CHARACTERIZING AND PREDICTING GROWTH IN READING SKILLS IN CHILDREN WITH DEVELOPMENTAL DYSLEXIA THROUGH FUNCTIONAL NEUROIMAGING

by

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ABSTRACT

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Children with developmental dyslexia exhibit deficits in a wide variety of reading skills that are attributable to underlying deficits in phonological processing. Functional neuroimaging studies show that these children exhibit differences in the activation of a distributed network of brain regions during reading tasks when compared to children without reading impairments. It is anticipated that children with dyslexia who are enrolled in a reading intervention will exhibit significant growth in reading skills over the course of their intervention. Furthermore, research has shown that activation of a distributed network of brain regions during reading tasks can be used to predict changes in children's reading skills over time. The present dissertation extends this research to a sample of children who completed a reading intervention. The specific goal of this dissertation is to predict children with dyslexia's growth in reading skills following a 2-year multisensory intervention through analyses of behavioral test scores and activation during two functional magnetic resonance imaging (fMRI) tasks completed prior to the intervention.

Analyses suggested that the children in the present study exhibited significant growth in their reading skills. Initial measures of single word reading predicted growth in phonological decoding and reading comprehension. Furthermore, brain activation across both tasks was associated with growth in reading skills throughout the intervention. A general pattern emerged from the fMRI analyses such that negative correlations with growth in reading were more likely to occur in occipito-temporal regions and positive correlations with growth in reading were more likely to occur in prefrontal regions. These analyses help to further identify pre-intervention factors that may facilitate reading skill improvements in children with developmental dyslexia.

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CHAPTER 1

INTRODUCTION

1.1 Reading and Developmental Dyslexia

Reading is a fundamental skill that assists individuals in acquiring information about the world around them. To be able to read alphabetic languages, such as English, one must be able to convert the symbols of written language into segmental units of sound. The awareness that spoken, as well as written, words are made up of separate sound units requires phonological processing abilities incorporating phonological awareness and phonics. These are basic skills that one must master to be able to read fluently and to comprehend text (Liberman, 1973; Liberman & Shankweiler, 1985). Unfortunately, approximately 5—17% of children experience such extensive difficulties learning to read that they are diagnosed with developmental dyslexia (Lyon, Shaywitz, & Shaywitz, 2003; 2007). Reading difficulties can lead to problems in multiple areas of an individual's life. Children who fail to learn to read are more likely to experience limited occupational and social advancements, suffer persistent health problems, become a teen parent, and end up in prison (Alliance for Excellent Education, 2008; 2006a; 2006b; Bureau of Justice Statistics, 2005; Harlow, 2003).

When provided with appropriate instruction, children with dyslexia can learn to read (e.g., Lovett et al., 2000). Yet, a nontrivial number of children with developmental dyslexia fail to respond to interventions (e.g., Torgesen, 2000). It is important to identify which child will succeed and which child may require more intensive instruction in order to learn to read so that interventions can be refined to better assist those children who continue to struggle with reading despite completing current interventions. In this regard, being able to predict whether a child with dyslexia will have a positive response to reading interventions may help to identify additional skills that should be emphasized during interventions designed for children who do not respond to current treatments (Frijters et al., 2011; Hoeft, Ueno et al., 2007; Hoeft et al., 2011; Shaywitz et al., 2004).

In the present dissertation, I used data acquired as part of a longitudinal study of children with developmental dyslexia to investigate the ability to predict growth in reading skills during a 2-year intervention using standardized reading test scores obtained throughout the intervention and brain activation evoked by phonological processing tasks obtained prior to the onset of the intervention. By doing so, I am extending the current literature on behavioral and functional neuroimaging factors associated with growth in reading skills. To date this research has focused on children with a wide range of reading skills who may or may not have been currently enrolled in a variety of reading intervention programs (Gantman, 2007; Hoeft Ueno et al., 2007; Hoeft et al., 2011). This study replicates the past research by predicting growth in phonological decoding using both standardized test scores and neuroimaging measures. More importantly, this study breaks new ground and extends the past research by focusing on a group of children with developmental dyslexia enrolled in a 2-year multisensory reading intervention and by predicting growth in both phonological decoding and reading comprehension. In order to be able to predict growth in reading skills in children with developmental dyslexia it is important to understand the cognitive processes needed to read and the specific areas where children with developmental dyslexia exhibit deficits in reading.

1.1.1 Components of Reading

Unlike spoken language, which is acquired naturally, reading is a relatively recent accomplishment in human evolution that requires extensive training in order for one to excel (Alexander & Slinger-Constant, 2004; Shaywitz, 2003; Turkletaub, Gareau, Flowers, Zeffrio, & Eden, 2003). In addition to the visual-spatial abilities needed to see written words, reading involves 3 component processes: orthographic, phonological, and semantic (Aaron, Joshi, & Williams, 1999; Fiez & Petersen, 1998; Price, 2000). First, orthographic processes refer to knowledge of letters and visual word forms (Aaron et al., 1999; Pugh et al., 1996). Next, phonological processes involve the ability to process the sound structure of language (National Institute of Child Health and Human Development, 2000). One specific phonological skill often observed to be deficient in children with dyslexia is phonological awareness. Phonological awareness is the ability to identify sublexical phonological components within a word. Examples of this ability include identifying the onset and rime of a word, segmenting the syllables in a word, blending phonemes to form words, and exhibiting awareness of the structure of the individual phonemes within a word (i.e., phonemic awareness). The mapping of the written letters (i.e., graphemes) to letter sounds (i.e., phonemes) is phonics, a fundamental skill that is taught as part of reading education. Additionally, children are taught to phonologically decode words in order to sound out and pronounce a written word (Beck & Juel, 1995; Liberman, 1973; Liberman & Shankweiler, 1985). Once individual words have been identified, readers must use semantic processes to identify the meaning of the words. Semantic processes involve using stored knowledge to comprehend material (Coltheart, Rastle, Perry, Landgon, & Ziegler, 2001; Poldrack et al., 1999).

1.1.2 Current Definition and Diagnosis of Dyslexia

Yet, not every person is able to effectively engage in the component processes of reading. When an individual experiences deficits in the ability to effectively and concurrently engage orthographic, phonological, and semantic processes that are unexpected given her cognitive abilities and exposure to effective classroom instruction, she is described as being dyslexic. Developmental dyslexia is a specific learning disability that is neurobiological in origin, and is characterized behaviorally by difficulties with accurate and/or fluent word recognition, spelling, and decoding abilities (Fletcher, Francis, Morris, & Lyon, 2005; Fletcher, Lyon, Fuchs, & Barnes, 2007; Lyon, 1995; Lyon et al., 2003; 2007). Diagnostic criteria for dyslexia often include a significant discrepancy between a child’s reading skills and intellectual abilities. However, in their meta-analysis, Steubing et al. (2002) observed negligible differences in reading skills between children diagnosed with dyslexia who did and did not exhibit a discrepancy between their intellectual abilities and reading skills. Additionally, brain activation in poor readers does not differ based on whether children exhibit a discrepancy between reading skills and IQ measures (Tanaka et al, 2011). Fletcher et al. (2005) recommend against using an aptitude-achievement discrepancy model for diagnosing learning disorders because such models do not predict response to intervention. Furthermore, children with mild to moderate mental retardation who received a comprehensive reading instruction demonstrated greater gains in phonemic awareness and phonological decoding than children with similar intellectual abilities who did not receive specialized reading instruction (Allor, Mathes, Roberts, Cheatham, & Champlin, 2010). These results suggest that children with mild mental retardation can positively respond to comprehensive reading instruction. In regards to the primary deficits associated with developmental dyslexia, there are several theories and the most prominent is the phonological deficit hypothesis (for a review see Ramus et al., 2003). This theory posits that children with dyslexia experience a core deficit in their ability to isolate the individual sublexical units of sounds that comprise words.

1.1.3 Phonological Deficits

In this regard, reading involves understanding the alphabetic principle. In other words, a child needs to know that words consist of phonemes, the smallest unit of sound in a language, and that the letters in written words correspond to these phonemes. In accordance with the phonological deficit hypothesis, children with developmental dyslexia tend to be unable to break spoken words down into their individual phonemes and this prevents children from mapping those sounds to their corresponding letter or letter combinations. In short, the children have deficits in phonological awareness and phonemic awareness (Ramus et al., 2003; Shaywitz, Mody, & Shaywitz, 2006; Shaywitz & Shaywitz, 2005). This inability to isolate the individual phonemes within words prevents them from learning the correspondence between phonemes and graphemes.

Although there is evidence for difficulties in rapid auditory processing, as well as deficits in visual, magnocellular, and cerebellar domains, these deficits do not appear to be necessary nor sufficient to diagnose dyslexia (Demonet, Taylor, & Chaix, 2004; Eden, Stein, Wood, & Wood, 1994; Fawcett, Nicholson, & Dean, 1996; Lyon & Krasnegor, 1996; McCrory, Mechelli, Firth, & Price, 2005; Ramus, 2003; Ramus et al., 2003; Tallal, Miller, & Fitch, 1993; Temple et al., 2000; Wolf & Bowers, 1999). Rather, an overarching language deficit in phonological awareness and phonological processing is present with each of these specific sensorimotor factors (Shaywitz, Lyon, & Shaywitz, 2006; Shaywitz & Shaywitz, 2005; Shaywitz et al., 1998).

Phonological awareness is a fundamental skill needed to read languages, such as English, that are based on the alphabetic principle. If individuals are unable to effectively map phonemes and graphemes due to deficits in phonological awareness, then they are highly likely to experience difficulties in phonological decoding of written words. Furthermore, measures of phonology have been shown to account for a substantial proportion of the variance in young children's single word reading skills (Hammill, Mather, Allen, & Roberts, 2002). In this regard, deficits in phonological awareness may lead to deficits in phonological decoding and single word identification. Deficits in the ability to read isolated words can lead to decreased reading fluency and reading comprehension. Reading comprehension is more easily obtained when individuals read fluently and have an adequate vocabulary in order to support meaning-based processing of words. Deficits in phonological decoding and single word reading may impair a child's ability to read fluently because cognitive resources are needed to decode each individual word (Chard, Vaughn, & Tyler, 2002; Meyer & Felton, 1999). Thus, children with developmental dyslexia experience an inability to read due to phonological deficits that impair phonological decoding and single word identification. Decreased phonological decoding and single word identification make it more difficult for a child to read text fluently. Furthermore, reading slowly and laboriously makes it more difficult for the child to understand and comprehend information presented in text (Lyon, 1995; Lyon et al., 2003; Meyer & Felton, 1999).

1.2 Neurobiology of Dyslexia

Developmental dyslexia is neurobiological in origin (Fawcett & Nicolson, 2007). Historically, descriptions of patients with intact speech abilities and intellect who were unable to read began appearing in the 19th century at roughly the same time that scientists began to demonstrate that some cognitive functions could be localized to specific brain regions. Two of the most famous pieces of evidence for functional specialization are that damage to Broca's area, the posterior portion of the third convolution in the left hemisphere (i.e., the posterior left inferior frontal gyrus), results in the loss of the ability to speak, and that damage to Wernicke's area, the left posterior superior temporal gyrus, results in a loss of the understanding of speech (Geschwind, 1972; Price, 2000; Richardson, 2001). Advances in functional neuroimaging have tremendously increased the ability to investigate the brain regions associated with different component reading processes and the phonological deficits characteristic of developmental dyslexia.

1.2.1 Brain Regions Associated with Reading

Researchers who have conducted functional neuroimaging studies requiring children and adults to engage in reading-related processes have identified a distributed network of brain regions associated with reading (e.g., Price, 2000; Pugh et al., 1996; Pugh et al., 2000; Shaywitz & Shaywitz, 2005). Research suggests single word reading to activate a distributed network encompassing 3 major brain areas, (1) the frontal lobe, (2) the parieto-temporal region, and (3) the occipito-temporal region (Epelbaum et al., 2008; Hoeft, Mayler et al., 2007; Hoeft et al., 2006; Horwitz, Rumsey, & Donohue, 1998; McCandliss, Cohen, & Dehaene, 2003; Price, 2000; Pugh et al., 1996; Pugh et al., 2000; Shaywitz et al., 2002; Shaywitz & Shaywitz, 2005).

First, several frontal lobe regions, including the lateral orbital gyrus, dorsolateral prefrontal cortex, and the inferior frontal gyrus exhibit activation during single word reading (Pugh et al., 1996; Pugh et al., 2000; Seghier & Price, 2010). Activation of Broca's region, encompassing Brodmann areas (BA) 44 and 45, in particular, is associated with reading (for a review see Heim et al., 2005). Although reading recruits both BA 44 and BA 45, there appears to be a dissociation in function such that more dorsal and posterior regions of the left inferior frontal gyrus (i.e., BA 44 and the opercularis) are recruited during phonological decoding (e.g., reading pseudowords; Bokde, Tagamets, Friedman, & Horwitz, 2001; Crosson et al., 1999; Heim et al., 2005; Jobard, Crivello, & Tzourio-Mazoyer, 2003; Kircher, Nagels, Kirner-Veselinovic, & Krach, 2011). In contrast, ventral and anterior regions of the inferior frontal gyrus (i.e., BA 45 and the triangularis) are recruited during tasks requiring semantic or meaning-based processing, such as retrieving real words from a mental lexicon (Crosson et al., 1999; Heim et al., 2005; Meinzer et al., 2009).

Second, parieto-temporal brain regions activated during single word reading tasks include the left middle and superior temporal gyri, supramarginal gyrus, and inferior parietal gyrus (Pugh et al., 2000; Seghier, Schofield, Ellis, & Price, 2008; Vigneau et al., 2011; Wise et al., 1991). Left posterior superior temporal activation (i.e., BA 22) appears to be a potential early predictor of reading skills because it is associated with phonological awareness abilities (Torgesen, 2000). Furthermore, rhyme judgments and listening to speech activates the left posterior superior temporal gyrus (Crosson et al., 2007; Pugh et al., 1996). In addition, semantic category judgments also activate this area (Pugh et al., 1996). Meanwhile, the left inferior parietal and supramarginal gyri are involved in the storage and manipulation of verbal information in working memory (Vigneau et al., 2011; Wise et al., 1991).

Third, single word reading also evokes activation in occipito-temporal areas. The left posterior fusiform gyrus (i.e., BA 20) is often referred to as the visual word form area (VWFA; McCandliss et al., 2003; McCandliss, & Noble, 2003). This brain region integrates visual form information with other properties that are essential in uniquely identifying a word, such as meaning and sound patterns (Devlin, Jamison, Gonnerman, & Matthews, 2006; McCandliss et al., 2003; Vigneau, Jobard, Mazoyer, & Tzourio-Mazoyer, 2005).

As reading skills (i.e., phonological decoding, single word reading, reading rate and reading accuracy) improve between 6 to 22 years of age, reading-related brain activation becomes more strongly lateralized to the left hemisphere. Specifically, brain activation increases in left middle temporal and inferior frontal gyri, and decreases in right extrastriate areas associated with visual and orthographic processing (Turkeltaub et al., 2003). However, homologous regions in the right hemisphere are often engaged when typically developing individuals read or listen to words. Activation of the right inferior frontal gyrus, particularly BA 44, occurs during language tasks requiring verbal material to be manipulated in working memory, especially when there is an increase in working memory load. Activation of the right superior temporal gyrus facilitates auditory processing (Gaillard et al., 2003; Vigneau et al., 2011). Furthermore, evidence suggests that left and right inferior frontal regions are structurally and functionally connected to each other and this may facilitate bilateral frontal activation (Ben-Shachar, Eckert, & Dougherty, 2006; Bokde et al., 2001; Farris et al., 2011; Gathercole, 1999; Stanberry et al., 2006; Toro, Fox, & Paus, 2008). Therefore, although reading predominantly involves activation of frontal, parieto-temporal, and occipito-temporal areas in the left hemisphere, homologous activation in right hemisphere areas may facilitate phonological processing.

1.2.2 Neurobiological Evidence of Dyslexia

Although there is inter-subject variability in the absolute level of brain activation, children with dyslexia do not activate the reading network brain regions in the same manner that typical readers do. Unlike typically developing children, individuals with dyslexia do not engage the left posterior temporo-parietal and occipito-temporal portions of this network of brain regions (Backes et al., 2002; Cao, Bitan, & Booth, 2008; Cao, Bitan, Chou, Burman, & Booth, 2006; Hoeft et al., 2006; Hoeft, Mayler et al., 2007; Lyon et al. 2003; Maisog, Einbinder, Flowers, Turkeltaub, & Eden, 2008; Meyler, Keller, Cherkassky, Gabrieli, & Just, 2008; Pugh et al., 2000; Richlan, Kronbichler, & Wimmer, 2009; Schulz et al., 2009; Shaywitz, 2003; Shaywitz et al., 2006; Shaywitz & Shaywitz, 2005; Shaywitz et al., 2004; Shaywitz et al., 2003; Simos et al., 2002; Simos, Breier, Fletcher, Foorman, & Mouzaki, 2001; Temple et al., 2001). Instead, children with dyslexia commonly exhibit bilateral activation of the left and right inferior frontal lobes (Brunswick, McCrory, Price, Firth, & Firth, 1999; Hoeft, Mayler et al., 2007; MacSweeney, Brammer, Waters, & Goswami, 2008; Odegard, Ring, Smith, Biggan, & Black, 2008; Salmelin, Service, Kiesila, Uutela, & Salonen, 1996; Shaywitz et al., 2002; Shaywitz & Shaywitz, 2004; Simos et al., 2007a, 2007b).

Upon completion of reading interventions, especially those focused on phonological awareness and decoding skills, children with dyslexia exhibit activation of bilateral inferior frontal gyrus, and left posterior parieto-temporal and occipito-temporal areas, including the left posterior superior temporal gyrus and fusiform gyrus (Davis et al., 2011; Eden et al., 2004; Meyler et al., 2008; Odegard et al., 2008; Shaywitz et al., 2004; Simos et al., 2002; Simos et al., 2007a; 2007b; Temple et al., 2003). For example, Shaywitz et al. (2004) observed children with dyslexia who completed a year-long phonologically-based intervention to exhibit increased activation in the left inferior frontal and middle temporal gyri during a letter identification task as compared to their brain activation measured pre-intervention. Also, using a longitudinal design, Simos et al. (2002) observed increased left posterior superior temporal gyrus activation after children with dyslexia completed an eight-week phonological intervention. Such findings of changes in brain activation patterns suggest that children with dyslexia exhibit neurological changes that complement the behavioral evidence of reading skill growth.

In this regard, Simos et al. (2002) observed that the amount of growth in measures of phonological decoding exhibited by children with dyslexia after an intervention could be accounted for by the amount of increased activation observed in the left posterior superior temporal gyrus during a pseudoword rhyming task. Similarly, Temple et al. (2003) observed increased activation in left temporo-parietal cortex during a letter rhyming task to be positively correlated with changes in oral language abilities in children with dyslexia who completed a month long auditory and language processing intervention. Furthermore, improvements in a behavioral measure of phonological awareness positively correlated with increased right inferior frontal activation following the intervention (Temple et al., 2003).

