Colleagues (2014-2015), we employed image scrubbing techniques and applied stringent thresholds for detecting motion artifacts. We also excluded participants with less than 4.5 minutes of high quality data (with little or no motion artifacts) (Power et al., 2012; Power et al., 2014). As a result, we excluded 25.86 % of the data because of excessive head motion; this rate of exclusion criteria is close to the percentage of subjects excluded in previous pediatric studies (approximately 30%) (Vanderwal, Kelly, Eilbott, Mayes, & Castellanos, 2015; Yuan et al., 2009). Also, to account for the variation in the amount of data censoring between subjects (*range* = 4:32 – 8 minutes of usable data; *M*= 1.4, *SD* =0.93 minutes), we decided to add the number of censored high motion volumes as a covariate to our group-level statistical model. Even if data censoring and subject exclusion biased our sample, head motion did not significantly correlate with our language scores, which means that our data was not systematically biased by variations in motion artifacts across our subjects.

We played a movie for the child during the MRI scan to help the child feel more comfortable during the scan and reduce the frequency of head motion. However, because we focused our analyses to the low-frequency spontaneous fluctuations of the BOLD signal (similar to resting state fMRI studies), having an external stimulus present during the fMRI scan may have reduced the strength of the FC patterns, particularly between regions of the language and default mode network as these networks function in opposition during resting and task states. Despite the potential drawbacks of playing a movie during scanning, previous studies report that the benefits of reduced head motion associated with movie watching far outreached the source of random error in the data caused by the presence of a passive stimulus. Playing a movie during the MRI scan was associated with greater participant compliance, increased participant comfort level, lower frequency of head motion, and an overall increase in sample size (Vanderwal et al., 2015). In addition, the authors found highly comparable results between traditional resting state and passive movie watching within-scanner conditions for adults with consistent high-quality, low-motion data (Kauppi, Jaaskelainen, Sams, & Tohka, 2010; Pamilo et al., 2012).

Therefore, we are confident that our results can be reliability compared to studies utilizing traditional resting state methods.

4.6 Future Directions

Despite major scientific and technological advancements, the exact etiology and developmental trajectory underlying a specific reading disability are still largely unknown. The most prominent theories of developmental dyslexia stem from the opposing (but partially overlapping) cognitive deficit models of developmental dyslexia. More specifically, the single deficit phonological processing model, the double-deficit phonological processing-speeded naming model, the speeded naming subtype model, and the multiple cognitive deficit model (van Bergen et al., 2014). In our study, we used language measures that are predictive of future reading abilities, specifically phonological processing and speeded naming. Future studies should follow-up our results and directly compare the FC patterns associated with speeded naming and phonological processing to gain a clearer understanding of how these language skills are interconnected and help us identify the brain areas that uniquely contribute to these specific language skills.

To further identify the distinct, yet interconnected language networks within the larger language network, future studies should include additional language measures (such as verbal IQ, verbal comprehension, verbal expression, vocabulary, and orthographic processing). Incorporating additional language measures, would help to increase our confidence in our ability to predict future reading skills in young children that could be utilized to help identify children at risk for developing a reading disability. In addition, gaining a better understanding of the specific cognitive-FC patterns associated with reading would help scientists further characterize children diagnosed with a reading specific impairment into specific subtypes, based on their distinct cognitive profiles. Finally, this information could be used to help researchers develop more targeted therapies for children at risk of developing a reading disability (van Bergen et al., 2014). In addition to language, future studies should examine the relationship between the brain systems associated with language and other highly-comorbid neurodevelopmental disorders, such as attention deficit hyperactivity disorder (ADHD) (Germano, Gagliano, & Curatolo, 2010) and specific language impairment (SLI) (van Bergen et al., 2014). It is important to understand the developmental trajectories and dynamic relationship between the language and executive functional systems when studying the underlying cause of a specific reading impairment because a deficit in attention, verbal working memory, task-shifting, or oral language ability can exacerbate the symptoms of a specific reading impairment (Germano, Gagliano, & Curatolo, 2010; van Bergen et al., 2014). Therefore, all reading, and language associated cognitive factors should be considered when developing assessment tools and interventions for children with reading difficulties. In addition, examining the relationship between reading, language, and executive function impairments would provide researchers with the insight needed to develop more targeted interventions aimed at reducing symptoms common to each of these comorbid neurodevelopmental disorders. Finally, longitudinal fMRI studies following children from early to late childhood are needed to determine the underlying neurological cause of a reading impairment and determine what language measures should be used to predict a child’s future reading ability.

4.5 Conclusion

Although the language network has been reliably mapped in adults, language networks in children are less well characterized, especially for children younger than five years of age. According to previous fMRI longitudinal studies the language network follows a strong neurodevelopmental pattern that can be moderated by language ability (Barquero, Davis, & Cutting, 2014; Davis et al., 2011; Simos et al., 2007). In the current study, we found that age and language ability positively correlated with the FC strength between language areas but negatively correlated with the FC patterns between our ROI, nearby areas, as well as language and sensory brain areas associated with rudimentary language processes. More specifically, speeded naming ability positively correlated with the FC strength between our language areas involved in orthographic processing, executive and semantic processing, including the bilateral inferior frontal gyrus, left fusiform gyrus and left frontal operculum; whereas phonological processing ability positively correlated with regions involved in phonological awareness, semantic processing and sensorimotor mapping within the angular gyrus, supramarginal gyrus, middle temporal gyrus. We also identified similar FC patterns between the two statistical models within in the precentral motor cortex and angular gyrus. Our results are comparable to the language and reading network(s) of older children and adults, which suggests that the FC pathways involved in reading begin in early childhood.

As hypothesized, we found a positive relationship between age, language ability, and the strength of FC patterns between distant and interhemispheric FC patterns along the ventral and dorsal language pathways, including the inferior frontal gyrus, middle/inferior frontal gyrus and the precentral and postcentral gyrus (Brauer et al., 2013; Londei et al., 2010; Smits, Jiskoot, & Papma, 2014). Also, in partial support of our initial hypothesis, and previous findings in older school-aged children, we found that the strength of the FC between our ROI and the sensorimotor cortices significantly correlated with age and language ability. Although previous fMRI studies conducted on older children and adults found significant FC patterns between the language network and the *bilateral* sensorimotor cortices, our significant FC between our language regions with the sensorimotor cortex remain predominately lateralized to one hemisphere (Weiss-Croft & Baldeweg, 2015b). More specifically, we found that age positively correlated with FC patterns between the right posterior ROI (ANG and STG) and the *left* pre/postcentral gyrus, while Phonological Processing scores positively correlated with the strength of the FC between the left ANG and *right* pre/postcentral gyrus (Koyama, Di Martino, et al., 2011; Stoodley & Schmahmann, 2009; Tomasi & Volkow, 2012; Weiss-Croft & Baldeweg, 2015b). These findings suggest that FC patterns between the language regions and the sensorimotor cortex is still underdeveloped in preschool aged children. A developmental effect thought to be associated with reading automaticity (Weiss-Croft & Baldeweg, 2015b). These findings suggest that the brain undergoes rapid changes within the frontal-temporal and temporal-parietal language regions during early childhood, whereas language ability appears to reflect the maturity and complexity of the FC patterns between regions of the language network. Therefore, information regarding the FC strength between regions of the language network might help researchers gain insight into the early predictors of future reading abilities.

Similar to the FC patterns we found to negatively correlate with age, we found a negative relationship between language ability and the strength of the FC between brain areas involved in rudimentary language processes, including the occipital cortex for visual processing. We also found that speeded naming ability negatively correlated with the FC strength between right STG and the precuneus and the PCC of the DMN. These findings provide support for models of brain development describing increasing network integration and strengthening, coinciding with between network segregation (Dosenbach et al., 2010; Fair et al., 2009; Fair et al., 2007; Menon, 2013; Power et al., 2010). These findings add to our understanding of the language network and suggest that pre-readers with superior language abilities have developed a more mature arrangement of brain function. In addition, our results provide insight to the early neural correlates associated with early language development and support the double-deficit and multi-cognitive component theories of developmental dyslexia, which suggest speeded naming and phonological processing utilize (at least partially) separate, but interconnected neural networks (Vandermosten, Hoeft, & Norton, 2016). In conclusion, our results provide insight into the neural underpinnings associated with speeded naming and phonological processing in preschool-aged children. These findings highlight the enormous potential language researchers and professionals could have to identify a reading impairment early on and develop targeted interventions.

References

Afshin-Pour, B., Grady, C., & Strother, S. (2014). Evaluation of spatio-temporal decomposition techniques for group analysis of fMRI resting state data sets. *Neuroimage, 87*, 363-382. doi:10.1016/j.neuroimage.2013.10.062

Andres-Roqueta, C., Adrian, J. E., Clemente, R. A., & Villanueva, L. (2016). Social cognition makes an independent contribution to peer relations in children with Specific Language Impairment. *Res Dev Disabil, 49-50*, 277-290. doi:10.1016/j.ridd.2015.12.015

Argyropoulos, G. P. (2015). The cerebellum, internal models and prediction in 'non-motor' aspects of language: A critical review. *Brain Lang*. doi:10.1016/j.bandl.2015.08.003

Arnett, A. B., Pennington, B. F., Peterson, R. L., Willcutt, E. G., DeFries, J. C., & Olson, R. K. (2017). Explaining the sex difference in dyslexia. *J Child Psychol Psychiatry*. doi:10.1111/jcpp.12691

Barbu, S., Nardy, A., Chevrot, J. P., Guellai, B., Glas, L., Juhel, J., & Lemasson, A. (2015). Sex Differences in Language Across Early Childhood: Family Socioeconomic Status does not Impact Boys and Girls Equally. *Front Psychol, 6*, 1874. doi:10.3389/fpsyg.2015.01874

Barquero, L., Davis, N., & Cutting, L. (2014). Neuroimaging of reading intervention: a systematic review and activation likelihood estimate meta-analysis. *PLoS ONE, 9*(1).

Basso, W., Spanhauer, Z., Arnold, S., & Deplazes, P. (2014). Capillaria plica (syn. Pearsonema plica) infection in a dog with chronic pollakiuria: challenges in the diagnosis and treatment. *Parasitol Int, 63*(1), 140-142. doi:10.1016/j.parint.2013.09.002

Berninger, V. W., Richards, T. L., & Abbott, R. D. (2017). Brain and Behavioral Assessment of Executive Functions for Self-Regulating Levels of Language in Reading Brain. *J Nat Sci, 3*(11).

Berl, M. M., Mayo, J., Parks, E. N., Rosenberger, L. R., VanMeter, J., Ratner, N. B., . . . Gaillard, W. D. (2014). Regional differences in the developmental trajectory of lateralization of the language network. *Hum Brain Mapp, 35*(1), 270-284. doi:10.1002/hbm.22179

Bishop, D. V., & Edmundson, A. (1987). Specific language impairment as a maturational lag: evidence from longitudinal data on language and motor development. *Dev Med Child Neurol, 29*(4), 442-459.

Bishop, D. V., McDonald, D., Bird, S., & Hayiou-Thomas, M. E. (2009). Children who read words accurately despite language impairment: who are they and how do they do it? *Child Dev, 80*(2), 593-605. doi:10.1111/j.1467-8624.2009.01281.x

Biswal, B., Yetkin, F. Z., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med, 34*(4), 537-541.

Blank, I., Kanwisher, N., & Fedorenko, E. (2014). A functional dissociation between language and multiple-demand systems revealed in patterns of BOLD signal fluctuations. *J Neurophysiol, 112*(5), 1105-1118. doi:10.1152/jn.00884.2013

Blumenfeld, R. S., & Ranganath, C. (2007). Prefrontal cortex and long-term memory encoding: an integrative review of findings from neuropsychology and neuroimaging. *Neuroscientist, 13*(3), 280-291. doi:10.1177/1073858407299290

Bolger, D. J., Hornickel, J., Cone, N. E., Burman, D. D., & Booth, J. R. (2008). Neural correlates of orthographic and phonological consistency effects in children. *Hum Brain Mapp, 29*(12), 1416-1429. doi:10.1002/hbm.20476

Bolger, D. J., Perfetti, C. A., & Schneider, W. (2005). Cross-cultural effect on the brain revisited: universal structures plus writing system variation. *Hum Brain Mapp, 25*(1), 92-104. doi:10.1002/hbm.20124

Bowers, P. G., & Swanson, L. B. (1991). Naming speed deficits in reading disability: multiple measures of a singular process. *J Exp Child Psychol, 51*(2), 195-219.

Brauer, J., Anwander, A., Perani, D., & Friederici, A. D. (2013). Dorsal and ventral pathways in language development. *Brain Lang, 127*(2), 289-295. doi:10.1016/j.bandl.2013.03.001

Brauer, J., & Friederici, A. D. (2007). Functional neural networks of semantic and syntactic processes in the developing brain. *J Cogn Neurosci, 19*(10), 1609-1623. doi:10.1162/jocn.2007.19.10.1609

Brian Byrne , S. W., Robin Corley , Stefan Samuelsson , Peter Quain , John C. DeFries , Erik Willcutt & Richard K. Olson. (2005). Longitudinal Twin Study of Early Literacy Development: Preschool and Kindergarten Phases *Scientific Studies of Reading 9*(3), 219-235.

Broca, P. (1861). Remarques sur le sie´ge de la faculte´ du langage articule´, suivies d’une observation d’aphemie (Perte de la Parole). In (Vol. 6, pp. 330-357). Paris: Bulletin et mémoires de la Société Anatomique de Paris.

Burman, D. D., Bitan, T., & Booth, J. R. (2008). Sex differences in neural processing of language among children. *Neuropsychologia, 46*(5), 1349-1362. doi:10.1016/j.neuropsychologia.2007.12.021

Brian Byrne , S. W., Robin Corley , Stefan Samuelsson , Peter Quain , John C. DeFries , Erik Willcutt & Richard K. Olson. (2005). Longitudinal Twin Study of Early Literacy Development: Preschool and Kindergarten Phases *Scientific Studies of Reading 9*(3), 219-235.

Bulut, T., Hung, Y. H., Tzeng, O., & Wu, D. H. (2017). Neural correlates of processing sentences and compound words in Chinese. *PLoS ONE, 12*(12), e0188526. doi:10.1371/journal.pone.0188526

Callan, A. M., Callan, D. E., & Masaki, S. (2005). When meaningless symbols become letters: neural activity change in learning new phonograms. *Neuroimage, 28*(3), 553-562. doi:10.1016/j.neuroimage.2005.06.031

Carawan, L. W., Nalavany, B. A., & Jenkins, C. (2016). Emotional experience with dyslexia and self-esteem: the protective role of perceived family support in late adulthood. *Aging Ment Health, 20*(3), 284-294. doi:10.1080/13607863.2015.1008984

Carota, F., Kriegeskorte, N., Nili, H., & Pulvermuller, F. (2017). Representational Similarity Mapping of Distributional Semantics in Left Inferior Frontal, Middle Temporal, and Motor Cortex. *Cereb Cortex, 27*(1), 294-309. doi:10.1093/cercor/bhw379

Chang, T. T., Lee, P. H., & Metcalfe, A. W. S. (2017). Intrinsic insula network engagement underlying children's reading and arithmetic skills. *NeuroImage, 167*, 162-177. doi:10.1016/j.neuroimage.2017.11.027

Conti-Ramsden, G., & Durkin, K. (2007). Phonological short-term memory, language and literacy: developmental relationships in early adolescence in young people with SLI. *J Child Psychol Psychiatry, 48*(2), 147-156. doi:10.1111/j.1469-7610.2006.01703.x Conti-Ramsden, G., &

Durkin, K. (2012). Language development and assessment in the preschool period. *Neuropsychol Rev, 22*(4), 384-401. doi:10.1007/s11065-012-9208-z

Costafreda, S. G., Fu, C. H., Lee, L., Everitt, B., Brammer, M. J., & David, A. S. (2006). A systematic review and quantitative appraisal of fMRI studies of verbal fluency: role of the left inferior frontal gyrus. *Hum Brain Mapp, 27*(10), 799-810. doi:10.1002/hbm.20221

Costanzo, F., Menghini, D., Caltagirone, C., Oliveri, M., & Vicari, S. (2013). How to improve reading skills in dyslexics: the effect of high frequency rTMS. *Neuropsychologia, 51*(14), 2953-2959. doi:10.1016/j.neuropsychologia.2013.10.018

Cox, R. W. (1996). AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput Biomed Res*, *29*(3), 162-173.