Thus, it would appear that successfully remediating the behavioral reading deficits characteristic of dyslexia results in improved function in key brain regions. In particular, successful intervention is associated with increased activation in the superior temporal lobe and the inferior frontal gyrus (Shaywitz et al., 2004; Simos et al., 2002; Temple et al., 2003). Such findings are critically important because they provide compelling evidence of the impact that successful interventions can have on improving the actual brain function of children with dyslexia. However, not all children respond well to current intervention methods.

1.3 Predicting Growth in Reading Skills through Brain Activation

Thus, there is a critical need to be able to identify which children will best respond to current phonologically based intervention methods and which children will continue to struggle with reading even after receiving such interventions. Initial efforts in this area were aimed at predicting treatment outcomes using behavioral measures obtained prior to treatment onset. In this regard, measures of phonological awareness, rapid naming, phonological decoding, and single word reading have all been observed to reliably predict growth in reading outcomes in children with dyslexia (Frijters et al., 2011; Hammill et al., 2002; Morris et al., 1998; Nelson, Benner, & Gonzalez, 2003). While these efforts were informative, they failed to account for a substantial amount of the variance in treatment outcomes. Given that developmental dyslexia is neurobiological in origin there is reason to believe that predictive models including measurements of the underlying neurobiology of children with dyslexia obtained prior to intervention might help to account for variance in treatment outcomes.

More recently, this research has been expanded to identify how well measures of brain activation obtained prior to intervention can reliably predict reading outcomes (Maurer et al., 2009; Shaywitz et al., 2002; Hoeft Ueno et al., 2007; Hoeft et al., 2011). In one such study, behavioral measures of phonological skills and event-related brain potentials measuring speech-like sound processing obtained in kindergarten from children at risk for developing reading problems were used to predict performance on a general reading measure in second, third, and fifth grade (Maurer et al., 2009). Specifically, a measure of syllable segmentation abilities in kindergarten could explain 19% of the variance in the number of correct words read per minute in second, third, and fifth grades, whereas a regression model including the measure of syllable segmentation and event-related brain potentials measuring a late mismatch negativity to phonemes in kindergarten could explain 50% of the variance in the same outcome measures. While this study included children at risk for developing dyslexia due to the presence of a diagnosis in a first-degree relative, who are an important group to target for early interventions, the authors did not regulate the type of reading instruction the children received throughout the study. Furthermore, this study did not specifically examine the ability to predict reading comprehension, which is the ultimate goal of reading, from the measures that were obtained.

In a related study, Hoeft, Ueno et al. (2007) observed a combination of behavioral measures of reading ability, functional neuroimaging measures of brain activation, and structural neuroimaging measures of gray and white matter density to be better at predicting later decoding skills than behavioral reading measures alone. Specifically, in a group of children with a wide range of reading skills a regression model that included scores on measures of phonological decoding, calculation, and spelling could account for 65% of the variance in decoding skills measured approximately one academic year later. Yet, a regression model that included a combination of (1) scores on measures of phonological decoding, calculation, and spelling, (2) brain activation in the right fusiform gyrus during a word rhyming fMRI task, and (3) measures of gray and white matter density was able to account for 81% of the variance in later decoding skills (Hoeft, Ueno et al., 2007). While this study is informative in regards to reading development more generally, due to the heterogeneity of the sample, it can not speak directly to the ability of brain imaging data to predict growth in reading skills observed in children with developmental dyslexia.

Yet, researchers have looked specifically at children with developmental dyslexia. In one such study, right inferior frontal activation during a word rhyme task positively correlated with improvements observed in single word reading skills over 2.5 years in children with developmental dyslexia (Hoeft et al., 2011). Furthermore, extending past research to focus specifically on children with developmental dyslexia, regression models including either behavioral measures of reading skills, or functional and structural neuroimaging measures, or both behavioral and neuroimaging measures were used to predict changes in single word reading test scores over a 2 year period. Analogous to Hoeft Ueno et al. (2007), a model combining behavioral and neuroimaging measures exhibited the greatest predictive utility (Gantman, 2007). Specifically, a regression model including (1) baseline behavioral measures of phonological decoding and reading comprehension, (2) baseline measures of activation in the right inferior frontal gyrus during a word rhyme task, and (3) baseline measures of gray matter volume in the right parietal lobe explained 78% of the variance in the changes observed over 2 years in single word reading test scores of children diagnosed with developmental dyslexia (Gantman, 2007). While these researchers looked specifically at children with dyslexia, it is difficult to interpret their findings because it is unknown what the children did during the 2.5 years that elapsed between assessment periods. The children may have been receiving regular classroom instruction, or they may have been enrolled in a variety of different reading interventions.

Unfortunately, studies that investigate neural correlates that predict future reading abilities in children with dyslexia have not focused on a group of children who have all received a similar intervention (i.e., Gantman, 2007; Hoeft Ueno et al., 2007; Hoeft et al., 2011). Therefore, research is needed to attempt to replicate and extend findings of the ability to predict change in reading skills from behavioral and functional neuroimaging measures to a group of children enrolled in a specific reading intervention. Specifically, it would be informative to investigate whether such predictive models are able to account for changes in reading abilities in children for which substantial change in reading abilities is anticipated to occur over the course of intervention. To address this need the current study includes a sample of children diagnosed with developmental dyslexia who all completed a specific 2-year multisensory reading intervention.

In addition, comprehension is the ultimate goal of reading, yet many of the functional neuroimaging studies of interventions for children with dyslexia focus almost exclusively on developing phonological processing, emphasizing either phonological awareness or phonics skills or both skill sets (Alexander & Slinger-Constant, 2004; National Institute of Child Health and Human Development, 2000). Interventions are needed that provide direct instruction in vocabulary, reading fluency and reading comprehension and a question facing educators is the extent to which improving single word reading abilities in children with dyslexia will result in improvements in reading comprehension (Alexander, & Slinger-Constant 2004; National Institute of Child Health and Human Development, 2000). In this regard, Simos et al. (2007b) observed significant gains in phonological decoding, reading fluency, and reading comprehension following an 8-week phonological intervention in a group of children with persistent reading difficulties, as well as continued gains in those skills after a subsequent 8-week intervention focused on developing reading fluency. Furthermore, more persistent activation in bilateral posterior middle temporal gyrus was observed following each of the interventions (Simos et al., 2007b). Such findings suggest that the models using behavioral and functional neuroimaging measures to predict growth in phonological decoding and single word reading skills should be extended to investigate the ability to predict growth in other skills such as reading comprehension. To address this need the current research extends past studies predicting growth in phonological decoding to also predict growth in reading comprehension.

Furthermore, one of the overarching goals of research in developmental dyslexia is to improve current intervention methods not only for children who positively respond to current programs, but also, and perhaps more importantly, for children who do not exhibit growth in their reading skills after completing currently available intervention programs. It would be invaluable to be able to prevent any child from experiencing exacerbated levels of anxiety and frustration because all of the time and effort she has devoted to an intervention program does not appear to be paying off. Thus, being able to identify factors obtained pre-intervention that predict growth in reading skills may help educators to identify the children who are most likely to continue to struggle with reading. Potentially, the children who do not respond positively to intervention will be those children with the lowest measures of the pre-intervention factors associated with reading growth. Furthermore, the early identification of children who are less likely to respond to interventions and subsequent description of how these children differ from children who do respond to current interventions may help to motivate future research designed to modify intervention programs so that all children are successfully and effortlessly able to read. To address this need, the current study identifies pre-intervention factors associated with growth in reading that can hopefully be used in subsequent research to distinguish between children with dyslexia who are more or less likely to respond to reading interventions.

1.4 Goal of Proposed Study

The current study uses data acquired during a longitudinal study of reading development in children with unimpaired reading and children with dyslexia to identify whether functional neuroimaging data obtained prior to the onset of treatment can prospectively predict how well a child with dyslexia will respond to intervention. During the course of the longitudinal study, a sample of children diagnosed with developmental dyslexia completed a 2-year reading intervention using *Take Flight: A Comprehensive Intervention for Students with Dyslexia* (*Take Flight*; Avrit et al., 2006), which integrates the five components of effective reading instruction recommended by the National Reading Panel meta-analysis (i.e., phonemic awareness, phonics skills, vocabulary, fluency, and reading comprehension; National Institute of Child Health and Human Development, 2000). Behavioral assessments of reading (i.e., single word reading, phonological decoding, reading efficiency, reading fluency, and reading comprehension) and reading-related basic cognitive skills (i.e., phonological awareness, phonological memory, and rapid naming) were obtained prior to intervention, one year into the intervention and at the conclusion of the intervention. In addition, prior to intervention participants completed two functional tasks measuring phonological processing during MR scanning. One fMRI task measured brain activation observed while children completed a phonics task. For this task, children mapped phonemes and graphemes. The other fMRI task measured brain activation evoked by a phonological awareness task. For this task children identified if two words, which were represented by color line drawings, rhymed.

The goal of this dissertation is to identify which factors can best predict growth in phonological decoding and reading comprehension observed during the intervention. Specifically, whether baseline behavioral, baseline functional neuroimaging, or a combination of behavioral and functional neuroimaging measures acquired at baseline are best able to predict growth in reading skills. I hypothesize that a combination of pre-intervention measures of standardized tests of reading skills (i.e., behavioral measures) and functional neuroimaging activation during phonological tasks will be best able to predict growth in phonological decoding and reading comprehension compared to either behavioral or functional neuroimaging measures alone. In order to achieve this overarching goal I tested two sets of hypotheses.

1.4.1 Characterization of Growth in Reading

The first set of hypotheses allows me to examine any changes observed throughout this study in the reading skills of the children with dyslexia and the non-impaired readers. First, I hypothesize that children with dyslexia will experience growth such that all reading skills are within the average range by the end of the intervention. Second, I hypothesize that the reading test scores of children with dyslexia may still be significantly lower than those of the children without reading impairments. These two hypotheses and any potential growth in the children's reading skills can be characterized by addressing three questions with each question leading to one sub-hypothesis: (1) Does participation in *Take Flight* lead to growth in reading skills? Sub-hypothesis 1 states that growth will occur in all measures of reading and related skills by the end of the intervention for the children with dyslexia, but the growth may not be apparent during the first year for reading efficiency, reading fluency, and reading comprehension. (2) If growth occurs, do standardized assessments of reading skills place a child's abilities within the normal range? Sub-hypothesis 2 states that pre-intervention scores of the children with dyslexia will be below average, whereas one year into intervention and post-intervention scores will be within the average range by either not differing from the low end of average range, or being higher than the low end of the average range. (3) Are reading ability differences between children with dyslexia and age-matched non-reading impaired children eliminated? Sub-hypothesis 3 states that at pre-intervention children with dyslexia will score significantly less than children without reading impairments on measures of reading and related skills, and they may continue to do so at the end of the intervention.

1.4.2 Predicting Growth in Reading Skills

The second set of hypotheses address the primary goal of this dissertation, which is to identify factors associated with growth in reading skills in children with dyslexia. In order to achieve this goal it is helpful to present conceptual models of what factors predict growth in reading skills. First, there is a behavioral model (see Figure 1.1). The behavioral model can be used to determine the contribution of pre-intervention levels of phonological awareness, phonological memory, rapid naming, single word reading, reading efficiency, and reading fluency to growth in phonological decoding and/or reading comprehension.

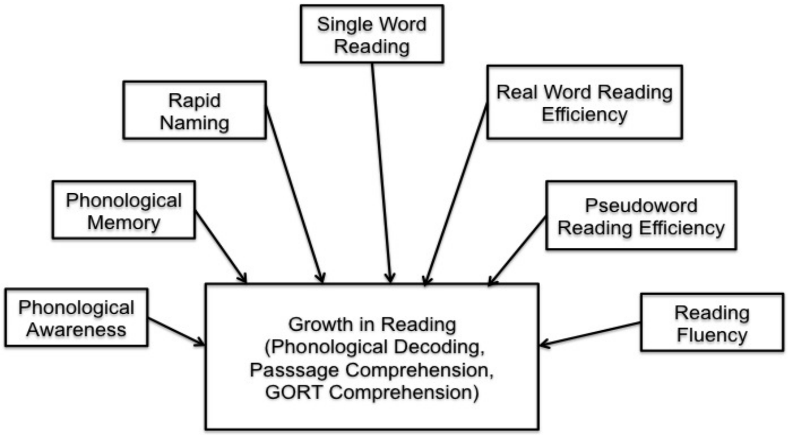

Figure 1.1 Behavioral model

Second, there is a functional neuroimaging model (see Figure 1.2). The functional neuroimaging model can be used to determine the contribution of voxelwise brain activation to phonological stimuli from each fMRI task completed prior to intervention on the growth observed in phonological decoding and reading comprehension.

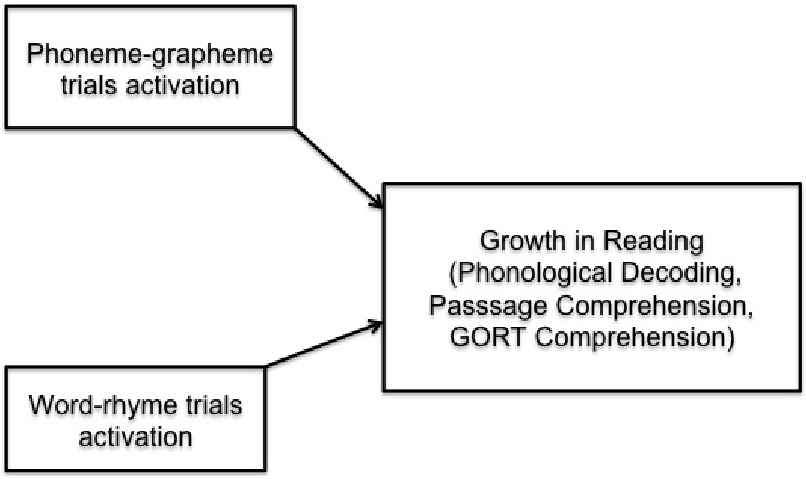

Figure 1.2 Functional neuroimaging model

Finally, the third conceptual model examines the contribution of both the pre-intervention measures of reading skills obtained behaviorally and through brain activation on growth in phonological decoding and reading comprehension (see Figure 1.3).

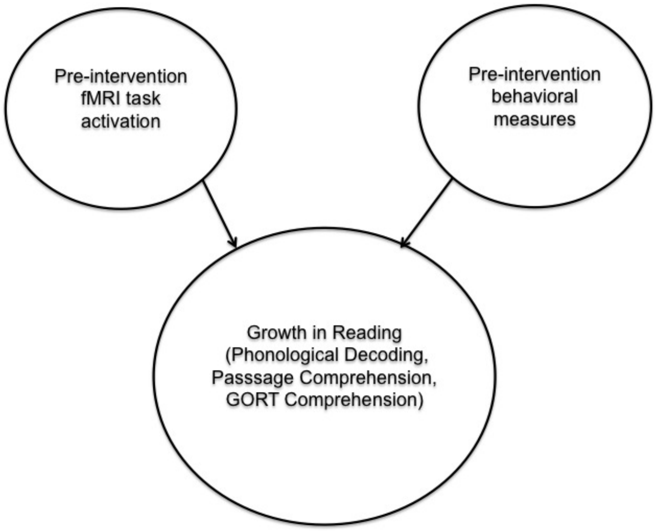

Figure 1.3 Combined model

The current study has a small sample size and thus lacks adequate statistical power to be able to properly test these conceptual models. However, critical components of the models can be tested by exploring the relationship between each of the potential predictor variables (i.e., pre-intervention reading skills and brain activation during phonological fMRI tasks) and the outcome variables (i.e., growth in phonological decoding and reading comprehension). It is especially important to examine the effect size of these relationships in order to refine the conceptual models so that they can be tested in future studies. As such, I have two hypotheses. First, I hypothesize that pre-intervention behavioral measures of reading skills will be correlated with growth in phonological decoding and reading comprehension. Second, I hypothesize that pre-intervention measures of fMRI activation during phonological processing tasks will be correlated with growth in phonological decoding and reading comprehension. Although, I predict that there will be significant correlations between my predictor variables and outcome measures, the direction of the relationship between each reading skill and each cluster of brain activation could vary such that some predictors are positively correlated with growth in phonological decoding and reading comprehension and other predictors are negatively correlated.

CHAPTER 2

METHOD

2.1 Participants

Thirty native English speakers (12 female; 29 right-handed) between the ages of 6 – 14 years old, who did not have hearing loss, neurological disorders, psychiatric problems, or implants or devices which included metal of any sort that were contraindicative for MRI scanning, participated in the study. Fifteen of the children were diagnosed with dyslexia. A diagnosis of dyslexia was made when reading skills were determined to be deficient and were unexpected given a child's age/grade and other cognitive abilities. These reading and cognitive abilities were measured through the norm-referenced instruments described below. The remaining children did not have reading impairments (i.e., control group of non-impaired readers). These two groups of children did not reliably differ from each other in age nor reported attention problems, as measured by the SNAP DSM-IV, which included Inattention, Hyperactivity, and Oppositional Defiant subscales (Bussing et al., 1998), all *t*s < 1.89. Although seven of the fifteen children with dyslexia had a comorbid diagnosis of an attention disorder, the certified academic language therapists who administered the intervention only noted attention problems as noticeably impacting classroom behavior in three children during the first year and two children during the second year of the intervention. Formal diagnostic information regarding attention disorders was not available for the non-impaired readers.

Additionally, chi-square analyses confirmed that gender and handedness, as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), were not significantly associated with being either a non-impaired reader or a child with dyslexia, all χ^2s < 1.04. Parent's education level provided a proxy for socioeconomic status. Information was available for 29 mothers and 28 fathers of the participants. Twenty-seven of the parents had a college or graduate level degree, 20 had completed some college, and the remaining 10 graduated from high school. Chi-square analyses confirmed that the amount of mother's and father's education was not significantly associated with the children belonging to either group of participants, $\chi^2(4) = 2.48$, $p = .65$; $\chi^{2(}4) = 4.36$, $p = .36$. A family history demographic questionnaire revealed that 10 of the children with dyslexia and 6 of the non-reading impaired children had a family member with either a diagnosis of a learning disability, dyslexia, or a history of trouble learning to read. The identified family member who also had trouble learning to read was limited to being a sibling or uncle for two of the dyslexic and two of the non-reading impaired children. The remaining identified family members were parents.

The children with dyslexia had full scale IQ scores within the average range ($M = 96.33$, $SE = 2.26$), but their IQ scores were significantly lower than the non-impaired readers ($M = 117.4$, $SE = 3.49$), $t(28) = 5.06$, $p < 0.001$. A listing of average demographic characteristics (i.e., age, gender, handedness, attention problems), and full scale IQ for each group of children is provided in Table 2.1, along with mean performance on reading and reading-related basic cognitive skills obtained prior to the children with dyslexia beginning *Take Flight* (i.e., pre-intervention).