Croft, L. J., & Baldeweg, T. (2015). Maturation of language networks in children: A systematic review of 22 years of functional MRI. *Neuroimage*. doi:10.1016/j.neuroimage.2015.07.046

Davis, N., Barquero, L., Compton, D., Fuchs, L., Fuchs, D., Gore, J., & Anderson, A. (2011). Functional correlates of children's responsiveness to intervention. *Dev Neuropsychol, 36,* 288-301.

Dehaene, S., & Cohen, L. (2011). The unique role of the visual word form area in reading. *Trends Cogn Sci, 15*(6), 254-262. doi:10.1016/j.tics.2011.04.003

Dehaene, S., Le Clec, H. G., Poline, J. B., Le Bihan, D., & Cohen, L. (2002). The visual word form area: a prelexical representation of visual words in the fusiform gyrus. *NeuroReport*, *13*(3), 321-325.

Dennis, M., Francis, D. J., Cirino, P. T., Schachar, R., Barnes, M. A., & Fletcher, J. M. (2009). Why IQ is not a covariate in cognitive studies of neurodevelopmental disorders. *J Int Neuropsychol Soc*, *15*(3), 331-343. doi:10.1017/S1355617709090481

Devlin, J. T., Jamison, H. L., Gonnerman, L. M., & Matthews, P. M. (2006). The role of the posterior fusiform gyrus in reading. *J Cogn Neurosci, 18*(6), 911-922. doi:10.1162/jocn.2006.18.6.911

Devous, M. D., Sr., Altuna, D., Furl, N., Cooper, W., Gabbert, G., Ngai, W. T., . . . Tobey, E. A. (2006). Maturation of speech and language functional neuroanatomy in pediatric normal controls. *J Speech Lang Hear Res*, *49*(4), 856-866. doi:10.1044/1092-4388(2006/061)

Dick, A., & Tremblay, P. (2012). Beyond the arcuate fasciculus: consensus and controversy in the connectional anatomy of language. *Brain : a journal of neurology*(135), 3529-3550

Fair, D. A., Dosenbach, N. U., Church, J. A., Cohen, A. L., Brahmbhatt, S., Miezin, F. M., …Schlaggar, B. L (2007). Development of distinct control networks through segregation and integration. *Proc Natl Acad Sci U S A, 104*(33), 13507-13512. doi:10.1073/pnas.0705843104

Ferguson, M. A., Nielsen, J. A., & Anderson, J. S. (2014). Altered resting functional connectivity of expressive language regions after speed reading training. *J Clin Exp Neuropsychol, 36*(5), 482-493. doi:10.1080/13803395.2014.908825

Ferrer, E., Shaywitz, B. A., Holahan, J. M., Marchione, K., & Shaywitz, S. E. (2010). Uncoupling of reading and IQ over time: empirical evidence for a definition of dyslexia. *Psychol Sci, 21*(1), 93-101. doi:10.1177/0956797609354084

Ferrer, E., Shaywitz, B. A., Holahan, J. M., Marchione, K. E., Michaels, R., & Shaywitz, S. E. (2015). Achievement Gap in Reading Is Present as Early as First Grade and Persists through Adolescence. *Journal of Pediatrics, 167*(5), 1121-1140.

doi:10.1016/j.jpeds.2015.07.045
Ferretti, G., Mazzotti, S., & Brizzolara, D. (2008). Visual scanning and reading ability in normal and dyslexic children. *Behav Neurol, 19*(1-2), 87-92.
Fluss, J., Ziegler, J., Ecalle, J., Magnan, A., Warszawski, J., Ducot, B., . . . Billard, C. (2008). [Prevalence of reading disabilities in early elementary school: impact of socioeconomic environment on reading development in 3 different educational zones]. *Arch Pediatr, 15*(6), 1049-1057. doi:10.1016/j.arcped.2008.02.012
Fluss, J., Ziegler, J. C., Warszawski, J., Ducot, B., Richard, G., & Billard, C. (2009). Poor reading in French elementary school: the interplay of cognitive, behavioral, and socioeconomic factors. *J Dev Behav Pediatr, 30*(3), 206-216. doi:10.1097/DBP.0b013e3181a7ed6c
Fonov, V. S., et al. (2009). Unbiased nonlinear average age-appropriate brain templates from birth to adulthood. *Neuroimage, 47*(1), 70884-70885. doi:10.1016/S10538119(09)70884-5
Fox, M. D., & Greicius, M. (2010). Clinical applications of resting state functional connectivity. *Front Syst Neurosci, 4*, 19. doi:10.3389/fnsys.2010.00019
Fox, M. D., & Raichle, M. E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nat Rev Neurosci, 8*(9), 700-711. doi:10.1038/nrn2201
Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America, 102*(27), 9673-9678. doi:10.1073/pnas.0504136102
Franceschini, S., Gori, S., Ruffino, M., Pedrolli, K., & Facoetti, A. (2012). A causal link between visual spatial attention and reading acquisition. *Curr Biol, 22*(9), 814-819. doi:10.1016/j.cub.2012.03.013
Fransson, P. (2005). Spontaneous low-frequency BOLD signal fluctuations: an fMRI investigation of the resting-state default mode of brain function hypothesis. *Hum Brain Mapp, 26*(1), 15-29. doi:10.1002/hbm.20113
Fransson, P., Aden, U., Blennow, M., & Lagercrantz, H. (2011). The functional architecture of the infant brain as revealed by resting-state fMRI. *Cereb Cortex, 21*(1), 145-154. doi:10.1093/cercor/bhq071
Friederici, A. D. (2006). The neural basis of language development and its impairment. *Neuron, 52*(6), 941-952. doi:10.1016/j.neuron.2006.12.002
Gabrieli, J. D., Poldrack, R. A., & Desmond, J. E. (1998). The role of left prefrontal cortex in language and memory. *Proc Natl Acad Sci U S A, 95*(3), 906-913.
Gallagher, A., Tremblay, J., & Vannasing, P. (2016). Language mapping in children using resting-state functional connectivity: comparison with a task-based approach. *J Biomed Opt, 21*(12), 125006. doi:10.1117/1.jbo.21.12.125006
Gardner-Neblett, N., & Iruka, I. U. (2015). Oral narrative skills: Explaining the languageemergent literacy link by race/ethnicity and SES. *Dev Psychol, 51*(7), 889-904. doi:10.1037/a0039274
Germano, E., Gagliano, A., & Curatolo, P. (2010). Comorbidity of ADHD and dyslexia. *Dev Neuropsychol, 35*(5), 475-493. doi:10.1080/87565641.2010.494748

Geschwin.N. (1965). Disconnexion Syndromes in Animals and Man. *Brain, 88*, 585-599. doi:10.1093/brain/88.3.585

Glover, G. H. (2011). Overview of functional magnetic resonance imaging. *Neurosurg Clin N Am, 22*(2), 133-139, vii. doi:10.1016/j.nec.2010.11.001

Greicius, M. (2008). Resting-state functional connectivity in neuropsychiatric disorders. *Curr Opin Neurol, 21*(4), 424-430. doi:10.1097/WCO.0b013e328306f2c5

Greicius, M. D., Supekar, K., Menon, V., & Dougherty, R. F. (2009). Resting-state functional connectivity reflects structural connectivity in the default mode network. *Cereb Cortex, 19*(1), 72-78. doi:10.1093/cercor/bhn059

Gonzalez-Garrido, A. A., Alejandro Barrios, F., Gomez-Velazquez, F. R., & Zarabozo-Hurtado, D. (2017). The supramarginal and angular gyri underlie orthographic competence in Spanish language. *Brain Lang, 175*, 1-10. doi:10.1016/j.bandl.2017.08.005

Hampson, M., Tokoglu, F., Sun, Z., Schafer, R. J., Skudlarski, P., Gore, J. C., & Constable, R. T. (2006). Connectivity-behavior analysis reveals that functional connectivity between left BA39 and Broca's area varies with reading ability. *Neuroimage, 31*(2), 513-519. doi:10.1016/j.neuroimage.2005.12.040

Hartwigsen, G., Golombek, T., & Obleser, J. (2015). Repetitive transcranial magnetic stimulation over left angular gyrus modulates the predictability gain in degraded speech comprehension. *Cortex, 68*, 100-110. doi:10.1016/j.cortex.2014.08.027

Heilman, K., & Scholes, R. J. (1976). The nature of comprehension errors in Broca's conduction and Wernicke's aphasics. *Cortex, 12*(3), 258-265.

Heim, S., Opitz, B., Muller, K., & Friederici, A. D. (2003). Phonological processing during language production: fMRI evidence for a shared production-comprehension network. *Brain Res Cogn Brain Res, 16*(2), 285-296.

Hickok, G. (2012a). Computational neuroanatomy of speech production. *Nat Rev Neurosci, 13*(2), 135-145. doi:10.1038/nrn3158

Hickok, G. (2012b). The cortical organization of speech processing: feedback control and predictive coding the context of a dual-stream model. *J Commun Disord, 45*(6), 393-402. doi:10.1016/j.jcomdis.2012.06.004

Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nat Rev Neurosci, 8*(5), 393-402. doi:10.1038/nrn2113

Hoeft, F., McCandliss, B. D., Black, J. M., Gantman, A., Zakerani, N., Hulme, C., . . . Gabrieli, J. D. (2011). Neural systems predicting long-term outcome in dyslexia. *Proc Natl Acad Sci U S A, 108*(1), 361-366. doi:10.1073/pnas.1008950108

Honey, C. J., Sporns, O., Cammoun, L., Gigandet, X., Thiran, J. P., Meuli, R., & Hagmann, P. (2009). Predicting human resting-state functional connectivity from structural connectivity. *Proc Natl Acad Sci U S A, 106*(6), 2035-2040. doi:10.1073/pnas.0811168106

Horowitz-Kraus, T., DiFrancesco, M., Kay, B., Wang, Y., & Holland, S. K. (2015). Increased resting-state functional connectivity of visual- and cognitive-control brain networks after training in children with reading difficulties. *Neuroimage Clin, 8*, 619-630. doi:10.1016/j.nicl.2015.06.010

Horowitz-Kraus, T., Toro-Serey, C., & DiFrancesco, M. (2015). Increased Resting-State Functional Connectivity in the Cingulo-Opercular Cognitive-Control Network after Intervention in Children with Reading Difficulties. *PLoS One, 10*(7), e0133762.

doi:10.1371/journal.pone.0133762
Horwitz, B., Rumsey, J. M., & Donohue, B. C. (1998). Functional connectivity of the angular gyrus in normal reading and dyslexia. *Proc Natl Acad Sci U S A, 95*(15), 8939-8944.
Houde, O., Rossi, S., Lubin, A., & Joliot, M. (2010). Mapping numerical processing, reading, and executive functions in the developing brain: an fMRI meta-analysis of 52 studies including 842 children. *Dev Sci, 13*(6), 876-885. doi:10.1111/j.1467-7687.2009.00938.
Hussey, E. K., Ward, N., Christianson, K., & Kramer, A. F. (2015). Language and Memory Improvements following tDCS of Left Lateral Prefrontal Cortex. *PLoS ONE, 10*(11), doi:10.1371/journal.pone.0141417
Jap, B. A. J., Borleffs, E., & Maassen, B. A. M. (2017). Towards identifying dyslexia in Standard Indonesian: the development of a reading assessment battery. *Read Writ, 30*(8), 1729-1751. doi:10.1007/s11145-017-9748-y
Jenkinson, M., Beckmann, C. F., Behrens, T. E., Woolrich, M. W., & Smith, S. M. (2012). Fsl. *Neuroimage, 62*(2), 782-790. doi:10.1016/j.neuroimage.2011.09.015
Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: a metanalysis of 35 neuroimaging studies. *Neuroimage, 20*(2), 693-712. doi:10.1016/S1053-8119(03)00343-4
Johnson, M. D., & Ojemann, G. A. (2000). The role of the human thalamus in language and memory: evidence from electrophysiological studies. *Brain Cogn, 42*(2), 218-230. doi:10.1006/brcg.1999.1101
Kaplan BJ, G. G., Leung B.M., Field C.J, Dewey D., Bell R.C., Manca D.P., O'Beirne M., Johnston D.W., Pop V.J., Singhal N., Gagnon L., Bernier F.P., Eliasziw M., McCargar L.J., Kooistra L., Farmer A., Cantell M., Goonewardene L., Casey L.M., Letourneau N., Martin J.W., Team A.P.S. (2014). The Alberta Pregnancy Outcomes and Nutrition (APrON) cohort study: rationale and methods. . *Maternal & child nutrition, 10*, 44-60.
Karahmadi, M., Shakibayee, F., Amirian, H., Bagherian-Sararoudi, R., & Maracy, M. R. (2014). Efficacy of parenting education compared to the standard method in improvement of reading and writing disabilities in children. *Iran J Psychiatry Behav Sci, 8*(1), 51-58.
Kauppi, J. P., Jaaskelainen, I. P., Sams, M., & Tohka, J. (2010). Inter-subject correlation of brain hemodynamic responses during watching a movie: localization in space and frequency. *Front Neuroinform, 4*, 5. doi:10.3389/fninf.2010.00005
Kelly, C., Biswal, B. B., Craddock, R. C., Castellanos, F. X., & Milham, M. P. (2012). Characterizing variation in the functional connectome: promise and pitfalls. *Trends Cogn Sci, 16*(3), 181-188. doi:10.1016/j.tics.2012.02.001
Kirby, J. R., Parrila, R. K., & Pfeiffer, S. L. (2003). Naming speed and phonological awareness as predictors of reading development. *Journal of Educational Psychology, 95*(3), 453464. doi:10.1037/0022-0663.95.3.453
Kjaer TW, N. M., Kjaer KW, Lou AR, Lou HC. (2001). Precuneus-prefrontal activity during awareness of visual verbal stimuli. *Conscious Cogn., 10*(3), 356-365. doi:10.1006/ccog.2001.0509
Klawiter, E. C. (2013). Current and new directions in MRI in multiple sclerosis. *Continuum (Minneap Minn), 19*(4 Multiple Sclerosis), 1058-1073. doi:10.1212/01.CON.0000433283.00221.37
Korkman, M., Kirk, U., & Kemp, S. (2007). *NEPSY II, Clinical and interpretative manual.* San Antonio, TX: The Psychological corporation.