Table 2.1. Group profiles prior to intervention

	Control children (n=15) Prior to Intervention	Children with Dyslexia (n=15) Prior to Intervention
Age in months	112 (24.24)	111.2 (24.21)
Gender[1]	0.40 (0.51)	0.40 (0.51)
Handedness[2]	0.00 (0.00)	0.07 (0.26)
Full-scale IQ[3]	117.4 (13.52)	96.33 (8.77)
Attention Problems[4]		
Inattention	0.57 (0.54)	0.97 (0.66)
Hyperactivity	0.32 (0.40)	0.47 (0.36)
Oppositional Defiant	0.33 (0.29)	0.37 (0.50)
Reading Related Skills		
Phonological Memory SS[5]	105.4 (7.53)	98 (11.66)
Rapid Naming SS[5]	95.5 (13.20)	79.64 (11.48)
Phonological awareness SS[5]	109.47 (16.54)	89.07 (11.67)
Reading Skills		
Single Word Reading[6]	117.07 (17.44)	84.13 (7.51)

Table 2.1 - *Continued*

Phonological Decoding[7]	115.8 (15.98)	86.6 (7.69)
Reading Efficiency		
Pseudowords[8]	107.73 (14.90)	81.67 (6.03)
Real words[9]	106.07 (14.78)	78.33 (9.20)
Fluency[10]	10.33 (3.54)	3.4 (1.68)
Comprehension		
GORT Comprehension[11]	13.13 (2.39)	7.4 (2.26)
WRMT Passage Comprehension[12]	109.93 (9.39)	82.53 (9.57)

Note. Standard deviations are provided in parentheses; SS = Standard Score. [1] Percent Female; [2] Percent left-handed; [3]Wechsler Full-Scale IQ; [4]SNAP-IV DSM inattention, hyperactivity, and oppositional defiant subscales; [5]Comprehensive Test of Phonological Processing; [6] Woodcock Reading Mastery Test Word Identification; [7] Woodcock Reading Mastery Test Word Attack; [8] Test of Word Reading Efficiency Phonemic Decoding; [9] Test of Word Reading Efficiency Sight Words; [10]Gray Oral Reading Test Fluency; [11]Gray Oral Reading Test Comprehension; [12]Woodcock Reading Mastery Test Passage Comprehension.

Furthermore, Table 2.2 provides demographic characteristics and full scale IQ for the children with dyslexia who do and do not have a comorbid diagnosis of an attention disorder. These children did not differ from each other in regards to age or full scale IQ, all ts < 1.49, and gender and handedness were not significantly associated with the children with dyslexia having a comorbid diagnosis of attention disorders, all χ^2s < 0.95. The children without comorbid diagnoses of attention disorders had higher reading fluency scores prior to intervention, $t(13) = 3.02$, $p = 0.01$, but did not differ from the children with comorbid dyslexia and attention disorder diagnoses on any of the other reading skills prior to intervention, all ts < 1.01.

Table 2.2. Group profiles prior to intervention for children with dyslexia who did and did not have a comorbid diagnosis of attention disorders

	Children with Dyslexia & Attention Disorder (n=7) Prior to Intervention	Children with Dyslexia (n=8) Prior to Intervention
Age in months	120.71 (27.24)	102.88 (19.15)
Gender[1]	0.43 (0.54)	0.38 (0.52)
Handedness[2]	0.00 (0.00)	0.13 (0.35)
Full-scale IQ[3]	96.71 (8.94)	96 (9.23)
Attention Problems[4]		
Inattention	1.38 (0.45)	0.61 (0.62)
Hyperactivity	0.67 (0.37)	0.29 (0.27)
Oppositional Defiant	0.59 (0.65)	0.17 (0.22)
Reading Related Skills		
Phonological Memory SS[5]	96.14 (16.04)	99.63 (6.70)
Rapid Naming SS[5]	80.29 (12.11)	79 (11.75)

Table 2.2 - *Continued*

Phonological awareness SS[5]	92.29 (9.14)	86.25 (13.47)
Reading Skills		
Single Word Reading[6]	84.71 (3.90)	83.63 (9.96)
Phonological Decoding[7]	85.43 (7.28)	87.63 (8.38)
Reading Efficiency		
Pseudowords[8]	80 (6.76)	83.13 (5.33)
Real words[9]	77 (10.28)	79.5 (8.68)
Fluency[10]	2.29 (1.38)	4.38 (1.30)
Comprehension		
GORT Comprehension[11]	7.57 (2.07)	7.25 (2.55)
WRMT Passage Comprehension[12]	82.29 (7.43)	82.75 (11.65)

Note. Standard deviations are provided in parentheses; SS = Standard Score. [1] Percent Female; [2] Percent left-handed; [3]Wechsler Full-Scale IQ; [4]SNAP-IV DSM inattention, hyperactivity, and oppositional defiant subscales; [5]Comprehensive Test of Phonological Processing; [6] Woodcock Reading Mastery Test Word Identification; [7] Woodcock Reading Mastery Test Word Attack; [8] Test of Word Reading Efficiency Phonemic Decoding; [9] Test of Word Reading Efficiency Sight Words; [10]Gray Oral Reading Test Fluency; [11]Gray Oral Reading Test Comprehension; [12]Woodcock Reading Mastery Test Passage Comprehension.

2.2 Behavioral Measures

Participants' performance on reading and reading-related basic cognitive skills were obtained through individually administered norm-referenced tests acquired prior to intervention, one year into the intervention, and in the case of the children with dyslexia, at the conclusion of the 2-year intervention program. Graduate research assistants with advanced training in neuropsychological assessments conducted the behavioral testing under the supervision of research personnel and licensed diagnosticians at Texas Scottish Rite Hospital for Children (TSRHC). Measures were selected based on 1) their alignment with converging evidence relevant to the measurement of component skills essential to the development of proficient reading; 2) their established psychometric properties; and 3) their frequent use in studies of dyslexia.

Prior to the intervention, children were screened for attention problems by obtaining parental reports through the SNAP-IV Rating Scale for children. The SNAP-IV Rating Scale was a revision of the Swanson, Nolan and Pelham (SNAP) Questionnaire (Bussing et al., 1998), which contained items that summarized the DSM-IV (1994) criteria for both subsets of symptoms (i.e., inattention and hyperactivity/impulsivity) for Attention-Deficit/Hyperactivity

Disorder (ADHD), as well as items from the DSM-IV criteria for Oppositional Defiant Disorder since it often is present in children with ADHD. The SNAP-IV was based on a 0 to 3 rating scale (Not at All = 0, Just A Little = 1, Quite A Bit = 2, and Very Much = 3). Subscale scores on the SNAP-IV were calculated by summing the scores on the items in each subset and dividing by the number of items in that subset. The score for any subset was expressed as the Average Rating-Per-Item.

Handedness was determined using the Edinburgh Handedness Inventory (Oldfield, 1971). The child heard a list of 22 activities (i.e., writing, drawing, throwing) and indicated which hand she preferred to use to complete the activity. A laterality quotient was calculated by subtracting the sum of left hand responses from those for the right hand, dividing this number by the sum of left and right hand responses, then multiplying the result by 100. Handedness scores were converted into a dichotomous variable such that positive values for the laterality quotient indicated right-handedness and negative values indicated left-handedness.

The assessment of IQ only occurred at the first time point or through diagnosis of dyslexia to ensure comparability in IQ between groups of participants. Since the assessment of intelligence occurred through the diagnostic procedure for the children with dyslexia, full-scale IQ scores were obtained from a variety of norm-referenced instruments. Eight children with dyslexia had scores from the Wechsler Intelligence Scale for Children Fourth Edition (WISC-IV; Psychological Corporation, 2003a; 2003b), one child had scores from the WISC Third Edition (WISC-III, Wechsler, 1991), one child had scores from the Wechsler Preschool and Primary Scale of Intelligence Third Edition (WPPSI-III; Wechsler, 2002), and the remaining five children with dyslexia had scores from the Wechsler Abbreviated Scale of Intelligence (WASI; Psychological Corporation, 1999). All of the children without reading impairments completed the WASI as part of their pre-intervention testing session.

Three reading-related cognitive skills were measured: phonological memory, rapid naming, and phonological awareness, as indicated in Table 2.3. Phonological memory was assessed with the *Phonological Memory* composite score of the Comprehensive Test of Phonological Processing (CTOPP; Wagner, Torgeson, & Rashotte, 1999). This measure had subtests that required children to repeat strings of digits and isolated nonwords. Rapid naming was assessed with the *Rapid Naming* composite score of the CTOPP (Wagner et al., 1999). This measure had subtests that required children to name a series of digits or letters that were presented on a page. The child's awareness of and ability to access the sound structure of spoken language was assessed with the *Phonological Awareness* composite score of the CTOPP (Wagner et al., 1999). The phonological awareness subtests had participants blend spoken word parts together (e.g., "put together /bl/ /end/") and delete word parts ("say tiger. Now say tiger without the /g/"). These composite scores had reported coefficient alphas of 0.83, 0.92, and 0.90 (Wagner et al., 1999). These skills have been observed to reliably predict treatment response as well as to be deficient in children with dyslexia (Frijters et al., 2011; Morris et al., 1998; Nelson et al., 2003; Torgesen, 2000; Torgesen, Wagner, & Rashotte, 1999).

Table 2.3. Measures of reading and reading-related skills

Skill	Tests
Reading Related Skills	
Phonological Memory	CTOPP Phonological Memory
Rapid Naming	CTOPP Rapid Naming
Phonological Awareness	CTOPP Phonological Awareness
Reading Skills	
Single Word Reading	WRMT Word Identification
Phonological Decoding	WRMT Word Attack
Reading Efficiency	TOWRE Sight Words; TOWRE Phonemic Decoding
Reading Fluency	GORT Fluency
Reading Comprehension	GORT Comprehension; WRMT Passage Comprehension

Five types of reading skills were also investigated: single word reading, phonological decoding, reading efficiency, reading fluency, and reading comprehension, as indicated in Table 2.3. *Single Word reading* was measured by the Word Identification subtest of the Woodcock Reading Mastery Test – Revised/NU (WRMT; Woodcock, 1998), which had children read isolated real words. *Phonological decoding* was measured by the Word Attack subtest of the WRMT, which required children to read isolated pseudowords. The Word Attack subtest had a reported split-half reliability of 0.89 and the Word Identification subtest had a reported split-half reliability of 0.91 (Woodcock, 1998). Reading pseudowords requires phonological decoding, whereas real words can be read by sight using knowledge from memory. Yet, intercorrelation coefficients between performance on the Word Attack and Word Identification subtests range from 0.70 to 0.79 for children in first, third, and fifth grades (Woodcock, 1998).

R*eading efficiency* involves the children's ability to read lists of isolated pseudowords and real words under timed conditions. *Reading efficiency* was measured by the Sight Words and Phonemic Decoding subtests of the Test of Word Reading Efficiency (TOWRE; Torgeson et al., 1999), which had a reported coefficient alpha of 0.94. For these measures the children were timed while reading columns of real words or pseudowords.

The children's *reading fluency*, or the ability to read text accurately and fluently, was measured by the Gray Oral Reading Test 4 (GORT; Wiederholt & Bryant, 2001), which had a reported coefficient alpha of 0.94. For this measure the time a child took to read a passage out loud and the number of errors made were calculated and combined.

Finally, *reading comprehension* was assessed in two ways. The Passage Comprehension subtest of the WRMT (Woodcock, 1998) assessed comprehension through the children's single word responses to silently read CLOZE-type probes and had a reported split-half reliability of 0.90. GORT Comprehension scores reflected the children's ability to correctly respond to orally presented multiple-choice questions after having read a story aloud (Wiederholt & Bryant, 2001) and had a reported coefficient alpha of 0.95.

Most of the children with dyslexia had their reading abilities initially evaluated by licensed diagnosticians at TSRHC several months prior to the pre-intervention testing. The median time that elapsed between this initial evaluation and pre-intervention testing was 7.23 months (*SD* = 8.57). During the initial evaluation, some of the behavioral measures of reading were different from the ones included in the present study.

Importantly, *phonological awareness* and *rapid naming* were assessed using the corresponding composite scores from the CTOPP (Wagner et al., 1999) that were included in the present study. There were no statistically reliable differences between the children's phonological awareness and rapid naming abilities during the initial evaluation (M = 94.9, SE = 3.29; M = 82.55, SE = 3.55) and pre-intervention testing sessions (M = 95.5, SE = 2.58; M = 81.45, SE = 3.15), $t(9) = 0.28$, $p = 0.79$; $t(10) = 0.43$, $p = 0.68$.

Single word reading was assessed with a different measure than the one included in the present study. Specifically, *single word reading* was initially measured in fourteen of the children with dyslexia by the Word Reading subtest of the Wechsler Individual Achievement Test Second Edition (WIAT-II; Psychological Corporation, 2002), which had children read isolated real words. There were no statistically reliable differences between the children with dyslexia's single word reading abilities during the initial evaluation (M = 81.07, SE = 2.04) and pre-intervention (M = 78.14, SE = 2.15) testing sessions on this measure, $t(13) = 1.94$, $p = 0.70$.

The initial evaluation measures were only available from some of the children with dyslexia included in the present study, yet these analyses suggest that the children's reading skills did not significantly change during the time that elapsed between their initial evaluation and the pre-intervention testing. Furthermore, in a sample of 93 children who had completed the same intervention, a similar pattern was observed such that there was no significant growth in phonological awareness or single word reading between the initial evaluation and pre-intervention testing (*Take Flight* Research Summary, 2011).

Additionally, the Numerical Operations subtest of the WIAT-II, which has a reported internal consistency of 0.91 (Psychological Corporation, 2002), was included as a measure of the children's mathematical skills in order to provide another means to validate if the intervention would lead to changes in the reading skills of the children with dyslexia over and above any changes that may be observed over time. Children were required to solve computational problems of increasing complexity including addition, subtraction, multiplication, and division.

2.3 Intervention

All participants with dyslexia received treatment for their reading difficulties over a 2-year intervention period at a hospital-based learning disabilities clinic, the Luke Waites Center for Dyslexia and Learning Disorders at TSRHC, using *Take Flight* (Avrit et al., 2006), a published curriculum that integrates the five components of effective reading instruction recommended by the National Reading Panel meta-analysis (National Institute of Child Health and Human Development, 2000). *Phonemic Awareness* included a systematic exploration of the articulation of phonemes that was taught explicitly first, then fully integrated into other skills. All phoneme-grapheme correspondence rules were introduced and time was allotted for practice towards automaticity in the application of *Phonics Skills* as well as guided reading practice with controlled and regular text. In order to emphasize articulation, students were instructed to reference mouth position and movement through the use of mirrors, mouth pictures and instructor modeling during phonological awareness, reading and spelling instruction. Morphological knowledge was used to build *Vocabulary*, and word relationships were taught in the context of reading text. *Fluency* instruction incorporated guided and timed repeated reading of decodable words, phrases, and connected text. A combination of strategies and techniques were used for instruction in *Reading Comprehension*, including comprehension monitoring, question generation, story structure, summarizing, and making inferences. Students also learned how to utilize graphic and semantic organizers when reading narrative and expository texts. The instruction was delivered over 132 lessons to small groups of 4 - 6 students by certified academic language therapists, who had acquired a minimum of 700 supervised clinical teaching hours delivering reading instruction to children with developmental dyslexia. The intervention lasted for approximately 90 minutes a day for 4 days each week over 2 academic years for a total of 230 hours of direct instruction. The median time elapsed between the pre-intervention testing and start of the intervention was 11 days (*SD* = 6.14).

In addition, seven of the children with dyslexia had received some form of specialized reading tutoring (n = 4) or speech therapy (n = 2) or both (n = 1) prior to beginning *Take Flight*. Although the children received various forms of treatment for different lengths of time, all seven of these children received this supplemental instruction before the initial evaluation at TSRHC. Furthermore, Table 2.4 provides demographic characteristics and full scale IQ for the children with dyslexia who did and did not receive specialized reading or speech therapy instruction prior to *Take Flight*. These children did not differ from the other children with dyslexia in regards to full scale IQ or attention problems, all *t*s < 1.58, and gender and handedness were not significantly associated with the children with dyslexia having received prior specialized reading instruction or speech therapy, all χ^2s < 1.61. However, the children with dyslexia who received additional instruction prior to *Take Flight* were younger than the other children with dyslexia *t*(13) = 2.38, *p* = 0.03. Prior to beginning *Take Flight* children who received additional specialized instruction had higher reading fluency scores and marginally lower phonological awareness scores than the children with dyslexia who did not receive additional specialized instruction, *t*(13) = 2.14, *p* = 0.05, *t*(13) = -1.97, *p* = 0.07. The children did not reliably differ on other reading skills when they began *Take Flight*, all *t*s < 1.40. Additionally, there were only two children who had a comorbid diagnosis of attention disorders and dyslexia and had received some form of specialized instruction prior to beginning *Take Flight*.

Table 2.4. Group profiles prior to intervention for children with dyslexia who had and had not received reading tutoring and/or speech therapy prior to *Take Flight*

	Children with Dyslexia & Prior Tutoring (n=7) Prior to Intervention	Children with Dyslexia & No Prior Tutoring (n=8) Prior to Intervention
Age in months	97.43 (9.09)	123.25 (27.32)
Gender[1]	0.57 (0.54)	0.25 (0.46)
Handedness[2]	0.00 (0.00)	0.13 (0.35)
Full-scale IQ[3]	92.71 (8.85)	99.5 (7.89)

Table 2.4 - *Continued*

Attention Problems[4]		
Inattention	0.84 (0.64)	1.08 (0.70)
Hyperactivity	0.32 (0.17)	0.60 (0.44)
Oppositional Defiant	0.18 (0.24)	0.53 (0.62)
Reading Related Skills		
Phonological Memory SS[5]	97.86 (5.40)	98.13 (15.71)
Rapid Naming SS[5]	84 (6.75)	76.38 (13.55)
Phonological awareness SS[5]	83.29 (9.46)	94.13 (11.53)
Reading Skills		
Single Word Reading[6]	84.71 (10.23)	83.63 (4.75)
Phonological Decoding[7]	86.57 (8.06)	86.63 (7.91)
Reading Efficiency		
Pseudowords[8]	79.86 (6.31)	83.25 (5.70)
Real words[9]	78.14 (8.97)	78.50 (10.01)
Fluency[10]	4.29 (1.38)	2.63 (1.60)
Comprehension		
GORT Comprehension[11]	6.57 (2.15)	8.13 (2.23)
WRMT Passage Comprehension[12]	81.86 (10.90)	83.13 (8.97)

Note. Standard deviations are provided in parentheses; SS = Standard Score. [1] Percent Female; [2] Percent left-handed; [3]Wechsler Full-Scale IQ; [4]SNAP-IV DSM inattention, hyperactivity, and oppositional defiant subscales; [5]Comprehensive Test of Phonological Processing; [6] Woodcock Reading Mastery Test Word Identification; [7] Woodcock Reading Mastery Test Word Attack; [8] Test of Word Reading Efficiency Phonemic Decoding; [9] Test of Word Reading Efficiency Sight Words; [10]Gray Oral Reading Test Fluency; [11]Gray Oral Reading Test Comprehension; [12]Woodcock Reading Mastery Test Passage Comprehension.

2.4 Image Acquisition

MR images were acquired from each participant during a separate session before the children with dyslexia began the intervention program. During their scanning session, participants were first prepared through training in a full-scale mock-up MR scanner. Whole brain images were acquired on a 3-T Siemens Trio MR scanner (Siemens Medical Solutions, Erlangen, Germany). Structural images were acquired from 160 0.94 mm sagittal slices using a multiplanar rapidly-acquired gradient echo sequence (flip angle = 9°; TE = 3.96 ms; TR = 2250 ms; inplane resolution = 0.94 mm x 0.94 mm; matrix size = 256 x 240). For active-state fMRI, a 129 volume timeseries of 46 2.97 mm axial slices was acquired using a T2*-weighted echo planar imaging (EPI) sequence (flip angle = 90°; TE = 20 ms; TR = 2000 ms; voxel dimension = 2.97 mm x 2.97 mm x 3 mm; inplane resolution = 2.97 mm x 2.97 mm; matrix size = 74 x 74; slice thickness = 3 mm; slice-to-slice gap = 3 mm). Each child completed one run of each of the tasks described below.

2.5 Active-state fMRI Tasks

Participants completed two event-related active-state tasks measuring brain activation associated with reading. Visual stimuli were projected onto a screen placed at the foot of the MR scanner gurney using a front projection system connected to a computer running E-Prime (Psychology Software Tools, Inc.), a suite of computer applications that allowed for the development of customized stimulus delivery and data collection programs. Participants viewed the screen using a mirror mounted to the head coil. Auditory stimuli were presented to participants over a pair of headphones. Behavioral responses were recorded with a pair of 2-button fiber-optic response boxes.

2.5.1 Phoneme-Grapheme Mapping Task

The event-related phoneme-grapheme mapping task was a modified version of the phonics task that was used in the Connecticut Longitudinal study of reading development (e.g., Pugh et al., 2000; Shaywitz & Shaywitz, 2005; Shaywitz et al. 2002). This modified task has previously been used to investigate differences in brain activation and functional connectivity between children who had completed *Take Flight* and did or did not exhibit improvements in decoding skills as well as children without reading impairments (Farris et al., 2011; Odegard et al., 2008). For phoneme-grapheme trials, the child heard a spoken phoneme (e.g. /b/) and two letters (B, D) were presented in the center of the screen for 4 seconds. The child pressed a button in her right or left hand to indicate the side of the screen where the letter matching the sound was displayed (see Figure 2.1A). Tone-symbol control trials were used to control for the effects of simple sensory, motor, and decision responses involved in the phoneme-grapheme trials (see Figure 2.1B). For these trials, a 220-Hz tone was presented and two visual symbols (. * or *.) were shown. The child pressed a button to identify the position of the asterisk relative to the period (i.e., left or right). Each phoneme-grapheme or tone-symbol trial lasted 4 seconds followed by a fixation point at the center of the screen that remained visible for 2 to 10 seconds for an average inter-stimulus interval of 6 seconds resulting in a run of this task lasting 4.5

minutes. Before MR scanning, the task was completed on a laptop computer outside the MR scanner to verify that the child understood the instructions.

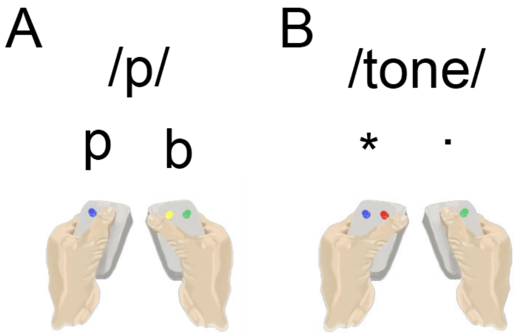

Figure 2.1 Phoneme-grapheme mapping task. Representation of (A) phoneme-grapheme trials and (B) tone-symbol trials.

See Tables 2.5 and 2.6 for accuracy and response time on the phoneme-grapheme and tone-symbol trials of the phoneme-grapheme mapping task completed inside the scanner for each group of participants. There were no differences in accuracy or latency to respond for either the phoneme-grapheme trials or the tone-symbol trials between the children with dyslexia and non-impaired readers, or between the subsamples of the children with dyslexia with and without comorbid diagnoses of attention disorders, or between those who did or did not receive prior instruction, all *t*s < 1.84.

Table 2.5. Group profiles on the phoneme-grapheme mapping task

	Control children (n=15)	Children with Dyslexia (n=15)
Accuracy		
Phoneme	0.91 (0.07)	0.88 (0.13)
Tone	0.99 (0.03)	0.98 (0.06)
Latency		
Phoneme	1661.02 (409.79)	1820.22 (317.86)
Tone	1229.54 (300.74)	1427.65 (293.49)

Note. Accuracy reported as proportion correct and latency reported in milliseconds. Standard deviations are provided in parentheses.

Table 2.6. Group profiles for the subgroups of children with dyslexia on the phoneme-grapheme mapping task

	Dyslexia & Attention Disorder (n=7)	Dyslexia (n=8)	Prior Instruction (n=7)	Dyslexia & No Prior Instruction (n=8)
Accuracy				
Phoneme	0.94 (0.04)	0.83 (0.16)	0.88 (0.08)	0.89 (0.16)
Tone	0.96 (0.09)	1.00 (0.0)	0.96 (0.09)	1.00 (0.0)
Latency				
Phoneme	1748.82 (373.64)	1882.69 (259.91)	1940.94 (423.94)	1714.58 (406.61)
Tone	1347.45 (351.39)	1497.81 (233.20)	1489.60 (240.12)	1373.44 (340.08)

Note. Accuracy reported as proportion correct and latency reported in milliseconds. Standard deviations are provided in parentheses.

2.5.2 Picture-Word Rhyming Task

A novel event-related picture-word rhyming task measuring phonological awareness was administered to the children in the present study. For this task, 24 color line drawings of monosyllabic real word objects were combined to form 12 rhyming pairs and 12 non-rhyming pairs. For training and explanation purposes, four additional words representing two rhyming pairs, which could be recombined to form two non-rhyming pairs, were also included. Prior to scanning all children identified each of the pictures that would be presented in the task to verify that they knew the name of the item and the label used in this study. If the child provided an incorrect response (i.e., rope instead of hose), she was provided the correct response and the item was repeated. All children provided the correct response to the items upon repetition and prior to scanning.

For word-rhyme trials the child saw two pictures of objects (i.e., dog and frog). The child pressed a button with her right or left hand to indicate if the pictures represented words that rhymed or not (see Figure 2.2A). Color-match trials were used to control for the effects of simple sensory, motor, and decision responses involved in the word-rhyme trials (see Figure 2.2B). For these trials two blocks of color (i.e., red and green) were presented and the child indicated if they matched (i.e., were the same color) or not. Each word-rhyme or color-match trial lasted 4 seconds followed by a fixation point at the center of the screen that remained visible for 2 to 10 seconds for an average inter-stimulus interval of 6 seconds resulting in a run of this task lasting 4.5 minutes. Before MR scanning, the task was completed on a laptop computer outside the MR scanner to verify that the child understood the instructions.

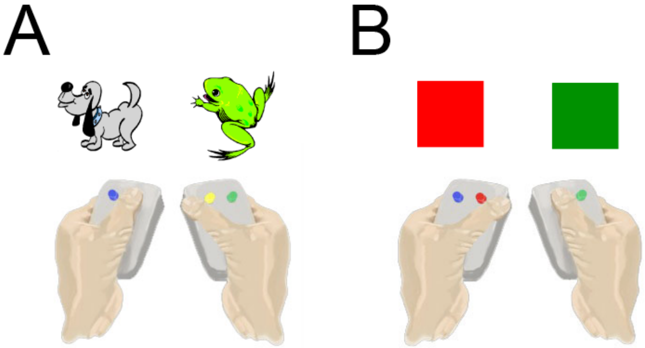

Figure 2.2 Picture-word rhyming task. Representation of (A) word-rhyme trials and (B) color-match trials.

See Tables 2.7 and 2.8 for accuracy and response time on the word-rhyme and color-match trials of the picture-word rhyming task completed inside the scanner for each group of participants. The non-impaired readers were more accurate on the word-rhyme trials than the children with dyslexia, $t(28) = 3.36$, $p = 0.002$. The children with a comorbid dyslexia and attention diagnosis were more accurate than the children with a single diagnosis of dyslexia, $t(13) = 2.46$, $p = 0.03$ on the word-rhyme trials, and the children who did not receive specialized instruction prior to *Take Flight* were more accurate than those who did, $t(13) = 3.12$, $p = 0.008$. There were no other significant differences in accuracy or latency on the picture-word rhyming task between any of the subgroups of children with dyslexia or between the children with dyslexia and the non-reading impaired children, all *t*s < 2.11.

Table 2.7. Group profiles on the picture-word rhyming task

	Control children (n=15)	Children with Dyslexia (n=15)
Accuracy		
Word	0.91 (0.11)	0.68 (0.24)
Color	0.98 (0.03)	0.92 (0.12)
Latency		
Word	2554.34 (338.58)	2415.95 (604.30)
Color	1322.65 (188.52)	1471.94 (558.46)

Note. Accuracy reported as proportion correct and latency reported in milliseconds. Standard deviations are provided in parentheses.

Table 2.8. Group profiles for the subgroups of children with dyslexia on the picture-word rhyming task

	Dyslexia & Attention Disorder (n=7)	Dyslexia (n=8)	Prior Instruction (n=7)	Dyslexia & No Prior Instruction (n=8)
Accuracy				
Word	0.82 (0.16)	0.56 (0.23)	0.52 (0.19)	0.82 (0.18)
Color	0.96 (0.09)	0.89 (0.14)	0.86 (0.15)	0.98 (0.06)
Latency				
Word	2591.84 (526.38)	2262.05 (659.44)	2326.73 (609.54)	2494.02 (630.05)
Color	1527.17 (1423.63)	1423.63 (357.83)	1504.89 (423.94)	1443.12 (317.66)

Note. Accuracy reported as proportion correct and latency reported in milliseconds. Standard deviations are provided in parentheses.

2.6 Data Processing (fMRI tasks)

Analyses of activation during the fMRI tasks was processed using procedures similar to those in Farris et al. (2011). Using Analysis of Functional NeuroImages software (AFNI; Cox, 1996) the slices within each volume were time-shifted to align the individual slices to the same temporal origin. Next, head motion was corrected using three-dimensional rigid body registration, the first 3 volumes from each EPI run collected prior to the magnetization stabilizing were discarded, and linear drift correction was applied. Then, AFNI's deconvolution was used to estimate hemodynamic response functions (HRF) for the phonological and control trials from each task (i.e., phoneme-grapheme and tone-symbol, or word-rhyme and color-match trials) relative to the fixation point baseline (Glover, 1999). The estimated HRF began at the onset of the event and included 16 s of signal. The estimated HRFs were spatially standardized to a pediatric brain template that had been created using pediatric brains acquired as part of the NIH MRI study of normal brain development (Fonov, Evans, McKinstry, Almli, & Colins, 2009; Fonov et al., 2011), and were spatially smoothed with a Gaussian filter with a full-width half-maximum value of 6 mm.

CHAPTER 3

DATA ANALYSIS AND ANTICIPATED RESULTS

Statistical analyses of behavioral measures were performed using the SPSS software package (SPSS inc, 2010), while a combination of SPSS and AFNI (Cox, 1996) was used for analyses incorporating fMRI data. The specific data analysis procedures for each hypothesis are described below.

3.1 Characterization of Growth in Reading Skills

Prior to addressing the primary goal of this dissertation, I will be characterizing any changes observed throughout this study in the reading skills of the participants. I hypothesize that the children with dyslexia who participated in the current longitudinal study will have experienced growth in reading skills, specifically in phonological awareness, single word reading, phonological decoding, reading efficiency, reading fluency, and reading comprehension. Additionally, it is not anticipated that the children will experience growth in their mathematics abilities. In order to test these hypotheses all of the standardized test scores from each participant at each time point have been entered into a SPSS database. Potential covariates of age, and attention problems will be examined through bivariate Pearson product-moment correlations to determine if these demographic characteristics are systematically related to each of the tested reading abilities of the children with dyslexia. If these variables are significantly correlated with reading performance (i.e., $p < 0.05$), they will be included as covariates in the following analyses. If the demographic characteristics are not systematically related to reading performance after controlling statistically for multiple comparisons, then they will not be included in the following analyses. Intellectual abilities will not be considered as a potential covariate as they do not predict response to intervention in learning-disabled populations, nor are they associated with reliable differences in brain activation during a phonological task (Fletcher et al., 2005; Steubing et al., 2002; Tanaka et al., 2011).

For the children with dyslexia, a series of 1 (skill) X 3 (time: pre-intervention, one year into intervention, end of intervention) within-participants repeated measures ANOVAs and subsequent pair-wise comparisons will be conducted for the measures of phonological awareness, phonological memory, rapid naming, reading fluency, WRMT passage comprehension, GORT comprehension, and numerical operations. Growth in the reading comprehension measures will be examined in separate analyses given that the tests are not only on different scales, but that they measure comprehension in different ways. Furthermore, standardized Z scores for the reading comprehension measures analyzed through repeated measures MANOVA yielded results that were similar to the univariate analyses.

Single word reading and phonological decoding involve reading isolated lists of real or pseudowords, whereas real and pseudoword reading efficiency involve reading isolated lists of real or pseudowords under timed conditions. As such, single word reading, phonological decoding, and real and pseudoword reading efficiency measurements obtained from subtests comprising the WRMT and the TOWRE will be examined through a 2 (word type: pseudoword, real word) x 2 (test form: untimed, timed) x 3 (time: pre-intervention, one year into intervention, end of intervention) repeated measures MANOVA with subsequent univariate analyses. Then, all reading and reading-related skills measured at each time point will be entered into a series of one-sample t-tests against a baseline identified as the low end of the average range for each particular measure in order to determine if the children with dyslexia have test scores that are not significantly different from the average range.

The reading skills of the children without reading impairments were only measured prior to intervention and one year later, thus, any changes in their reading skills and numerical operation abilities will be measured through t-tests comparing the first and second time points with the following exception. Change over time in single word reading, phonological decoding and real and pseudoword reading efficiency will be evaluated with a 2 (word type: real word, pseudoword) x 2 (test form: timed, untimed) x 2 (time: pre-intervention, one year into intervention) repeated measures MANOVA since the measurement of these constructs were obtained from subtests of the WRMT and TOWRE as described above. Finally, a series of two-sample t-tests will compare performance between the children with dyslexia and children without reading impairments for phonological memory, rapid naming, phonological awareness, single word reading, phonological decoding, real and pseudoword reading efficiency, reading fluency, both measures of reading comprehension, and numerical operation skills at both the first and second time points. Means and standard errors as well as significance tests will be reported and graphical depictions may also be included. Finally, in order to control the family-wise error rates significance levels of $p < 0.005$ will be considered significant in accordance with having applied a Bonferroni correction to analyses of the 10 reading and related skills. Thus, significance levels between $0.05 < p < 0.005$ will be considered marginally significant.

I hypothesize that by the end of the intervention, the children with dyslexia, as a group, will have exhibited growth in all of the measured reading and reading-related skills (i.e., phonological memory, rapid naming, phonological awareness, single word reading, phonological decoding, real and pseudoword reading efficiency, reading fluency, and reading comprehension). Although the children with dyslexia may have obtained scores within the average range, they may still exhibit lower scores than our particular sample of children without reading impairments.

3.2 Predicting Growth in Reading Skills

The following set of analyses will address the primary goal of this dissertation, which is to identify factors associated with growth in reading skills. I will be testing critical components of the behavioral, functional neuroimaging, and combined models that I outlined earlier by examining the relationship between each of the potential predictor variables (i.e., pre-intervention reading skills and brain activation during phonological fMRI tasks) and the outcome variables. Due to concerns about having sufficient statistical power given my small sample size, I will be examining measures of effect size in addition to noting significance levels for my analyses. Specifically, r^2 values, representing the proportion of variance accounted for by the relationship between the particular reading skill or area of task-associated brain activation under investigation and a particular measure of growth in reading, will be interpreted as a measure of effect size. According to Cohen (1988), values of 0.1 represent a small effect, 0.3 represent a medium effect, and 0.5 represent a large effect (Cohen, 1992).

The critical outcomes measures will be growth in phonological decoding and growth in two separate measures of reading comprehension. Specifically, the change over time (i.e., slope) measured between pre-intervention and the end of the intervention for WRMT Word Attack (i.e., phonological decoding), WRMT Passage Comprehension (i.e., first measure of reading comprehension), and GORT Comprehension (i.e., second measure of reading comprehension) standard scores will be the 3 separate dependent variables. First, I hypothesize that pre-intervention behavioral measures of reading skills will be correlated with growth in phonological decoding and reading comprehension. Second, I hypothesize that pre-intervention measures of fMRI activation during phonological processing tasks will be correlated with growth in phonological decoding and reading comprehension. Partial correlations between each dependent variable (i.e., change in WRMT Word Attack, WRMT Passage Comprehension, and GORT Comprehension) and potential covariates of age at time 1, and attention problems at time 1 controlling for pre-intervention scores on each of the dependent variables (i.e., pre-intervention WRMT Word Attack, WRMT Passage Comprehension, and GORT Comprehension) will be calculated to identify whether the potential covariates are systematically related to the outcome measures. If the potential covariates of age at time 1, and attention problems at time 1 are systematically related (i.e., $p < 0.05$) to the dependent variables after correcting for multiple comparisons, they will be included in the following analyses. Otherwise, covariates will not be included in the analyses.

Two sets of analyses will be conducted for each dependent variable. First, behavioral measures of reading will be analyzed to determine the contribution of pre-intervention levels of phonological awareness, phonological memory, rapid naming, single word reading, reading efficiency, and reading fluency to growth in the dependent variables (i.e., growth in phonological decoding and two measures of reading comprehension). To determine whether each measure of reading is related to the dependent variable of interest, bivariate Pearson product-moment correlations will be conducted between each of the dependent variables (i.e., growth in phonological decoding and reading comprehension) and each reading skill (i.e., phonological memory, rapid naming, phonological awareness, single word reading, reading efficiency, and reading fluency). In addition, partial correlations between growth in each of the dependent variables and each reading skill controlling for pre-intervention measures of the dependent variables will also be examined. These partial correlations will help to examine the contribution of initial levels of performance on the ability to predict changes in a particular reading skill based on pre-intervention performance on other measures of reading. Results of these analyses will be reported and will make up the proposed behavioral model for growth in phonological decoding (i.e., change in WRMT Word Attack) and reading comprehension (i.e., change in WRMT Passage Comprehension, and change in GORT Comprehension). I hypothesize that the behavioral scores may predict change in reading skills. Although, there may also not be any behavioral scores that predict change in reading skills over time, as was observed by Hoeft et al. (2011). However, if the children with developmental dyslexia in this study exhibited significant growth in reading skills during the course of the intervention, then it may be more likely that some of the behavioral scores measured prior to intervention can predict growth in the reading skills of interest.

The second set of analyses will also include the slope (i.e., change over time between pre-intervention and the end of the intervention) of WRMT Word Attack, WRMT Passage Comprehension, and GORT Comprehension standard scores as 3 separate dependent variables. However, the independent variables in these analyses will be the amount of activation to phonological stimuli (i.e., phoneme-grapheme, and word-rhyme trials) after controlling for the amount of activation to control stimuli (i.e., tone-symbol and color-match trials) for each fMRI task. Activation evoked by each fMRI task will be analyzed separately. Specifically, a series of voxelwise correlation analyses will be conducted between activation for each task and each of the three dependent variables. Age at time 1 will be included as a covariate if it was significant when tested prior to analyzing the behavioral data.