Korpilahti, P., Valkama, M., & Jansson-Verkasalo, E. (2016). Event-Related Potentials Reflect Deficits in Lexical Access: The N200 in Prematurely Born School-Aged Children. *Folia Phoniatr Logop, 68*(4), 189-198. doi:10.1159/000450886

Koyama, M. S., Di Martino, A., Zuo, X. N., Kelly, C., Mennes, M., Jutagir, D. R., . . . Milham, M. P. (2011). Resting-state functional connectivity indexes reading competence in children and adults. *J Neurosci, 31*(23), 8617-8624. doi:10.1523/JNEUROSCI.486510.2011

Koyama, M. S., Kelly, C., Shehzad, Z., Penesetti, D., Castellanos, F. X., & Milham, M. P. (2010). Reading networks at rest. *Cereb Cortex, 20*(11), 2549-2559. doi:10.1093/cercor/bhq005

Koyama, M. S., Stein, J. F., Stoodley, C. J., & Hansen, P. C. (2011). Functional MRI evidence for the importance of visual short-term memory in logographic reading. *Eur J Neurosci, 33*(3), 539-548. doi:10.1111/j.1460-9568.2010.07534.x

Kwong, K. K., Belliveau, J. W., Chesler, D. A., Goldberg, I. E., Weisskoff, R. M., Poncelet, B. P., . . . et al. (1992). Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc Natl Acad Sci U S A, 89*(12), 5675-5679.

Largo, R. H., Molinari, L., Comenale Pinto, L., Weber, M., & Duc, G. (1986). Language development of term and preterm children during the first five years of life. *Dev Med Child Neurol, 28*(3), 333-350.

Lebel, C., & Beaulieu, C. (2009). Lateralization of the arcuate fasciculus from childhood to adulthood and its relation to cognitive abilities in children. *Hum Brain Mapp, 30*(11), 3563-3573. doi:10.1002/hbm.20779

Lee, M. H., Hacker, C. D., Snyder, A. Z., Corbetta, M., Zhang, D., Leuthardt, E. C., & Shimony, J. S. (2012). Clustering of resting state networks. *PLoS One, 7*(7), e40370. doi:10.1371/journal.pone.0040370

Leonard, L. B. (1998). *Children with specific language impairment* (Second edition. ed.).

Lidzba, K., Schwilling, E., Grodd, W., Krageloh-Mann, I., & Wilke, M. (2011). Language comprehension vs. language production: age effects on fMRI activation. *Brain Lang, 119*(1), 6-15. doi:10.1016/j.bandl.2011.02.003

Ling, D. (1989). *Foundations of spoken language for hearing-impaired children.* . Washington, D.C.: Alexander Graham Bell Association for the Deaf.

Londei, A., D'Ausilio, A., Basso, D., Sestieri, C., Del Gratta, C., Romani, G. L., & Belardinelli, M. O. (2010). Sensory-Motor Brain Network Connectivity for Speech Comprehension. *Hum Brain Mapp, 31*(4), 567-580. doi:10.1002/hbm.20888

Lonigan, C. J., Anthony, J. L., Phillips, B. M., Purpura, D. J., Wilson, S. B., & McQueen, J. D. (2009). The Nature of Preschool Phonological Processing Abilities and Their Relations to Vocabulary, General Cognitive Abilities, and Print Knowledge. *J Educ Psychol, 101*(2), 345-358. doi:10.1037/a0013837

Mar, R. A. (2011). The neural bases of social cognition and story comprehension. *Annu Rev Psychol, 62*, 103-134. doi:10.1146/annurev-psych-120709-145406

Maria de la Iglesia-Vaya, J. M.M., Escarti-Fabra M.J., Kanaan A.S., & Martí-Bonmati L. (2013). Brain Connections – Resting State fMRI Functional Connectivity. In K. N. Fountas (Ed.), *Novel Frontiers of Advanced Neuroimaging* (pp. 1-17). Rijeka, Croatia: InTech.

Marinus, E., Nation, K., & de Jong, P. F. (2015). Density and length in the neighborhood: Explaining cross-linguistic differences in learning to read in English and Dutch. *J Exp Child Psychol, 139*, 127-147. doi:10.1016/j.jecp.2015.05.006

Martinez Perez, T., Majerus, S., Mahot, A., & Poncelet, M. (2012). Evidence for a specific impairment of serial order short-term memory in dyslexic children. *Dyslexia, 18*(2), 94109. doi:10.1002/dys.1438

Martinez Perez, T., Majerus, S., & Poncelet, M. (2012). The contribution of short-term memory for serial order to early reading acquisition: evidence from a longitudinal study. *J Exp Child Psychol, 111*(4), 708-723. doi:10.1016/j.jecp.2011.11.007

Mattheiss, S. R., Alexander, E. J., & Graves, W. W. (2017). Elaborative feedback: Engaging reward and task-relevant brain regions promotes learning in pseudoword reading aloud. *Cogn Affect Behav Neurosci*. doi:10.3758/s13415-017-0553-5

McCandliss, B. D., Cohen, L., & Dehaene, S. (2003). The visual word form area: expertise for reading in the fusiform gyrus. *Trends Cogn Sci, 7*(7), 293-299.

McKean, C., Reilly, S., Bavin, E. L., Bretherton, L., Cini, E., Conway, L., . . . Mensah, F. (2017). Language Outcomes at 7 Years: Early Predictors and Co-Occurring Difficulties. *Pediatrics, 139*(3). doi:10.1542/peds.2016-1684

Mermelshtine, R. (2017). Parent-child learning interactions: A review of the literature on scaffolding. *Br J Educ Psychol, 87*(2), 241-254. doi:10.1111/bjep.12147

Messer, D., & Dockrell, J. (2011). Lexical access and literacy in children with word-finding difficulties. *Int J Lang Commun Disord, 46*(4), 473-480. doi:10.1111/j.14606984.2011.00009.x

Meyer M.S., W. F., Hart L.A., Felton R.H. (1998). Selective predictive value of rapid automatized naming in poor readers. *J. Learn. Disabil., 31*(1), 106–117.

Miller, B., Vaughn, S., & Freund, L. (2014). Learning Disabilities Research Studies: Findings from NICHD funded Projects. *J Res Educ Eff, 7*(3), 225-231. doi:10.1080/19345747.2014.927251

Mohr, J. P., Pessin, M. S., Finkelstein, S., Funkenstein, H. H., Duncan, G. W., & Davis, K. R. (1978). Broca aphasia: pathologic and clinical. *Neurology, 28*(4), 311-324.

Morken, F., Helland, T., Hugdahl, K., & Specht, K. (2014). Children with dyslexia show cortical hyperactivation in response to increasing literacy processing demands. *Front Psychol, 5*, 1491. doi:10.3389/fpsyg.2014.01491

Moseley, R. L., Pulvermuller, F., & Shtyrov, Y. (2013). Sensorimotor semantics on the spot: brain activity dissociates between conceptual categories within 150 ms. *Sci Rep, 3*, 1928. doi:10.1038/srep01928

Neef, N. E., Muller, B., Liebig, J., Schaadt, G., Grigutsch, M., Gunter, T. C., . . . Friederici, A. D. (2017). Dyslexia risk gene relates to representation of sound in the auditory brainstem. *Dev Cogn Neurosci, 24*, 63-71. doi:10.1016/j.dcn.2017.01.008

Nguyen, V. T., Sonkusare, S., Stadler, J., Hu, X., Breakspear, M., & Guo, C. C. (2017). Distinct Cerebellar Contributions to Cognitive-Perceptual Dynamics During Natural Viewing. *Cereb Cortex, 27*(12), 5652-5662. doi:10.1093/cercor/bhw334

Norton, E. S., Beach, S. D., & Gabrieli, J. D. (2015). Neurobiology of dyslexia. *Curr Opin Neurobiol, 30*, 73-78. doi:10.1016/j.conb.2014.09.007

Norton, E. S., Black, J. M., Stanley, L. M., Tanaka, H., Gabrieli, J. D., Sawyer, C., & Hoeft, F. (2014). Functional neuroanatomical evidence for the double-deficit hypothesis of developmental dyslexia. *Neuropsychologia, 61*, 235-246. doi:10.1016/j.neuropsychologia.2014.06.015

O'Brien, B. A., Wolf, M., Miller, L. T., Lovett, M. W., & Morris, R. (2011). Orthographic processing efficiency in developmental dyslexia: an investigation of age and treatment factors at the sublexical level. *Ann Dyslexia, 61*(1), 111-135. doi:10.1007/s11881-0100050-9

Ogawa, S., Lee, T. M., Kay, A. R., & Tank, D. W. (1990). Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci U S A, 87*(24), 98689872.