To control for multiple comparisons, the results of fMRI analyses will be viewed at an uncorrected $p < 0.001$, with a spatially corrected p value < 0.01, and spatial clustering threshold set to 10 voxels, with each voxel sharing a face with at least one other voxel in the cluster (i.e., NN = 1). Clusters of voxels demonstrating significant correlations between activation for phoneme-grapheme and word-rhyme trials and each dependent variable will be identified and their location will be labeled with a Talairach atlas (Talairach & Tournoux, 1988). More lenient statistical thresholds, up to an uncorrected $p < 0.05$, and spatial clustering of 5 voxels, may be examined if the threshold stated above results in a lack of clusters surviving the statistical threshold. The significant clusters for the relationship of each task to each reading outcome will be reported.

A mask of the significant clusters observed for each task will also be generated and combined in a conjunction analysis to identify areas of activation in common across both fMRI tasks that are related to growth in each of the reading skills of interest (i.e., growth in phonological decoding and two measures of reading comprehension). Results of these analyses will be reported and will make up the proposed neuroimaging model for growth in phonological decoding (i.e., change in WRMT Word Attack) and reading comprehension (i.e., change in WRMT Passage Comprehension, and change in GORT Comprehension). I hypothesize that significant clusters of activation and the resulting functional neuroimaging model will include some combination of clusters in bilateral inferior frontal, superior and middle temporal, supramarginal, and fusiform gyri.

Thus, with this dissertation I propose to obtain (1) a description of the growth observed in reading and reading-related skills as children with dyslexia participate in a 2-year multisensory reading intervention, *Take Flight*, and (2) knowledge of the ability to predict growth in reading skills across the intervention through standardized reading test scores and functional neuroimaging measures of brain activation during phonological processing fMRI tasks completed prior to the intervention. Knowledge obtained from these analyses will help to demonstrate the effectiveness of *Take Flight* as a reading intervention intended to improve not just phonological awareness abilities but also phonics skills, reading fluency, and reading comprehension. Furthermore, gaining a better understanding of how brain activation measured prior to intervention is related to growth observed in reading skills can help educators to identify which children are most likely to respond to interventions. Once educators are able to identify which children will respond to a reading intervention they can begin to investigate ways to refine their instructional methods in hopes that some day all children with dyslexia will exhibit improvements following intervention and will not continue to struggle to read.

CHAPTER 4

RESULTS

This dissertation aims to identify behavioral and functional neuroimaging factors that can be used to predict growth in phonological decoding and reading comprehension in a group of children with developmental dyslexia who completed a 2-year multisensory intervention. The first set of analyses characterize any growth observed in the children's reading skills throughout the intervention and the second set of analyses predict growth in phonological decoding and reading comprehension from both behavioral test measures and brain activation during phonological processing fMRI tasks.

4.1 Characterization of Growth in Reading

In the section that follows the changes observed throughout this study in the reading and related skills of the children with dyslexia and the control children are discussed. The reading-related skills included 1) phonological memory, 2) rapid naming, and 3) phonological awareness. The reading skills included 1) single word reading, 2) phonological decoding, 3) real word and pseudoword reading efficiency, 4) reading fluency, and 5) reading comprehension. Additionally, the mathematical skill of numerical operations was included in order to investigate if changes were limited to reading skills. Changes in skills during the intervention were assessed in several ways. First, it was possible to identify if participation in the intervention was associated with significant growth in these reading skills. Second, it was possible to identify if the growth placed these skills within the normal range of standardized tests assessing these reading skills. Finally, it was possible to identify if participation in the intervention eliminated the differences in these reading skills observed between the children with dyslexia and the control children with unimpaired reading.

Potential covariates of age, and attention problems were not systematically related to dyslexic children’s reading and reading-related skills at pre-treatment, with one exception. There was a negative relationship between age and pre-intervention reading fluency, $r(13) = -0.62$, $p = 0.01$, indicating that older children were more likely to have lower reading fluency scores. Thus, analyses of fluency were repeated treating age as a covariate of no interest.

4.1.1 Reading-related Skills

Basic cognitive skills related to reading were assessed using the phonological memory, rapid naming, and phonological awareness composite scores from the CTOPP (Wagner et al., 1999). These skills have been observed to reliably predict treatment response as well as to be deficient in children with dyslexia (Frijters et al., 2011; Morris et al., 1998; Nelson et al., 2003; Torgesen, 2000; Torgesen et al., 1999). Of these skills the specific intervention used in this study, *Take Flight*, was designed to remediate deficits in phonological awareness. In contrast, *Take Flight* was not specifically designed to remediate rapid naming or phonological memory.

4.1.1.1 Phonological Memory

Prior to treatment phonological memory abilities of the children with dyslexia ($M = 98$, $SE = 3.01$) were within the average range (i.e., 90 – 110 SS), although their standardized test scores were significantly lower than those of the non-impaired readers at a marginal level of significance when stringent criteria is used to control family-wise error rates ($M = 105.4$, $SE = 1.95$), $t(28) = 2.07$, $p < 0.05$. Growth was not observed in the standard score measurement of phonological memory abilities of the children with dyslexia throughout the intervention program, $F < 1$, or in standard score measurements of the non-impaired readers’ phonological memory abilities during the first year of the study, $t(14) = -1.72$, $p = 0.11$ (see Figure 4.1). However, at the conclusion of the first year of treatment the phonological memory abilities of the children with dyslexia ($M = 96.8$, $SE = 3.54$) did not differ from those of the non-impaired readers ($M = 100.4$, $SE = 2.27$), $t(28) = 0.86$, $p < 0.40$.

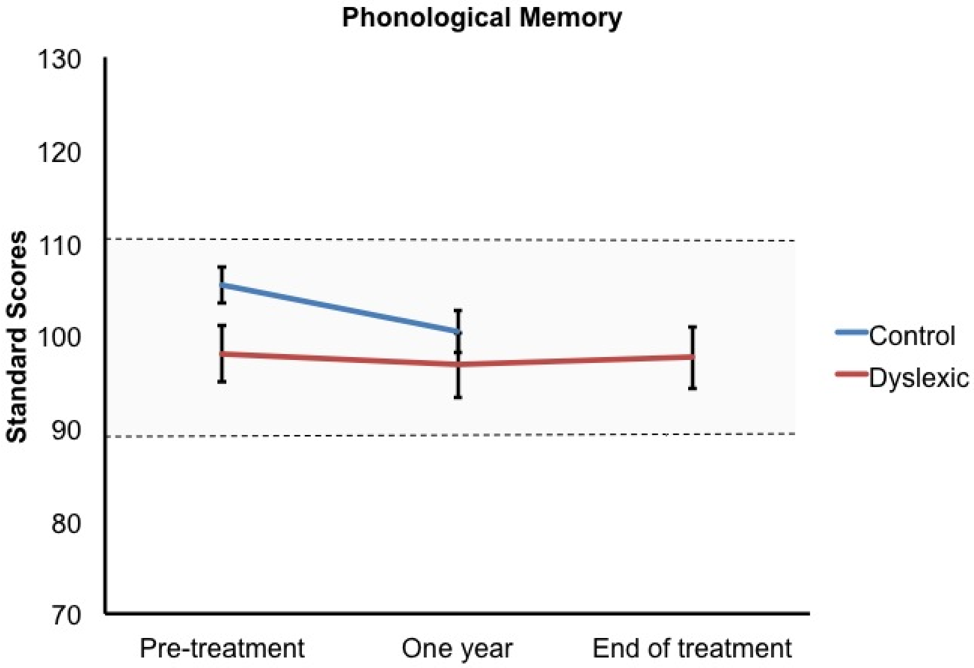

Figure 4.1 Phonological memory skills over time

Thus, the children with dyslexia began treatment with phonological memory abilities that were lower than the non-impaired readers, yet still within the average range. By the end of the first year of treatment there was no longer a significant difference between the children's phonological memory abilities even though no significant gains were observed in the children with dyslexia's standardized test scores throughout the 2-year treatment program. This was due to scores of the non-impaired readers regressing to the mean, and not due to significant growth in the children with dyslexia's skills.

4.1.1.2 Rapid Naming

During the pre-intervention assessment rapid naming scores were not available for one child with dyslexia and one non-impaired reader who each exhibited too many errors in rapidly naming a series of letters in order to obtain an accurate score. Prior to treatment the children with dyslexia exhibited below average range (i.e., 90 – 110 SS) rapid naming abilities (M = 79.64, SE = 3.07) that were also significantly lower than those of the non-impaired readers (M = 95.5, SE = 3.53), $t(26) = 3.39$, $p < 0.002$. The non-impaired readers did not exhibit improvements in standard score measurements of their rapid naming abilities during the first year of the study, $t(13) = .17$, $p = 0.87$. Although significant growth was not observed in the children with dyslexia's rapid naming abilities according to stringent statistical criteria needed to control for family-wise error, $F(2, 24) = 4.21$, $MSE = 39.98$, $\eta_p^2 = 0.26$, $p < 0.03$, after one year of the intervention they were not significantly different from the lower bounds of the average range (i.e., 90 SS), $t(13) = -.97$, $p = 0.35$ (see Figure 4.2). In addition, one year into the intervention the rapid naming abilities of the children with dyslexia ($M = 87.14$, $SE = 2.94$) were not significantly different from those of the non-impaired readers ($M = 93.53$, $SE = 4.26$), $t(27) = 1.22$, $p < 0.23$. The children with dyslexia did not exhibit growth in the standard score measurements of their rapid naming abilities during the second year of the intervention program, $t(13) = .11$, $p = 1.00$. Thus, after one year of *Take Flight* the rapid naming abilities of the children with dyslexia had increased and were not significantly outside of the average range, nor did they differ from those of the non-impaired readers.

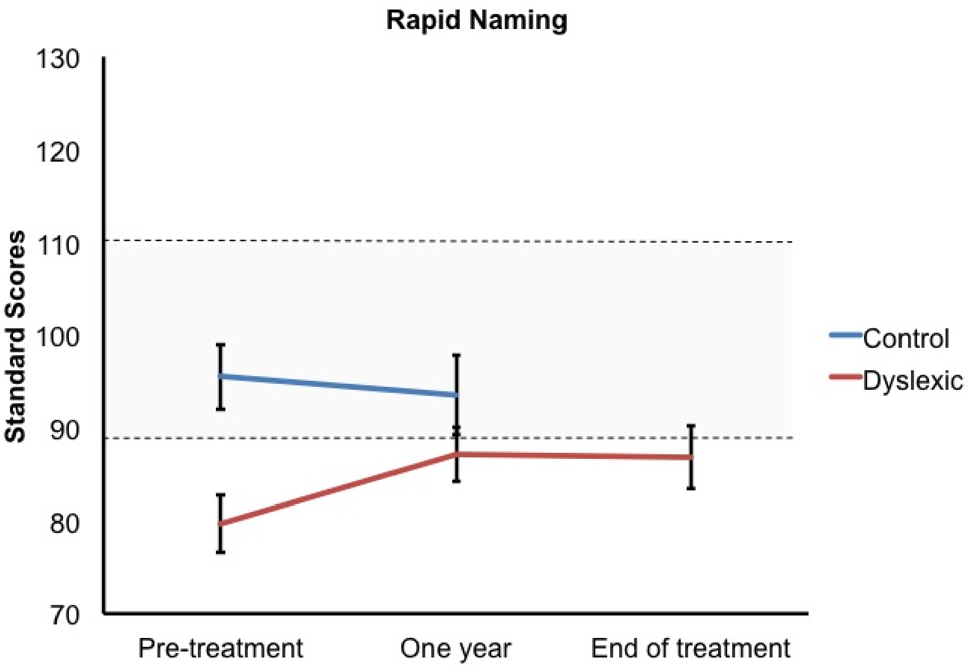

Figure 4.2 Rapid naming skills over time

4.1.1.3 Phonological Awareness

Prior to treatment phonological awareness abilities of the children with dyslexia (*M* = 89.07, *SE* = 3.01) were not statistically less than the average range (i.e., 90 – 110 SS), *t*(14) = -.31, *p* = 0.76, although their standardized test scores were significantly lower than those of the non-impaired readers (*M* = 109.47, *SE* = 4.27), *t*(28) = 3.90, *p* = 0.001. Although growth was not observed in the standard score measurements of the non-impaired readers' phonological awareness abilities during the first year of the study, *t*(14) =0.07, *p* = 0.94, the children with dyslexia exhibited growth in their phonological awareness abilities, *F*(2,28) = 9.71, *MSE* = 53.88, η_p^2 = 0.41, *p* = 0.001 (see Figure 4.3).

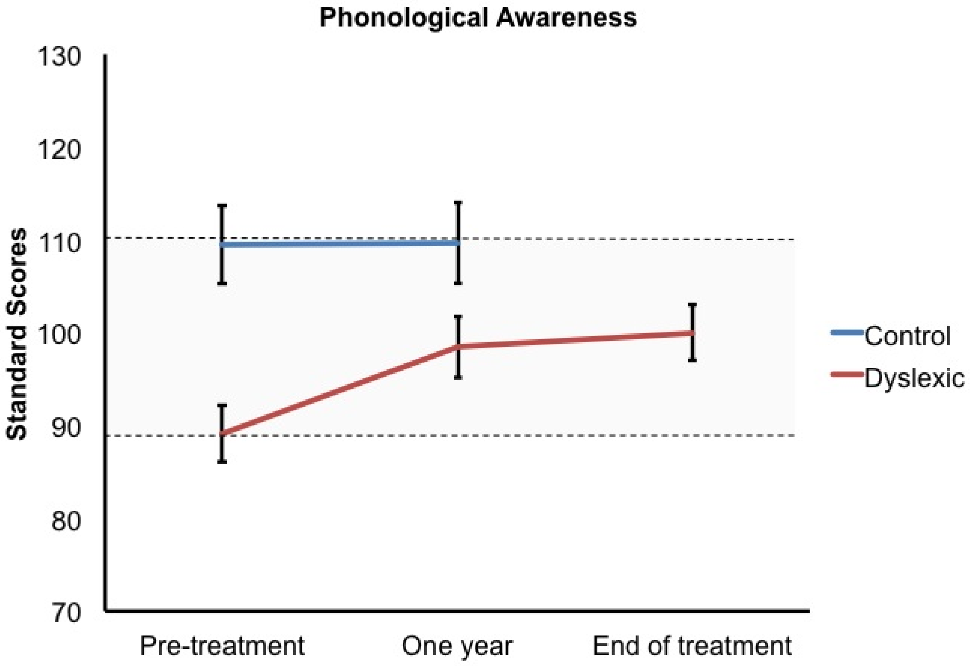

Figure 4.3 Phonological awareness skills over time

Specifically, the children with dyslexia exhibited standardized test scores (*M* = 98.4, *SE* = 3.25) within the average range after the first year of the intervention program. However, their phonological awareness abilities were still less than those of the non-impaired readers (*M* = 109.67, *SE* = 4.07), *t*(28) = 3.57, *p* = 0.001. Additionally, the children with dyslexia did not exhibit additional growth in standard score measurements of phonological awareness during the second year of the intervention program, $t(14) = .52$, $p = 0.61$. Thus, the phonological awareness abilities of the children with dyslexia remained significantly lower than those of the non-impaired readers even though they increased from being outside, but not statistically different from the average range, to being numerically within the average range.

4.1.2 Reading Skills

This section contains assessments of changes observed in reading skills throughout the intervention. Five types of reading skills are investigated, 1) single word reading, 2) phonological decoding, 3) real word and pseudoword reading efficiency, 4) reading fluency, and 5) reading comprehension.

4.1.2.1 Single Word Reading, Phonological Decoding, and Reading Efficiency

Prior to treatment the children with dyslexia exhibited below average range (i.e., 90 – 110 SS) single word reading ($M = 84.13$, $SE = 1.94$), phonological decoding ($M = 86.6$, $SE = 1.99$), real word ($M = 78.33$, $SE = 2.38$) and pseudoword ($M = 81.67$, $SE = 1.56$) reading efficiency abilities that were also significantly lower than those of the non-impaired readers ($M = 115.6$, $SE = 4.13$; $M = 117.07$, $SE = 4.5$; $M = 107.73$, $SE = 3.85$; $M = 106.07$, $SE = 3.82$), $t(28) = 6.34$; $t(28) = 6.72$; $t(28) = 6.28$; $t(28) = 6.17$). The non-impaired readers did not exhibit improvements in any of these four measures of word reading, $F(2,13) = 1.37$, $\eta_p^2 = 0.17$, $p = 0.29$. However, the measures of phonological decoding ($M = 115.57$, $SE = 4.1$) and single word reading ($M = 117.53$, $SE = 4.15$) were greater than pseudoword ($M = 104.80$, $SE = 3.60$) and real word reading efficiency ($M = 103.83$, $SE = 3.54$) at both time points, $F(2,13) = 43.3$, $\eta_p^2 = 0.87$, $p < 0.001$.

In contrast, the children with dyslexia exhibited improvements in their word reading skills, $F(2,13) = 35.8$, $\eta_p^2 = 0.85$, $p < 0.001$. One year into the *Take Flight* program untimed phonological decoding scores were within the average range ($M = 95.87$, $SE = 1.23$) and single word reading ($M = 89.6$, $SE = 1.56$) was not significantly different from the lower bounds of the average range (i.e., 90 SS), *t*(14) = -0.26, $p = 0.80$. Yet, these scores were still significantly lower than those of the non-impaired readers, *t*(28) = 4.22, $p < 0.001$; *t*(28) = 6.66, $p < 0.001$. In addition, timed pseudoword and real word reading efficiency scores were still less than the lower bounds of the average range at a marginal level of significance after controlling family-wise error rates (i.e., 90 SS), *t*(14) = 2.80, $p < 0.01$; *t*(14) = -2.14, $p < 0.05$ after one year of the intervention. By the end of *Take Flight* timed pseudoword reading efficiency was not significantly different from the average range, *t*(14) = -1.52, $p < 0.15$. Thus, following one year of treatment the initially deficient phonological decoding and single word reading skills had increased to be within the average range and remained within the average range throughout the remainder of the intervention program. Reading efficiency scores also increased such that by the conclusion of the intervention pseudoword reading efficiency was not significantly outside of the average range (see Figure 4.4).