Olofsson, A. (2000). Naming speed, phonological awareness and the initial stage of learning to read. *Logoped Phoniatr Vocol, 25*(1), 35-40.

Pamilo, S., Malinen, S., Hlushchuk, Y., Seppa, M., Tikka, P., & Hari, R. (2012). Functional subdivision of group-ICA results of fMRI data collected during cinema viewing. *PLoS One, 7*(7), e42000. doi:10.1371/journal.pone.0042000

Pennington, B. F., Santerre-Lemmon, L., Rosenberg, J., MacDonald, B., Boada, R., Friend, A., . . . Olson, R. K. (2012). Individual prediction of dyslexia by single versus multiple deficit models. *J Abnorm Psychol, 121*(1), 212-224. doi:10.1037/a0025823

Plaza, M., & Cohen, H. (2007). The contribution of phonological awareness and visual attention in early reading and spelling. *Dyslexia, 13*(1), 67-76.

Pol, v. d. H. H. (2010). Exploring the brain network: A review on resting-state fMRI functional connectivity. *European Neuropsychopharmacology, 20*(8), 519-534.

Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *Neuroimage, 59*(3), 2142-2154. doi:10.1016/j.neuroimage.2011.10.018

Power, J. D., Cohen, A. L., Nelson, S. M., Wig, G. S., Barnes, K. A., Church, J. A., . . . Petersen, S. E. (2011). Functional network organization of the human brain. *Neuron, 72*(4), 665678. doi:10.1016/j.neuron.2011.09.006

Power, J. D., Fair, D. A., Schlaggar, B. L., & Petersen, S. E. (2010). The development of human functional brain networks. *Neuron, 67*(5), 735-748. doi:10.1016/j.neuron.2010.08.017

Power, J. D., Mitra, A., Laumann, T. O., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2014). Methods to detect, characterize, and remove motion artifact in resting state fMRI. *Neuroimage, 84*, 320-341. doi:10.1016/j.neuroimage.2013.08.048

Price, A. R., Bonner, M. F., Peelle, J. E., & Grossman, M. (2015). Converging evidence for the neuroanatomic basis of combinatorial semantics in the angular gyrus. *J Neurosci, 35*(7), 3276-3284. doi:10.1523/jneurosci.3446-14.2015

Price, C. J., Moore, C. J., Humphreys, G. W., & Wise, R. J. (1997). Segregating Semantic from Phonological Processes during Reading. *J Cogn Neurosci, 9*(6), 727-733. doi:10.1162/jocn.1997.9.6.727

Pugh KR1, M. W., Shaywitz B.A., Shaywitz S.E., Fulbright R.K., Constable R.T., Skudlarski P, Marchione K.E., Jenner A.R., Fletcher J.M., Liberman A.M., Shankweiler D.P., Katz L, Lacadie C., & Gore J.C. (2000). The angular gyrus in developmental dyslexia: taskspecific differences in functional connectivity within posterior cortex. *Psychol Sci, 11*(1), 51-56.

Puolakanaho A, A. T., Aro M., Eklund K., Leppanen P.H., Poikkeus A.M., Tolvanen A., Torppa M., Lyytinen H. (2007). Very early phonological and language skills: estimating individual risk of reading disability. *Journal of child psychology and psychiatry, and allied disciplines, 48*, 923-931.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proc Natl Acad Sci U S A, 98*(2), 676-682. doi:10.1073/pnas.98.2.676

Raschle, N. M., Chang, M., & Gaab, N. (2011). Structural brain alterations associated with dyslexia predate reading onset. *Neuroimage, 57*(3), 742-749. doi:10.1016/j.neuroimage.2010.09.055

Raschle, N. M., Stering, P. L., Meissner, S. N., & Gaab, N. (2014). Altered neuronal response during rapid auditory processing and its relation to phonological processing in prereading children at familial risk for dyslexia. *Cereb Cortex, 24*(9), 2489-2501. doi:10.1093/cercor/bht104

Rezai, K., Andreasen, N. C., Alliger, R., Cohen, G., Swayze, V., 2nd, & O'Leary, D. S. (1993). The neuropsychology of the prefrontal cortex. *Arch Neurol, 50*(6), 636-642.

Richels, C. G., Johnson, K. N., Walden, T. A., & Conture, E. G. (2013). Socioeconomic status, parental education, vocabulary and language skills of children who stutter. *J Commun Disord, 46*(4), 361-374. doi:10.1016/j.jcomdis.2013.07.002

Richlan, F., Kronbichler, M., & Wimmer, H. (2013). Structural abnormalities in the dyslexic brain: a meta-analysis of voxel-based morphometry studies. *Hum Brain Mapp, 34*(11), 3055-3065. doi:10.1002/hbm.22127

Ricketts, J., Jones, C. R., Happe, F., & Charman, T. (2013). Reading comprehension in autism spectrum disorders: the role of oral language and social functioning. *J Autism Dev Disord, 43*(4), 807-816. doi:10.1007/s10803-012-1619-4

Ries, S., Legou, T., Burle, B., Alario, F. X., & Malfait, N. (2015). Corrigendum to "Why does picture naming take longer than word naming? The contribution of articulatory processes". *Psychon Bull Rev, 22*(1), 309-311. doi:10.3758/s13423-014-0668-4
Richels, C. G., Johnson, K. N., Walden, T. A., & Conture, E. G. (2013). Socioeconomic status, parental education, vocabulary and language skills of children who stutter. *J Commun Disord, 46*(4), 361-374. doi:10.1016/j.jcomdis.2013.07.002
Ries, S. K., Karzmark, C. R., Navarrete, E., Knight, R. T., & Dronkers, N. F. (2015). Specifying the role of the left prefrontal cortex in word selection. *Brain Lang, 149*, 135-147. doi:10.1016/j.bandl.2015.07.007

Rohr, C. S., Vinette, S. A., Parsons, K. A. L., Cho, I. Y. K., Dimond, D., Benischek, A., . . . Bray, S. (2017). Functional Connectivity of the Dorsal Attention Network Predicts Selective Attention in 4-7 year-old Girls. *Cereb Cortex, 27*(9), 4350-4360. doi:10.1093/cercor/bhw236

Rosselli, M., Ardila, A., & Bernal, B. (2015). [Angular gyrus connectivity model for language: a functional neuroimaging meta-analysis]. *Rev Neurol, 60*(11), 495-503.