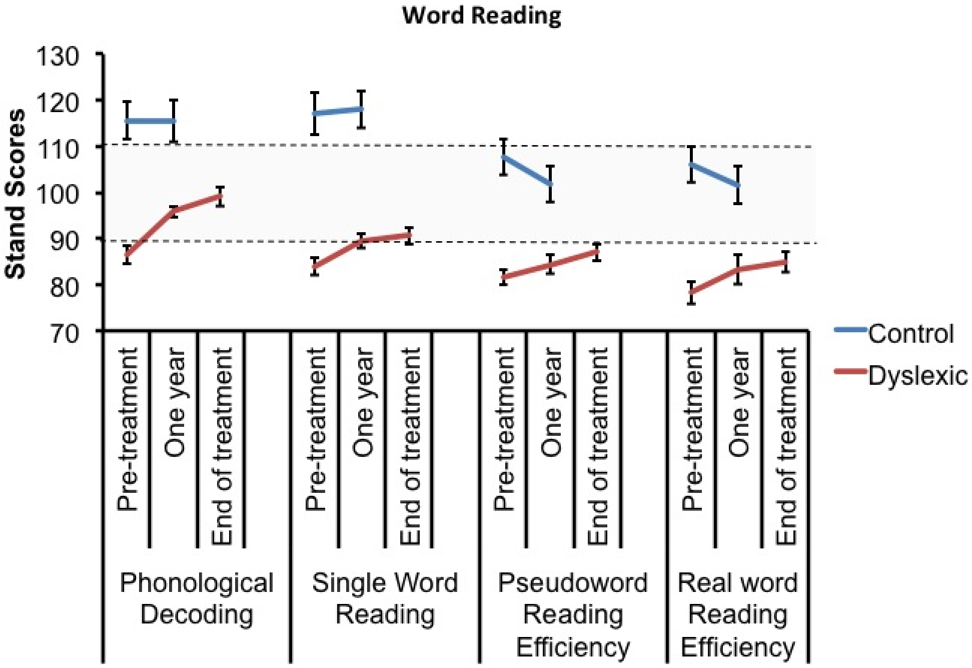

Figure 4.4 Word reading skills over time

4.1.2.2 Reading Fluency

Prior to treatment the children with dyslexia exhibited below average range (i.e., 8 - 12 SS) reading fluency (*M* = 3.40, *SE* = 0.43) that was also significantly lower than that of the non-impaired readers (*M* = 10.33, *SE* = 0.91), *t*(28) = 6.85, *p* < 0.001. The non-impaired readers exhibited marginally significant improvements in standard score measurements of their reading fluency during the first year of the study, *t*(14) = 2.44, *p* = 0.03, but the children with dyslexia did not, *t*(14) = 1.34, *p* = 0.20 (see Figure 4.5).

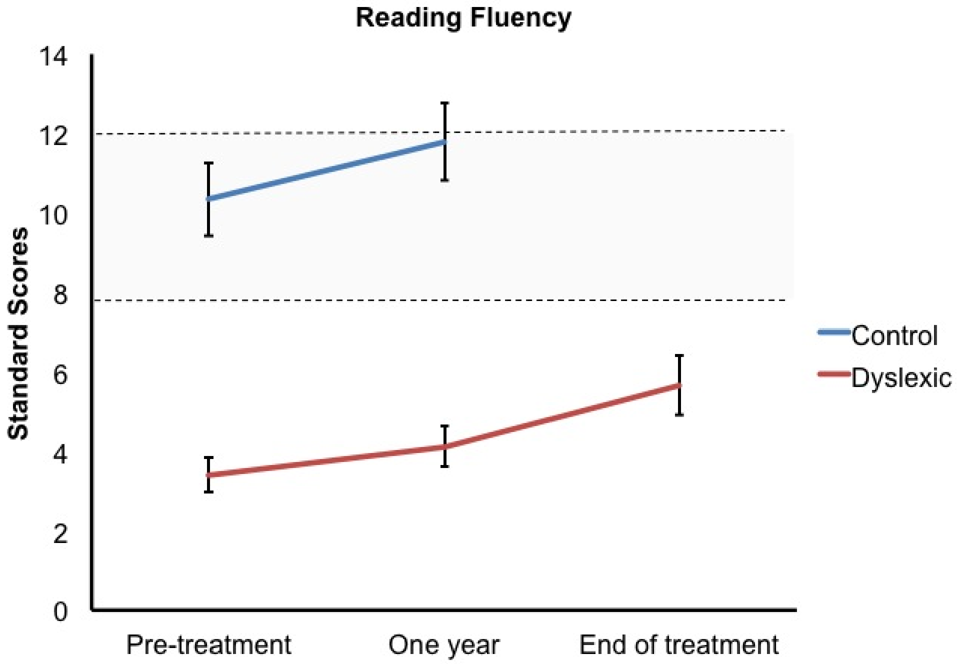

Figure 4.5 Reading fluency skills over time

However, the children with dyslexia exhibited significant improvements in standard score measurements of their reading fluency following the second year of the intervention, *F*(2, 28) = 7.22, *MSE* = 2.78, η_p^2 = 0.34, *p* = 0.003. Despite exhibiting significant growth in reading fluency, the children with dyslexia continued to demonstrate standard scores that were marginally below the lower bounds of the average range (i.e., 8 SS) at the end of the intervention program when relying on statistical criteria intended to control family-wise error rates (*M* = 5.67, *SE* = .75), *t*(14) = -3.10, *p* = 0.01. Given that pre-intervention reading fluency was correlated with age ($r(13) = -0.62$, $p = 0.01$), analyses were repeated including age as a covariate. Improvements in the reading fluency of the children with dyslexia and the non-reading impaired children were no longer significant after controlling for the effects of age, $F(2, 26) = 2.77$, $MSE = 2.16$, $\eta_p^2 = 0.18$, $p = 0.08$; $F(1, 13) = 0.08$, $MSE = 2.78$, $\eta_p^2 = 0.01$, $p = 0.78$.

4.1.2.3 Reading Comprehension

Reading comprehension was assessed in two ways. The Passage Comprehension subtest of the WRMT assesses comprehension through the child's single word responses to silently read CLOZE-type probes (Woodcock, 1998). GORT Comprehension scores reflect the child's ability to correctly respond to orally presented multiple-choice questions after having read a story aloud (Wiederholt & Bryant, 2001).

Prior to treatment, the children with dyslexia exhibited below average range (i.e., 90 - 110 SS) scores on the passage comprehension subtest of the WRMT ($M = 82.53$, $SE = 2.47$) that were also significantly lower than those of the non-impaired readers ($M = 109.93$, $SE = 2.43$), $t(28) = 7.92$, $p < 0.001$. The non-impaired readers did not exhibit improvements in standard score measurement of passage comprehension during the first year of the study, $t(14) = 0.79$, $p = 0.44$. However, the children with dyslexia exhibited growth between the pre-treatment assessment and end of the first year of the intervention as well as between the first and final year of the intervention, $F(2, 28) = 12.27$, $MSE = 35.62$, $\eta_p^2 = 0.47$, $p < 0.001$ (see Figure 4.6). Although the passage comprehension scores of the children with dyslexia ($M = 89.6$, $SE = 1.46$) were still lower than the non-impaired readers ($M = 111.73$, $SE = 3.69$) at the end of the first year of the intervention, $t(28) = 5.11$, $p < 0.001$, the test scores of the children with dyslexia were no longer significantly less than the lower bounds of the average range (i.e., 90 SS), $t(14) = 1.81$, $p = 0.09$. By the end of treatment, the passage comprehension standard scores of the children with dyslexia ($M = 93.13$, $SE = 1.73$) had further increased to be numerically within the average range, $t(14) = 3.13$, $p = 0.007$.

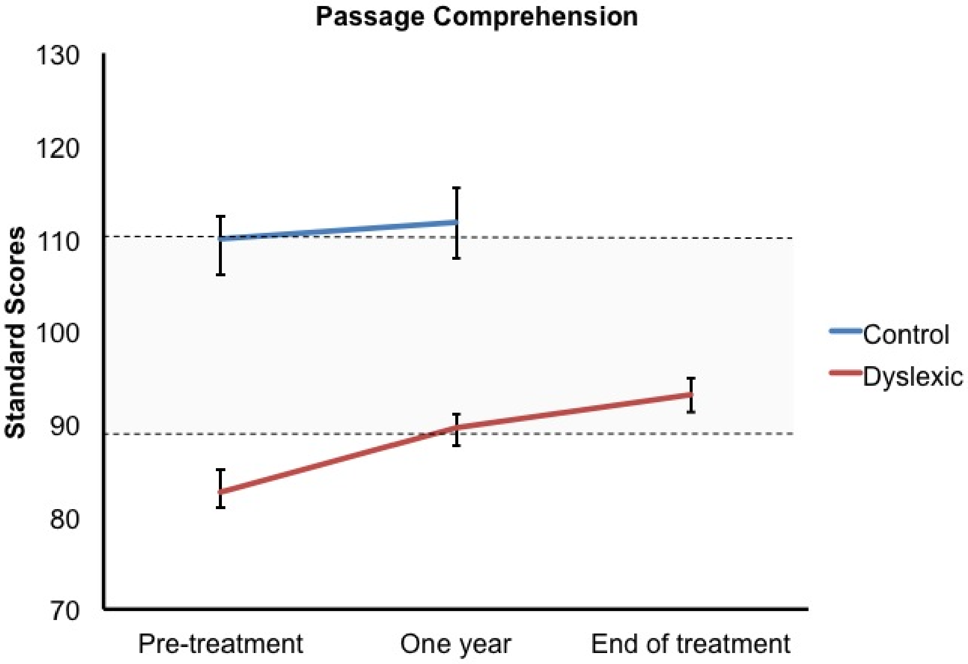

Figure 4.6 Passage comprehension skills over time

Prior to treatment, the children with dyslexia exhibited below average range (i.e., 8 - 12 SS) scores on GORT comprehension (*M* = 7.4, *SE* = 0.58) that were also significantly lower than those of the non-impaired readers (*M* = 13.13, *SE* = 0.62), $t(28) = 6.76$, $p < 0.001$. The non-impaired readers did not exhibit improvements in standard score measurement of reading comprehension during the first year of the study, $t(14) = -.52$, $p = 0.61$. Although no significant growth was observed after the first year of the intervention, $t(14) = .49$, $p = 0.63$, the GORT comprehension standard scores of the children with dyslexia (*M* = 7.67, *SE* = 0.60) were no longer significantly different from the lower bounds of the average range (i.e., 8 SS), $t(14) = -.56$, $p = 0.59$ at this second time point. However, the children with dyslexia exhibited significant growth between the end of the first year of the intervention and the conclusion of the intervention, $F(2, 28) = 14.26$, $MSE = 2.51$, $\eta_p^2 = 0.51$, $p < 0.001$ (see Figure 4.7). Specifically, the children with dyslexia exhibited growth in their GORT reading comprehension test scores, $t(14) = 4.75$, $p < 0.001$, such that by the conclusion of the 2-year intervention the test scores of the children with dyslexia (*M* = 10.2, *SE* = 0.53) were within the average range.

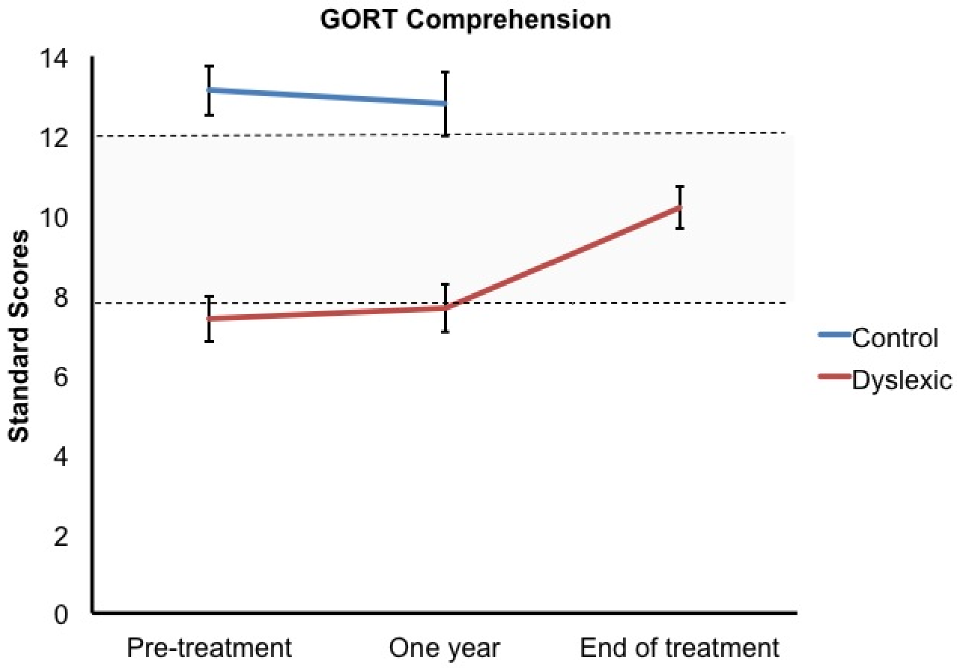

Figure 4.7 GORT comprehension skills over time

Thus, on both measures of reading comprehension the children with dyslexia began the intervention with scores significantly lower than the average range. Although the children with dyslexia did not achieve scores equivalent to the non-impaired readers, they did exhibit growth in their reading comprehension abilities. Specifically, following the first year of treatment standard scores on both measures of comprehension were no longer statistically outside of the average range. During the first year of treatment growth was observed in the children with dyslexia's ability to provide correct responses to CLOZE-type probes following silent reading. Growth continued to be observed in this measure of comprehension during the final year of the intervention program and now was also observed in the children with dyslexia's ability to respond to multiple-choice questions regarding passages they had read aloud.

4.1.3 Mathematical Skills

Prior to treatment the children with dyslexia exhibited numerical operations skills (M = 83.27, SE = 3.58) that were not statistically different from the low end of the average range (i.e., 90 SS), $t(14) = 1.88$, $p < 0.08$, although they were significantly lower than those of the non-impaired readers (*M* = 103.33, *SE* = 4.43), $t(28) = 6.85$, $p < 0.001$. The non-impaired readers did not exhibit changes in numerical operations skills during the first year of the study (*M* = 102.60, *SE* = 5.30), $t(14) = 0.21$, $p = 0.84$. The test scores of the children with dyslexia increased throughout the intervention, $F(2, 28) = 6.31$, *MSE* = 66.31, $\eta_p^2 = 0.31$, $p < 0.005$ (see Figure 4.8).

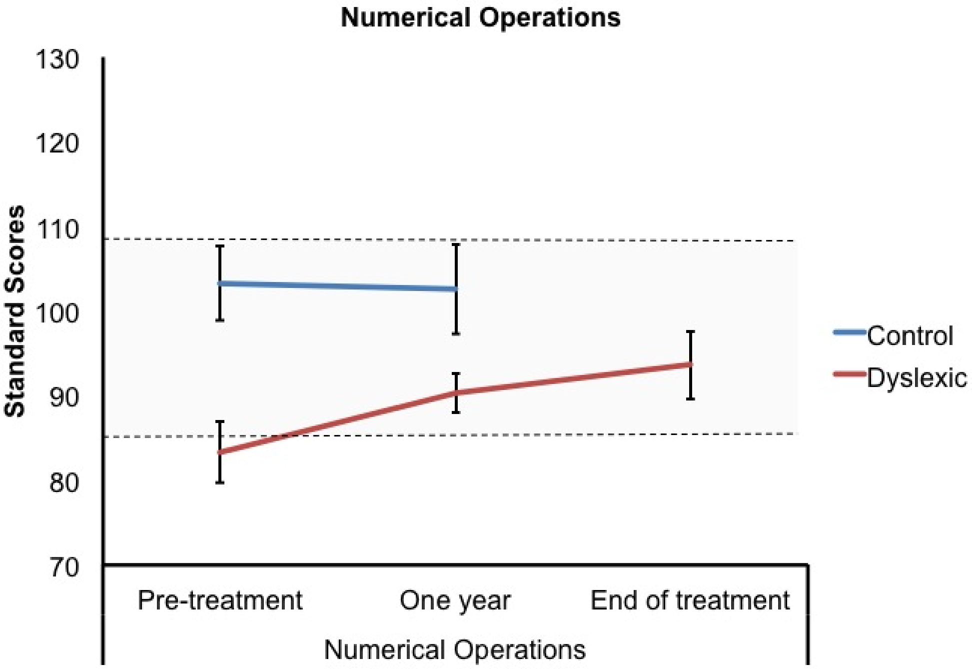

Figure 4.8. Numerical Operations skills over time

The test scores of the children with dyslexia were numerically within the average range by the end of the first year of the intervention (*M* = 90.27, *SE* = 2.29), and were still within the average range at the conclusion of the intervention (*M* = 93.60, *SE* = 4.04). Although the children with dyslexia did exhibit growth in their mathematical computation skills throughout the intervention the size of this effect ($\eta_p^2 = 0.31$) was smaller than those associated with growth in their reading skills (i.e., word reading skills, $\eta_p^2 = 0.85$).

4.1.4 Summary

Prior to the intervention, rapid naming abilities were the only measured reading-related skills of the children with dyslexia that were deficient such that scores were significantly less than the lower end of the average range. The reading-related skills of the children with dyslexia were all within the average ranges after one year of the intervention. Furthermore, at that time phonological memory and rapid naming abilities did not significantly differ from those of the non-impaired readers.

Prior to beginning *Take Flight* the children with dyslexia exhibited deficits in single word reading, phonological decoding, reading efficiency, reading fluency, and reading comprehension. Their test scores were not only significantly below the average range, but also lower than the reading skills of the non-impaired readers. By the conclusion of the intervention the children with dyslexia exhibited growth in all of the measured reading skills, however, there were differences in how early the growth became apparent and how much growth was observed. Single word reading, phonological decoding, and reading comprehension test scores increased such that they were within the average range by the end of the first year of the intervention. The children with dyslexia also exhibited growth in reading efficiency during this first year, but test scores remained below average. Phonological decoding and reading comprehension measures continued to exhibit growth between the end of the first year of the intervention and conclusion of treatment. By the conclusion of treatment, the reading efficiency test scores were also within the average range even though significant growth was not observed during the second year of the intervention. The children with dyslexia did not exhibit growth in reading fluency until the second year of the intervention. Unfortunately, even though reading fluency improved between the end of the first year of the intervention and the conclusion of the treatment, these scores were still below average. Thus, although growth was eventually observed in all reading skills, deficits were still present in reading fluency by the conclusion of treatment.

4.2 Predicting Growth in Reading Skills

In the section that follows the factors associated with growth in the children with dyslexia's reading skills are discussed. Growth in reading skills is defined as changes over time in phonological decoding and reading comprehension. The factors associated with growth in reading skills include 1) behavioral measures, and 2) functional neuroimaging measures.

4.2.1 Behavioral Measures

Pre-intervention reading and reading-related skills of the children with dyslexia correlated with growth in phonological decoding and reading comprehension observed across the intervention. Potential covariates of age, and attention problems were not systematically related to dyslexic children's changes in phonological decoding or reading comprehension scores over the course of the intervention, with two exceptions. There was a negative relationship between growth in phonological decoding and hyperactivity measured pre-intervention, $r(12) = -0.57$, $p = 0.03$, indicating that children with fewer indications of hyperactive behaviors are likely to exhibit more growth in phonological decoding. Thus, analyses of phonological decoding were repeated treating hyperactivity as a covariate of no interest through partial correlations. There was also a negative relationship between inattentive behaviors measured pre-intervention and growth in reading comprehension measured with the passage comprehension subtest of the WRMT, $r(12) = -0.55$, $p = 0.04$. In this case, children with fewer indications of inattentive behaviors are likely to exhibit more growth in their passage comprehension scores than children with more indications of inattentive behaviors. Thus, analyses of passage comprehension growth were repeated treating inattention as a covariate of no interest through partial correlations. No potential covariates were systematically associated with growth in GORT comprehension.