Rowlands, M. A., Scheinost, D., Lacadie, C., Vohr, B., Li, F., Schneider, K. C., . . . Ment, L. R. (2016). Language at rest: A longitudinal study of intrinsic functional connectivity in preterm children. *Neuroimage Clin, 11*, 149-157. doi:10.1016/j.nicl.2016.01.016

Ruben, R. J. (1999). A time frame of critical/sensitive periods of language development. *Indian J Otolaryngol Head Neck Surg, 51*(3), 85-89. doi:10.1007/bf02996542

Saur, D., Kreher, B. W., Schnell, S., Kummerer, D., Kellmeyer, P., Vry, M. S., . . . Weiller, C. (2008). Ventral and dorsal pathways for language. *Proc Natl Acad Sci U S A, 105*(46), 18035-18040. doi:10.1073/pnas.0805234105

Savage, R., Pillay, V., & Melidona, S. (2008). Rapid serial naming is a unique predictor of spelling in children. *J Learn Disabil, 41*(3), 235-250. doi:10.1177/0022219408315814

Schlaggar, B. L., & McCandliss, B. D. (2007). Development of neural systems for reading. *Annu Rev Neurosci, 30*, 475-503. doi:10.1146/annurev.neuro.28.061604.135645

Seghier, M. L. (2008). Laterality index in functional MRI: methodological issues. *Magn Reson Imaging, 26*(5), 594-601. doi:10.1016/j.mri.2007.10.010

Seghier, M. L. (2013). The angular gyrus: multiple functions and multiple subdivisions. *Neuroscientist, 19*(1), 43-61. doi:10.1177/1073858412440596

Seghier, M. L., Lazeyras, F., Pegna, A. J., Annoni, J. M., Zimine, I., Mayer, E., . . . Khateb, A. (2004). Variability of fMRI activation during a phonological and semantic language task in healthy subjects. *Hum Brain Mapp, 23*(3), 140-155. doi:10.1002/hbm.20053

Seghier, M. L. (2008). Laterality index in functional MRI: methodological issues. *Magn Reson Imaging, 26*(5), 594-601. doi:10.1016/j.mri.2007.10.010

Seghier, M. L. (2013). The angular gyrus: multiple functions and multiple subdivisions. *Neuroscientist, 19*(1), 43-61. doi:10.1177/1073858412440596

Seghier, M. L., Lazeyras, F., Pegna, A. J., Annoni, J. M., Zimine, I., Mayer, E., . . . Khateb, A. (2004). Variability of fMRI activation during a phonological and semantic language task in healthy subjects. *Hum Brain Mapp, 23*(3), 140-155. doi:10.1002/hbm.20053

Shaywitz, S. E., & Shaywitz, B. A. (2005). Dyslexia (specific reading disability). *Biol Psychiatry, 57*(11), 1301-1309. doi:10.1016/j.biopsych.2005.01.043

Shaywitz, S. E., Shaywitz, B. A., Fletcher, J. M., & Escobar, M. D. (1990). Prevalence of reading disability in boys and girls. Results of the Connecticut Longitudinal Study. *JAMA, 264*(8), 998-1002.

Shaywitz, S. E., Shaywitz, B. A., Pugh, K. R., Fulbright, R. K., Constable, R. T., Mencl, W. E., . . . Gore, J. C. (1998). Functional disruption in the organization of the brain for reading in dyslexia. *Proc Natl Acad Sci U S A, 95*(5), 2636-2641.

Siddiqui, S. V., Chatterjee, U., Kumar, D., Siddiqui, A., & Goyal, N. (2008). Neuropsychology of prefrontal cortex. *Indian J Psychiatry, 50*(3), 202-208. doi:10.4103/0019-5545.43634

Simos, P., Fletcher, J., Sarkari, S., Billingsley, R., Denton, C., & Papanicolaou, A. (2007). Altering the brain circuits for reading through intervention: a magnetic source imaging study. *Neuropsychology, 21*, 485-496.

Smallwood, J., Gorgolewski, K. J., Golchert, J., Ruby, F. J., Engen, H., Baird, B., . . . Margulies, D. S. (2013). The default modes of reading: modulation of posterior cingulate and medial prefrontal cortex connectivity associated with comprehension and task focus while reading. *Front Hum Neurosci, 7*, 734. doi:10.3389/fnhum.2013.00734

Smits, M., Jiskoot, L. C., & Papma, J. M. (2014). White matter tracts of speech and language. *Semin Ultrasound CT MR, 35*(5), 504-516. doi:10.1053/j.sult.2014.06.008

Sroka, M. C., Vannest, J., Maloney, T. C., Horowitz-Kraus, T., Byars, A. W., & Holland, S. K. (2015). Relationship between receptive vocabulary and the neural substrates for story processing in preschoolers. *Brain Imaging Behav, 9*(1), 43-55. doi:10.1007/s11682-0149342-8

Stanovich, K. E., & Siegel, L. S. (1994). Phenotypic Performance Profile of Children with Reading Disabilities - a Regression-Based Test of the Phonological-Core Variable-Difference Model. *J Educ Psychol, 86*(1), 24-53. doi:Doi 10.1037/0022-0663.86.1.24

Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *Neuroimage, 44*(2), 489-501.

Sun, X., Song, S., Liang, X., Xie, Y., Zhao, C., Zhang, Y., . . . Gong, G. (2017). ROBO1 polymorphisms, callosal connectivity, and reading skills. *Hum Brain Mapp*. doi:10.1002/hbm.23546

Szaflarski, J. P., Schmithorst, V. J., Altaye, M., Byars, A. W., Ret, J., Plante, E., & Holland, S. K. (2006). A longitudinal functional magnetic resonance imaging study of language development in children 5 to 11 years old. *Ann Neurol, 59*(5), 796-807. doi:10.1002/ana.20817

Tang, Y. Y., Tang, Y., Tang, R., & Lewis-Peacock, J. A. (2017). Brief Mental Training Reorganizes Large-Scale Brain Networks. *Front Syst Neurosci, 11*, 6. doi:10.3389/fnsys.2017.00006

Thothathiri, M., Kim, A., Trueswell, J. C., & Thompson-Schill, S. L. (2012). Parametric effects of syntactic-semantic conflict in Broca's area during sentence processing. *Brain Lang, 120*(3), 259-264. doi:10.1016/j.bandl.2011.12.004

Tomasi, D., & Volkow, N. D. (2012). Resting functional connectivity of language networks: characterization and reproducibility. *Mol Psychiatry, 17*(8), 841-854. doi:10.1038/mp.2011.177

van Bergen, E., van der Leij, A., & de Jong, P. F. (2014). The intergenerational multiple deficit model and the case of dyslexia. *Front Hum Neurosci, 8*, 346. doi:10.3389/fnhum.2014.00346

Vandermosten, M., Boets, B., Poelmans, H., Sunaert, S., Wouters, J., & Ghesquiere, P. (2012). A tractography study in dyslexia: neuroanatomic correlates of orthographic, phonological and speech processing. *Brain, 135*(Pt 3), 935-948. doi:10.1093/brain/awr363

Vandermosten, M., Hoeft, F., & Norton, E. S. (2016). Integrating MRI brain imaging studies of pre-reading children with current theories of developmental dyslexia: A review and quantitative meta-analysis. *Curr Opin Behav Sci, 10*, 155-161. doi:10.1016/j.cobeha.2016.06.007

Vanderwal, T., Kelly, C., Eilbott, J., Mayes, L. C., & Castellanos, F. X. (2015). Inscapes: A movie paradigm to improve compliance in functional magnetic resonance imaging. *Neuroimage*. doi:10.1016/j.neuroimage.2015.07.069

Verhoeven, L., van Leeuwe, J., Irausquin, R., & Segers, E. (2016). The unique role of lexical accessibility in predicting kindergarten emergent literacy. *Read Writ, 29*, 591-608. doi:10.1007/s11145-015-9614-8

Vigneau, M., Beaucousin, V., Herve, P. Y., Duffau, H., Crivello, F., Houde, O., . . . TzourioMazoyer, N. (2006). Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. *NeuroImage, 30*(4), 1414-1432. doi:10.1016/j.neuroimage.2005.11.002

Vogel, A. C., Petersen, S. E., & Schlaggar, B. L. (2014). The VWFA: it's not just for words anymore. *Front Hum Neurosci, 8*, 88. doi:10.3389/fnhum.2014.00088

Vukovic, R. K., & Siegel, L. S. (2006). The double-deficit hypothesis: a comprehensive analysis of the evidence. *J Learn Disabil, 39*(1), 25-47. doi:10.1177/00222194060390010401