4.2.1.1 Phonological Decoding

Bivariate correlations identified reading and reading-related skills associated with growth in phonological decoding as measured by the Word Attack subtest of the WRMT (Woodcock, 1998). A small negative relationship was observed between phonological awareness ($r(13) = -0.37$, $r^2 = 0.14$, $p = 0.18$), single word reading ($r(13) = -0.44$, $r^2 = 0.19$, $p =$

0.1) and real word reading efficiency ($r(13) = -0.46$, $r^2 = 0.21$, $p = 0.08$) and changes in phonological decoding (see Figure 4.9).

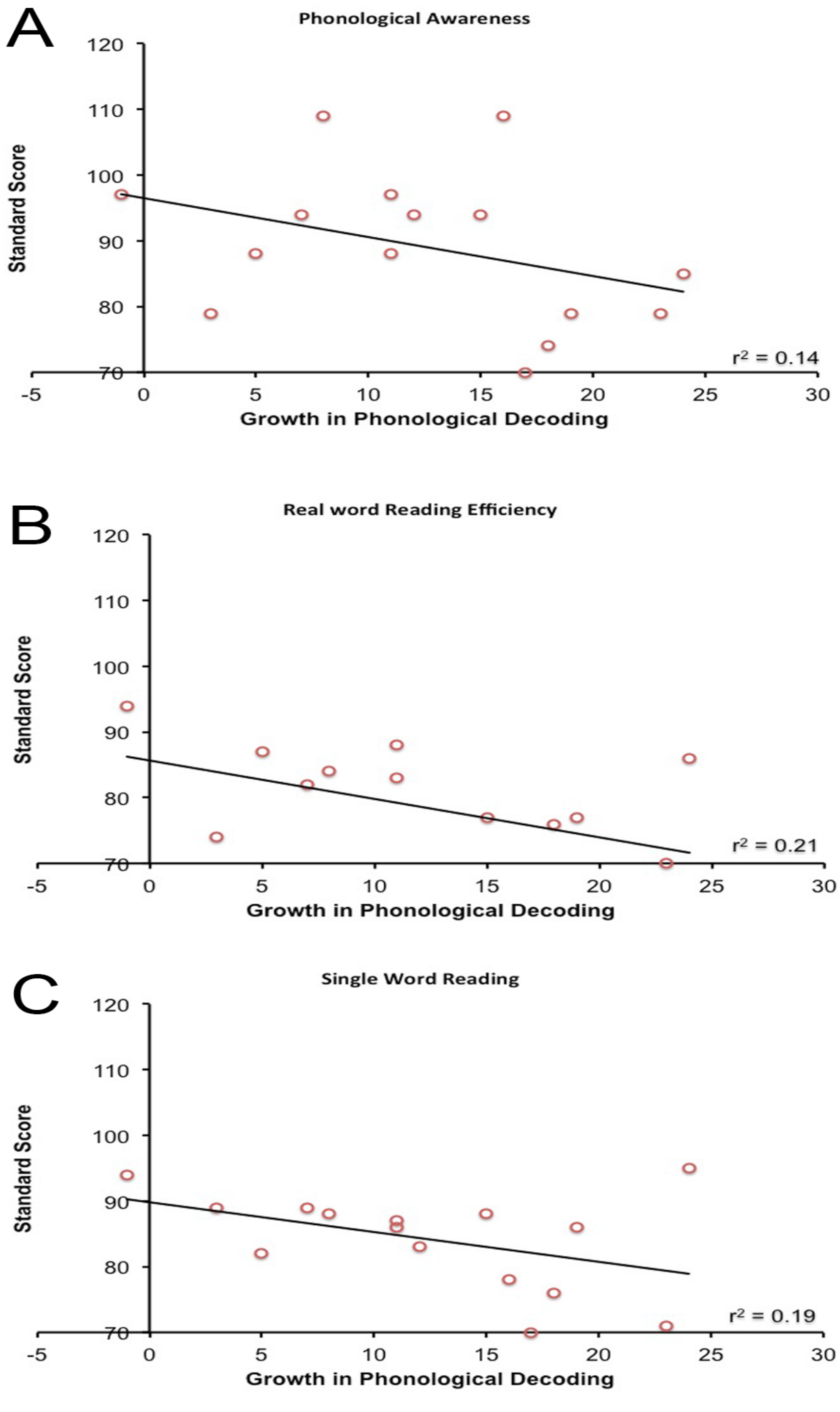

Figure 4.9 Growth in phonological decoding and pre-intervention (A) phonological awareness, (B) real word reading efficiency, and (C) single word reading.

However, these relationships were attenuated and no longer considered reliable when partial correlations controlling for initial levels of phonological decoding were analyzed ($r(12) = -0.27$, $r^2 = 0.07$, $p = 0.35$; $r(12) = -0.18$, $r^2 = 0.03$, $p = 0.54$; $r(12) = -0.28$, $r^2 = 0.08$, $p = 0.34$). There were no significant relationships between phonological memory, rapid naming, pseudoword reading efficiency, or reading fluency and growth in phonological decoding regardless of whether initial levels of phonological decoding were included or not (all *r's* < +/- 0.19; all *r's* < +/- 0.13). Thus, although lower initial performance on phonological awareness, single word reading, and real word reading efficiency tasks were associated with more growth in phonological decoding over the course of the intervention, much of these relationships could be accounted for by initial performance on phonological decoding measures.

Analyses were repeated using partial correlations controlling for initial parent ratings of hyperactivity. A small negative relationship was observed between both phonological awareness ($r\ (12) = -0.44$, $r^2 = 0.19$, $p = 0.11$) and real word reading efficiency ($r\ (12) = -0.46$, $r^2 = -0.21$, $p = 0.10$) and growth in phonological decoding. The negative relationship between single word reading and growth in phonological decoding was a stronger medium-sized effect ($r\ (12) = -0.55$, $r^2 = 0.30$, $p = 0.04$). Again, the relationship between real word reading efficiency and growth in phonological decoding ($r\ (11) = -0.14$, $r^2 = 0.02$, $p = 0.65$) and between single word reading and growth in phonological decoding ($r\ (11) = -0.22$, $r^2 = 0.05$, $p = 0.47$) were attenuated when initial levels of phonological decoding were also controlled in the analyses. However, a small effect was still observed for the relationship between phonological awareness and growth in phonological decoding ($r\ (11) = -0.35$, $r^2 = 0.12$, $p = 0.25$). No other reading skills were significantly related to growth in phonological decoding when initial parents ratings of hyperactivity were controlled, all *r's* < +/- 0.29, with the exception of a small positive relationship with pseudoword reading efficiency when initial levels of phonological decoding were also controlled ($r\ (11) = 0.36$, $r^2 = 0.13$, $p = 0.23$).

4.2.1.2 Passage Comprehension

Bivariate correlations revealed reading and related skills associated with growth in reading comprehension measured by the passage comprehension subtest of the WRMT (i.e., passage comprehension; Woodcock, 1998). Small to medium-sized negative relationships were observed between phonological awareness ($r(13) = -0.48$, $r^2 = 0.23$, $p = 0.07$), rapid naming ($r(12) = -0.53$, $r^2 = 0.28$, $p = 0.05$), single word reading ($r(13) = -0.54$, $r^2 = 0.29$, $p = 0.04$, real and pseudoword reading efficiency ($r(13) = -0.57$, $r^2 = 0.32$, $p = 0.03$; $r(13) = -0.33$, $r^2 = 0.11$, $p = 0.07$) and growth in passage comprehension (see Figure 4.10).

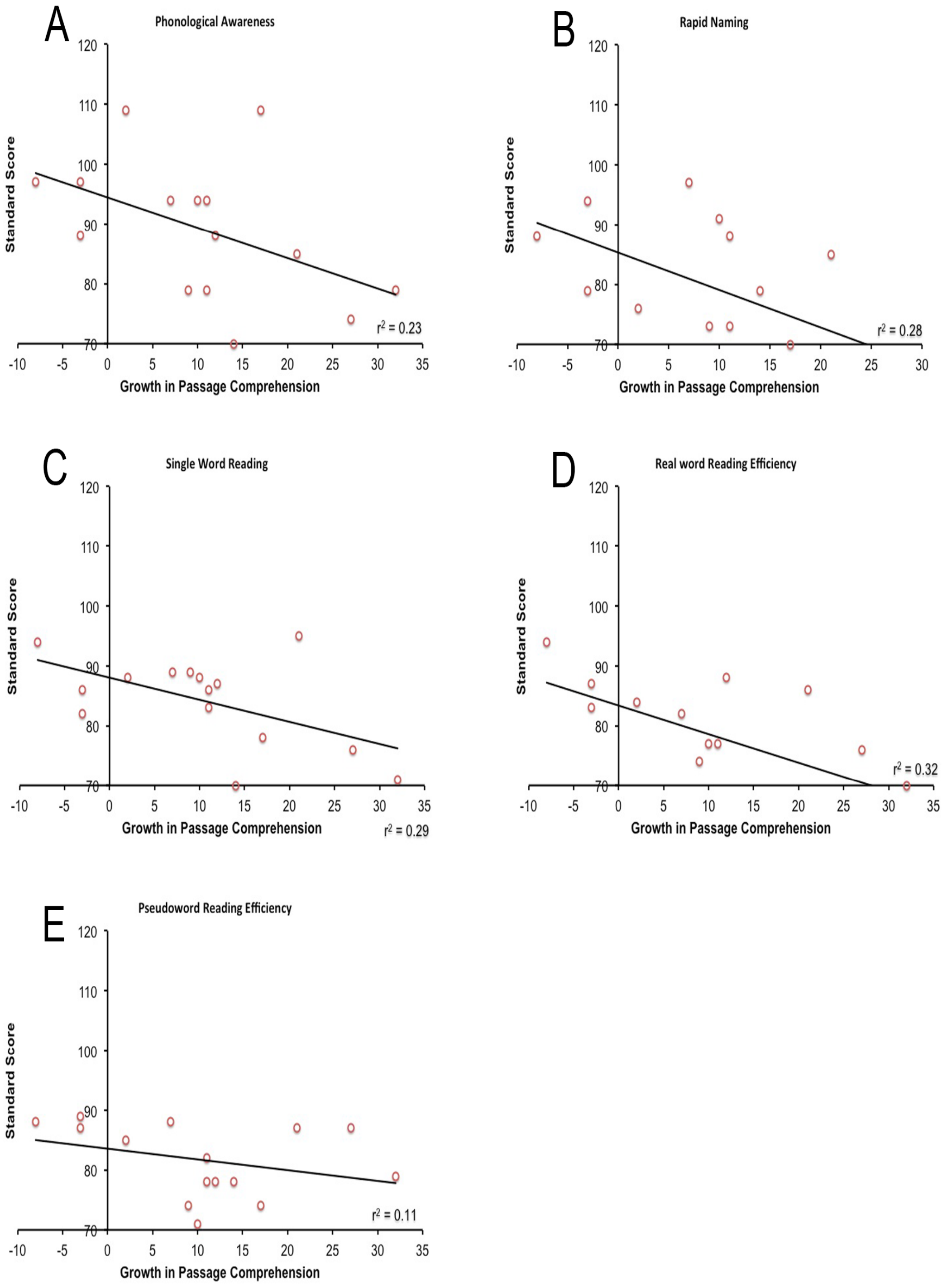

Figure 4.10. Growth in passage comprehension and pre-intervention (A) phonological awareness, (B) rapid naming, (C) single word reading, (D) real word reading efficiency, and (E) pseudoword reading efficiency.

The relationships between growth in passage comprehension and rapid naming, real and pseudoword reading efficiency were attenuated and no longer considered reliable when partial correlations controlling for initial levels of passage comprehension were analyzed ($r(11) = -0.24$, $r^2 = 0.06$, $p = 0.44$; $r(12) = 0.09$, $r^2 = 0.01$, $p = 0.75$; $r(12) = 0.12$, $r^2 = 0.01$, $p = 0.69$). However, there was still a small negative relationship between growth in passage comprehension and phonological awareness (($r(12) = -0.33$, $r^2 = 0.11$, $p = 0.25$). In addition, the relationship between growth in passage comprehension and single word reading had changed from being a medium-sized negative effect, to a small-sized positive effect once initial levels of passage comprehension were controlled ($r\ (12) = 0.44$, $r^2 = 0.19$, $p = 0.12$). Phonological memory and reading fluency were not significantly related to growth in passage comprehension, all *r's* < +/- 0.03. Although the relationship with phonological memory remained unreliable ($r\ (12) = 0.15$, $r^2 = 0.02$, $p = 0.60$), the relationship between reading fluency and growth in passage comprehension could be considered as a small effect when initial levels of passage comprehension were included in analyses ($r\ (12) = 0.31$, $r^2 = 0.10$, $p = 0.29$).

Analyses were repeated using partial correlations controlling for initial parent ratings of inattention. Results mirrored the initial analyses. Phonological memory and reading fluency were not reliably related to growth in passage comprehension regardless of whether initial levels of passage comprehension were controlled, all *r's* < +/- 0.13. Initially there were small to medium-sized negative relationships between growth in passage comprehension and phonological awareness ($r(12) = -0.51$, $r^2 = 0.26$, $p = 0.06$), rapid naming ($r(12) = -0.54$, $r^2 = 0.29$, $p = 0.06$), single word reading ($r(12) = -0.63$, $r^2 = 0.40$, $p = 0.02$), real word and pseudoword reading efficiency ($r(12) = -0.61$, $r^2 = 0.37$, $p = 0.02$; $r(12) = -0.38$, $r^2 = 0.14$, $p = 0.18$). Once initial levels of passage comprehension were included in the models, only the relationships with phonological awareness and single word reading remained reliable ($r\ (11) = -0.41$, $r^2 = 0.17$, $p = 0.16$; $r\ (11) = 0.37$, $r^2 = 0.14$, $p = 0.21$; all other *r's* < +/- 0.26). Furthermore, the relationship with single word reading was once again now in a positive direction.

4.2.1.3 GORT Comprehension

Bivariate correlations revealed reading and related skills associated with growth in reading comprehension measured by the GORT (Wiederholt & Bryant, 2001). A small negative relationship was observed between single word reading and growth in GORT comprehension, $r(13) = -0.35$, $r^2 = 0.12$, $p = 0.020$, whereas a medium-sized negative relationship was observed between real word reading efficiency and growth in GORT comprehension, $r(13) = -0.61$, $r^2 = 0.37$, $p = 0.02$. (see Figure 4.11).

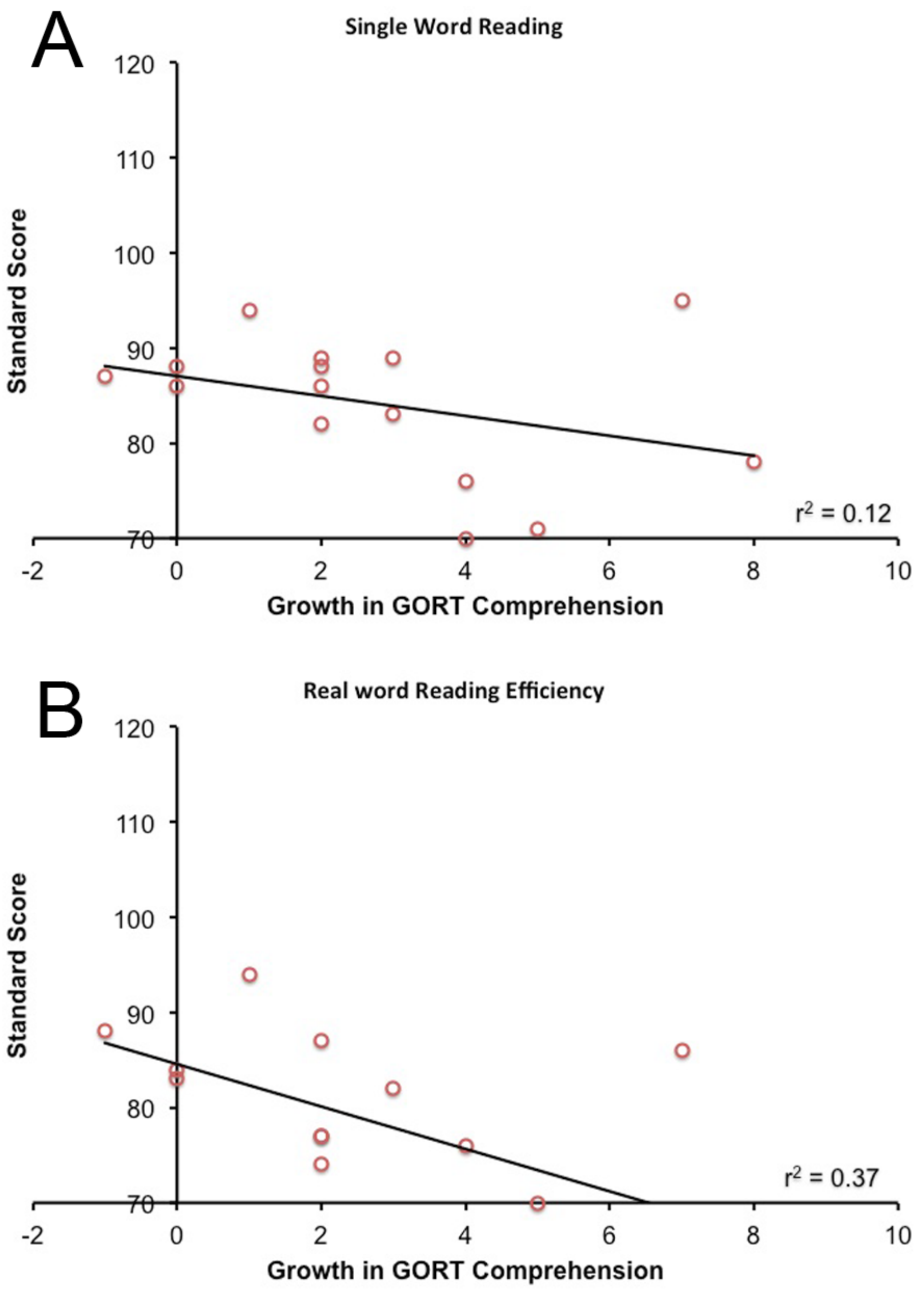

Figure 4.11. Growth in GORT comprehension and pre-intervention (A) single word reading, and (B) real word reading efficiency.

No other reading measures were reliably related to growth in GORT comprehension, all *r's* < -0.16. The relationship with single word reading was no longer reliable when partial correlations were calculated controlling initial levels of GORT comprehension ($r(12) = -0.02$, $r^2 = 0.0004$, $p = 0.95$). Although the relationship with real word reading efficiency was attenuated, it was still reliable ($r(12) = -0.46$, $r^2 = 0.21$, $p = 0.11$). Furthermore, a small positive relationship was observed between phonological awareness and GORT comprehension once initial levels of GORT comprehension were controlled ($r(12) = 0.33$, $r^2 = 0.11$, $p = 0.25$).