Vydrova, R., Komarek, V., Sanda, J., Sterbova, K., Jahodova, A., Maulisova, A., . . . Kyncl, M. (2015). Structural alterations of the language connectome in children with specific language impairment. *Brain Lang, 151*, 35-41. doi:10.1016/j.bandl.2015.10.003

Wagner, A. D., Pare-Blagoev, E. J., Clark, J., & Poldrack, R. A. (2001). Recovering meaning:

left prefrontal cortex guides controlled semantic retrieval. *Neuron, 31*(2), 329-338.
Wagner, R. K., & Torgesen, J. K. (1987). The nature of phonological processing and its causal role in the acquisition of reading skills. *Psychological Bulletin, 101*, 192-212.
Weiss-Croft, L. J., & Baldeweg, T. (2015a). Maturation of language networks in children: A systematic review of 22years of functional MRI. *Neuroimage*. doi:10.1016/j.neuroimage.2015.07.046
Weiss-Croft, L. J., & Baldeweg, T. (2015b). Maturation of language networks in children: A systematic review of 22years of functional MRI. *NeuroImage, 123*, 269-281. doi:10.1016/j.neuroimage.2015.07.046
Wiig, E. H., Nielsen, N. P., Minthon, L., McPeek, D., Said, K., & Warkentin, S. (2002). Parietal lobe activation in rapid, automatized naming by adults. *Percept Mot Skills, 94*(3 Pt 2), 1230-1244. doi:10.2466/pms.2002.94.3c.1230
Wilke, M. (2014). Isolated assessment of translation or rotation severely underestimates the effects of subject motion in FMRI data. *PLoS One, 9*(10), e106498. doi:10.1371/journal.pone.0106498
Willems, G., Jansma, B., Blomert, L., & Vaessen, A. (2016). Cognitive and familial risk evidence converged: A data-driven identification of distinct and homogeneous subtypes within the heterogeneous sample of reading disabled children. *Res Dev Disabil, 53-54*, 213-231. doi:10.1016/j.ridd.2015.12.018
Wilson, A. M., Deri Armstrong, C., Furrie, A., & Walcot, E. (2009). The mental health of canadians with self-reported learning disabilities. *J Learn Disabil, 42*(1), 24-40. doi:10.1177/0022219408326216
Wise, T., Marwood, L., Perkins, A. M., Herane-Vives, A., Joules, R., Lythgoe, D. J., . . . Arnone, D. Arnone, D. (2017). Instability of default mode network connectivity in major depression: a two-sample confirmation study. *Transl Psychiatry, 7*(4), e1105. doi:10.1038/tp.2017.40
Wolf, E. S. N. a. M. (2012). Rapid Automatized Naming (RAN) and Reading Fluency: Implications for Understanding and Treatment of Reading Disabilities. *Annu. Rev. Psychol., 63*(1), 427–452. doi:10.1146/annurev-psych-120710-100431
Wu, K., Taki, Y., Sato, K., Hashizume, H., Sassa, Y., Takeuchi, H., . . . Fukuda, H. (2013). Topological organization of functional brain networks in healthy children: differences in relation to age, sex, and intelligence. *PLoS One, 8*(2), e55347. doi:10.1371/journal.pone.0055347
Wu, S. Y., Li, Y. H., Ran, L., Fu, P., Li, Z. G., & Yao, J. H. (2003). [Active surveillance on Listeria monocytogenes in seven kinds of food in 11 provinces of China in 2001]. *Zhonghua Liu Xing Bing Xue Za Zhi, 24*(8), 657-660.
Xia, M., Wang, J., & He, Y. (2013). BrainNet Viewer: a network visualization tool for human brain connectomics. *PLoS One, 8*(7), e68910. doi:10.1371/journal.pone.0068910
Xiao, Y., Brauer, J., Lauckner, M., Zhai, H., Jia, F., Margulies, D. S., & Friederici, A. D. (2016). Development of the Intrinsic Language Network in Preschool Children from Ages 3 to 5 Years. *PLoS One, 11*(11), e0165802. doi:10.1371/journal.pone.0165802
Xiao, Y., Friederici, A. D., Margulies, D. S., & Brauer, J. (2015). Longitudinal changes in resting-state fMRI from age 5 to age 6years covary with language development. *Neuroimage, 128*, 116-124. doi:10.1016/j.neuroimage.2015.12.008

Yamada, Y., Stevens, C., Dow, M., Harn, B. A., Chard, D. J., & Neville, H. J. (2011). Emergence of the neural network for reading in five-year-old beginning readers of different levels of pre-literacy abilities: an fMRI study. *Neuroimage, 57*(3), 704-713. doi:10.1016/j.neuroimage.2010.10.057

Yuan, W., Altaye, M., Ret, J., Schmithorst, V., Byars, A. W., Plante, E., & Holland, S. K. (2009). Quantification of head motion in children during various fMRI language tasks. *Hum Brain Mapp, 30*(5), 1481-1489. doi:10.1002/hbm.20616

Zhang S, L. C. (2012). Functional connectivity mapping of the human precuneus by resting state fMRI. *Neuroimage, 59*(4), 3548-3562. doi:10.1016/j.neuroimage.2011.11.023.

Zhao, Z., Huang, T., Tang, C., Ni, K., Pan, X., Yan, C., . . . Luo, Y. (2017). Altered resting-state intra- and inter- network functional connectivity in patients with persistent somatoform pain disorder. *PLoS One*, *12*(4), e0176494. doi:10.1371/journal.pone.0176494

Zhong, J., Rifkin-Graboi, A., Ta, A. T., Yap, K. L., Chuang, K. H., Meaney, M. J., & Qiu, A. (2014). Functional networks in parallel with cortical development associate with executive functions in children. *Cereb Cortex, 24*(7), 1937-1947. doi:10.1093/cercor/bht051

Zhu, L., Fan, Y., Zou, Q., Wang, J., Gao, J. H., & Niu, Z. (2014). Temporal reliability and lateralization of the resting-state language network. *PLoS One, 9*(1), e85880. doi:10.1371/journal.pone.0085880

Zielinski, B. A., Gennatas, E. D., Zhou, J., & Seeley, W. W. (2010). Network-level structural covariance in the developing brain. *Proc Natl Acad Sci U S A, 107*(42), 18191-18196. doi:10.1073/pnas.1003109107

Zubrick, S. R., Taylor, C. L., & Christensen, D. (2015). Patterns and Predictors of Language and Literacy Abilities 4-10 Years in the Longitudinal Study of Australian Children. *PLoS One, 10*(9), e0135612. doi:10.1371/journal.pone.0135612

Appendix A

Regions of Interest	MNI Coordinates			Pediatric Coordinates		
	x	y	z	x	y	z
Left Hemisphere						
Angular gyrus (ANG)	-48	-52	38	-39	-42	30
Superior temporal gyrus (STG)	-53	-31	9	-43	-25	7
Inferior frontal gyrus, pars triangularis (IFGtr)	-48	32	6	-39	26	5
Right Hemisphere						
Angular gyrus (ANG)	48	-52	38	39	-42	30
Superior temporal gyrus (STG)	53	-31	9	43	-25	7
Inferior frontal gyrus, pars triangularis (IFGtr)	52	32	6	43	26	5

Table 2. Coordinates for regions of interest (ROI) in standard MNI and Pediatric Template space. The left hemispheric ROI were selected from word reading and linguistic task brain activation meta-analyses for children (Houde et al., 2010) and adults (Bolger, Perfetti, & Schneider, 2005). Where the right hemispheric ROI regions were manually selected to correspond to the same regions within the right hemisphere. All coordinates were expanded to create spheres of equal size (2mm^3, 6mm radius). The pediatric coordinates are based on the standard asymmetrical high-resolution 2mm^3 pediatric template, optimized for children aged 33- 44 months, developed by the McGill McConnell Brain Imaging Center (Fonov, 2009).