4.2.1.4 Summary of Behavioral Measures

My hypothesis was that pre-intervention measures of reading-related and reading skills would be correlated with growth throughout the intervention in phonological decoding and two measures of reading comprehension. The hypothesis was supported and small to medium negative correlations were observed between each of the outcome measures and pre-intervention measures of single word reading and real word reading efficiency. Thus, a child's pre-intervention ability to read isolated words could be used to predict changes in the child's ability to read isolated novel pseudowords, which requires knowledge of the sound structure of language and cannot depend on prior exposure or semantic memory. Furthermore, changes in comprehension measured by providing a missing word based on context (i.e., passage comprehension) or answering multiple-choice questions about a story (i.e., GORT comprehension) could be predicted through a child's pre-intervention ability to read isolated words.

In addition, a pre-intervention measure of phonological awareness was negatively correlated with growth in phonological decoding and passage comprehension. In this regard, a measure of a child's ability to identify sublexical components can predict changes in her ability to read isolated pseudowords. Rapid naming and pseudoword reading efficiency were also negatively correlated with growth in passage comprehension. Thus, changes in a child's ability to provide a missing word based on context can be predicted based on knowledge of her ability to rapidly name letters and numbers or to rapidly read isolated words.

However, once pre-intervention levels of each growth outcome measure were controlled in partial correlations, only the relationship between phonological awareness and growth in passage comprehension and between real word reading efficiency and GORT comprehension remained significant. Thus, initial performance on the measures of interest could account for a large portion of the changes that occurred in those skills throughout the intervention. In this regard proposed behavioral models predicting changes in each of the outcome measures would include pre-intervention measures of phonological awareness, single word reading, and real word reading efficiency.

In the present study, the direction of the relationships between pre-intervention reading skills and growth throughout the intervention in other reading skills was negative, suggesting that children with lower initial scores will be the ones who will exhibit the greatest gains in reading skills throughout the intervention. Furthermore, children with dyslexia's initial performance on the reading skills of interest accounted for much of the relationship between other reading or reading-related skills and changes in each particular growth measure. Children who had higher initial performance on measures of phonological decoding and reading comprehension exhibited less growth. The smaller amounts of growth are due, in part, to smaller increases being needed for children with dyslexia's scores to be within the average range by the end of the intervention. Additionally, the children who had lower initial scores were likely farther away from the average range than the children who had higher initial scores. Thus if all children's scores were within the average range at the end of treatment, only the children with dyslexia who had lower initial scores would have exhibited significant amounts of growth. It is possible that, as described above, a ceiling effect was observed such that skills increased to be within the average range, but did not excel past this level. The analyses in the next section address the question of whether measures of brain activation during phonological tasks can also be used to predict growth in phonological decoding and reading comprehension.

4.2.2 Functional Neuroimaging Measures

Whole brain voxelwise analyses revealed correlations between the amount of brain activation that occurred in response to phonological stimuli during the fMRI tasks and growth in phonological decoding and reading comprehension. The phoneme-grapheme mapping task is a phonics task in which the child must map phonemes to graphemes, whereas the picture-word rhyming task is a phonological awareness task in which the child must use her knowledge of the sound structure of language to determine if two words rhyme. The clusters of significant voxels reported in the following sections each represent large size effects (i.e., 0.5 and above), unless otherwise stated. Coordinates for the peak voxel in each cluster are provided in Talaraich coordinates along with information regarding the size, significance values, and location including Brodmann areas.

The models reported below show clusters of voxels that exhibited significant correlations between the amount of activation evoked by the phonological task stimuli (i.e., phoneme-grapheme or word-rhyme trials) and each particular measure of growth in reading. Clusters are also reported that either remained significant or became significant once activation evoked by the control task stimuli (i.e., tone-symbol or color-match trials) was included as a covariate of no interest. Furthermore, the analyses of the behavioral data reported above demonstrated that pre-intervention levels of the reading skills of interest accounted for much of the variance in the relationship between other reading skills and the measures of growth. Therefore, partial correlations controlling for participants' initial performance on the measures of growth in reading are also reported. Age at scanning was not included as a covariate in the fMRI analyses because it did not exhibit a significant relationship with the behavioral data, and there are concerns regarding low statistical power due to the small sample size. Appendix A contains a report of the cluster of voxels that were significantly correlated when age at scanning was included in the models, however, these results should be interpreted with caution.

Additionally, Appendix B contains a report of the clusters of voxels that were activated by the phonological stimuli in each fMRI task in order to aid in the interpretation of the results.

4.2.2.1 Phonological Decoding

The amount of brain activation evoked by phoneme-grapheme trials during the phoneme-grapheme mapping task was correlated with growth observed in phonological decoding across the intervention. Two clusters of voxels demonstrated significant negative correlations between phoneme-grapheme activation and growth in phonological decoding at an uncorrected threshold of $p < 0.001$ that was spatially corrected to $p < 0.01$ (see Figure 4.12).

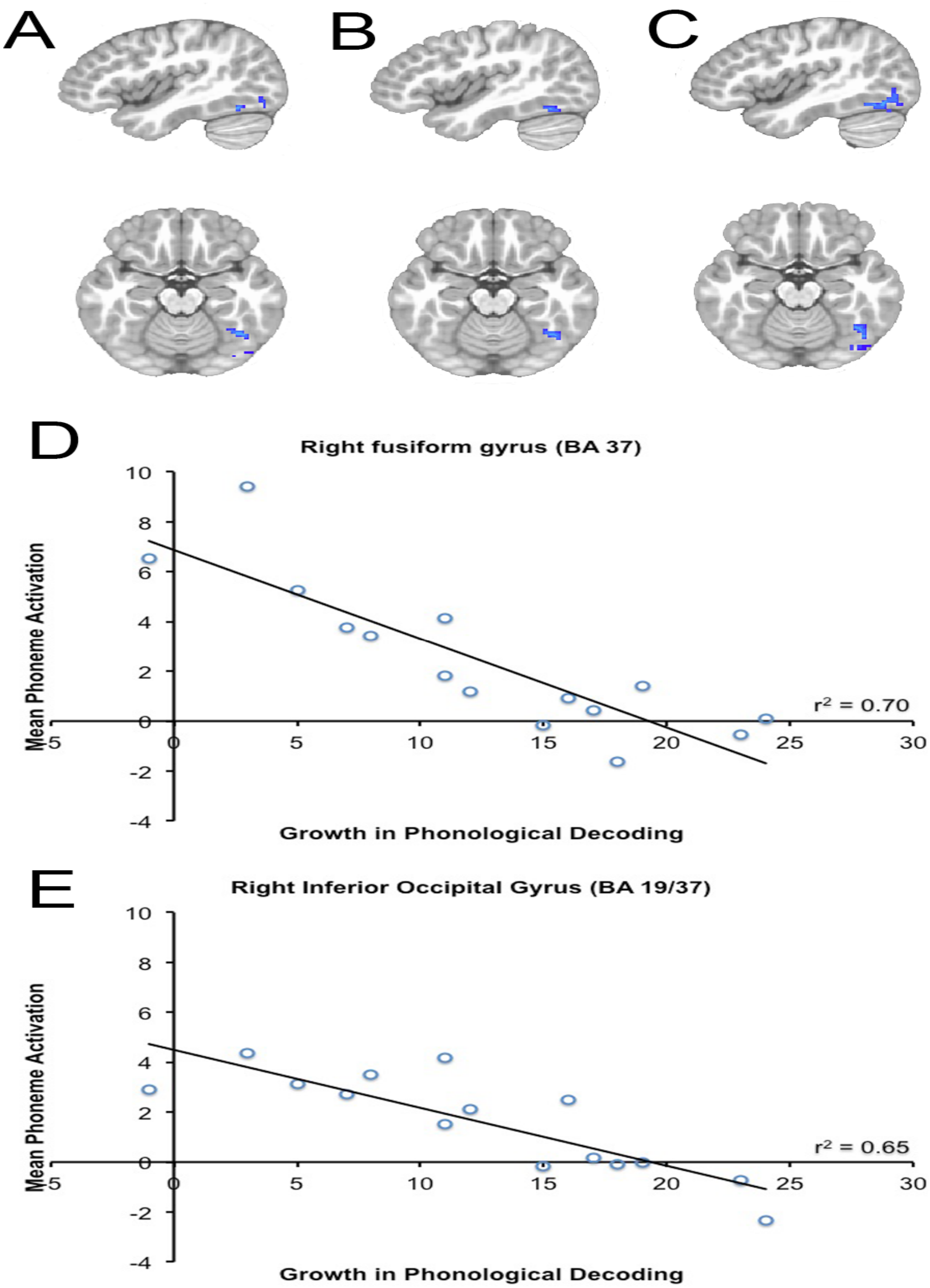

Figure 4.12. Sagittal (x = 43) and axial (z = -12) images depicting significant correlations between phoneme-grapheme activation and growth in phonological decoding when (A) no covariates, (B) tone-symbol trials, and (C) tone-symbol trials and time 1 phonological decoding were included in models. Scatterplots showing clusters in the (D) right fusiform, and (E) right inferior occipital gyrus when no covariates were in the model.

These clusters were in the right fusiform (BA 37) and right inferior occipital (BA 19) gyri. Furthermore, the cluster in the right fusiform gyrus (BA 37) remained significant when the activation evoked by tone-symbol trials, and pre-intervention levels of phonological decoding were included as covariates of no interest in separate as well as combined models (see Table 4.1).

Table 4.1 Voxelwise correlations of phoneme-grapheme trial activation with growth in phonological decoding

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Phoneme-grapheme trials						
Fusiform gyrus	R	37	-5.54	0.70	16	40, -58, -11
Inferior occipital gyrus	R	19	-4.97	0.65	10	40, -75, -8
Tone-symbols as covariate						
Fusiform gyrus	R	37	-5.32	0.68	20	40, -58, -11
Inferior/middle occipital gyrus	L	19/37	-4.90	0.65	13	-47, -66, -3
Time1 Phonological Decoding as covariate						
Fusiform/inferior occipital gyrus	R	19/37	-4.80	0.64	65	37, -75, -11
Tone-symbols and Time1 Phonological Decoding as covariates						
Fusiform gyrus	R	37	-4.56	0.62	46	43, -67, -11

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$. H = hemisphere, BA = Brodmann area, TLRC = Talaraich coordinates.

Additionally, a negative correlation was observed in the left inferior occipital gyrus (BA 19/37) when activation evoked by tone-symbol trials was included in the model. This cluster was no longer significant if pre-intervention measures of phonological decoding were included in the model. However, at a less stringent threshold of uncorrected $p < 0.01$ spatially corrected to $p < 0.01$ the negative correlation in the left inferior occipital gyrus (BA 19/37) was present in the initial model ($t(13) = -3.27$, voxels = 215, x = -17, y = -81, z = -8) as well as those with control stimuli or control stimuli and pre-intervention reading as covariates ($t(12) = -4.60$, voxels = 210, x = -38, y = -67, z = -1; $t\,(11) = -4.58$, voxels = 140, x = -38, y = -67, z = -1).

The amount of brain activation evoked by word-rhyme trials during the picture-word rhyming task was correlated with growth observed in phonological decoding across the intervention. A cluster of voxels in the left fusiform gyrus (BA 37/19) and a cluster of voxels in the left inferior occipital gyrus (BA 18/19) demonstrated significant negative correlations with growth in phonological decoding at an uncorrected threshold of $p < 0.001$ that was spatially corrected to $p < 0.01$ (see Table 4.2).

Table 4.2. Voxelwise correlations of word-rhyme trial activation with growth in phonological decoding

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Word-rhyme trials						
Inferior occipital/fusiform gyrus	L	18/19	-5.29	0.68	12	-26, -84, -5
Fusiform gyrus	L	37/19	-4.25	0.58	12	-41, -66, -6
Color-match as covariate						
No significant clusters						
Time1 Phonological Decoding as covariate						
Fusiform gyrus	L	37	-4.61	0.62	31	-41, -66, -8
Color-match and Time1 Phonological Decoding as covariates						
Fusiform gyrus	L	37	-5.25	0.68	44	-41, -66, -8
Insula	L	13	6.11	0.74	21	-29, 13, 17

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$. H = hemisphere, BA = Brodmann area, TLRC = Talaraich coordinates.

These clusters were no longer significant if activation evoked by color-match trials was included as a covariate of no interest. However, including pre-intervention levels of phonological decoding in the model resulted in the left fusiform gyrus cluster becoming significant regardless of whether either activation evoked by color-match trials was also in the model (see Figure 4.13).

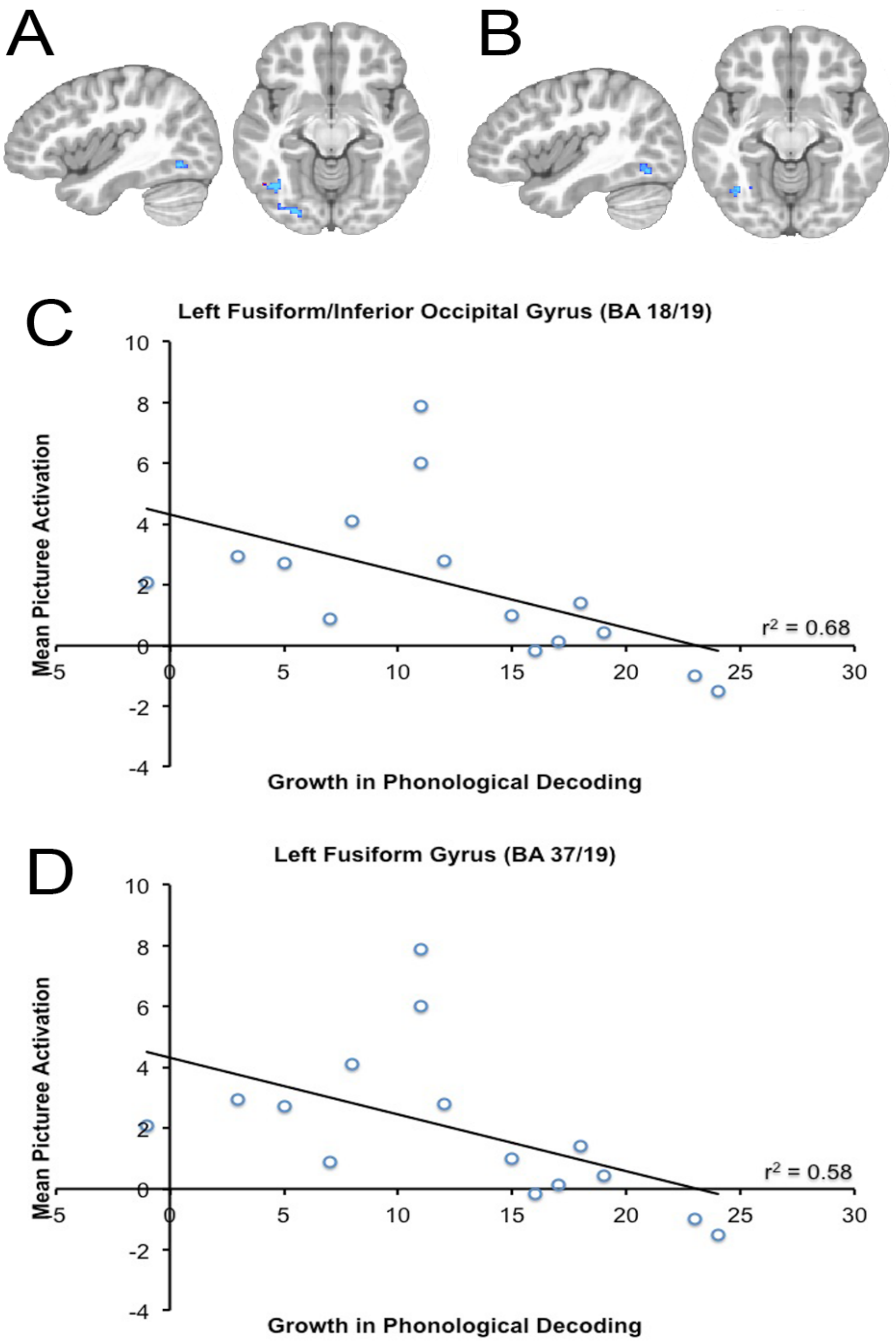

Figure 4.13. Sagittal (x = -41) and axial (z = -6) images depicting significant correlations between word-rhyme activation and growth in phonological decoding when (A) no covariates, and (B) color-match trials and time 1 phonological decoding were included in models. Scatterplots of clusters in the (C) left inferior occipital, and (D) left fusiform gyri when no covariates were in the model.

Additionally, when activation evoked by color-match trials and pre-intervention levels of phonological decoding were included as covariates of no interest there was a cluster of 21 voxels in the left insula (BA 13) that positively correlated with growth in phonological decoding (see Figure 4.14). A positive correlation was also present in a cluster in the left insula (BA 13) when only color-match activation was included as a covariate at an uncorrected threshold of $p < 0.01$ ($t\,(12) = 3.91$, voxels = 21, x = -32, y = -2, z = -2).

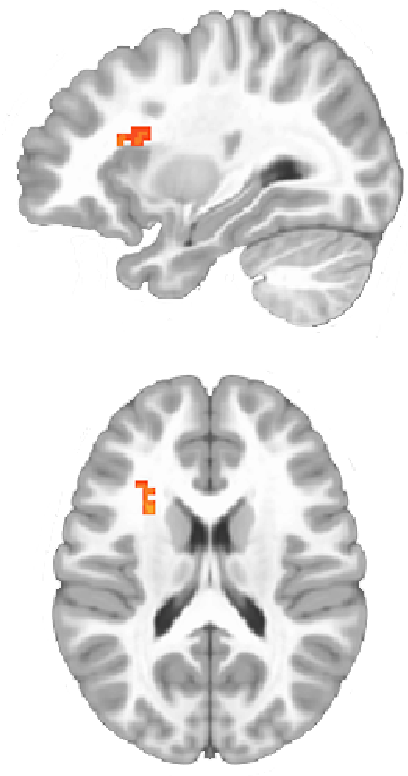

Figure 4.14. Sagittal (x = -30) and axial (z = 17) images depicting the positive correlation in the left insula between growth in phonological decoding and word-rhyme activation with color-match trials and time 1 phonological decoding as covariates in the model.

There was no overlap in the significant clusters associated with growth in phonological decoding across the phoneme-grapheme mapping and picture-word rhyming fMRI tasks.

4.2.2.2 Passage Comprehension

The amount of brain activation evoked by phoneme-grapheme trials during the phoneme-grapheme mapping task was not correlated with growth observed in passage comprehension across the intervention in any group of voxels that was large enough to survive the statistical thresholds of an uncorrected $p < 0.001$ that was spatially corrected to $p < 0.01$. There was a negative correlation in a cluster of voxels in the left posterior cingulate gyrus (BA 30/18) once activation evoked by tone-symbol trials was included as a covariate of no interest (see Table 4.3).

Table 4.3. Voxelwise correlations of phoneme-grapheme trial activation with growth in passage comprehension

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Phoneme-grapheme trials						
No significant clusters						
Tone-symbols as covariate						
Posterior cingulate gyrus	L	30/18	-4.84	0.62	14	-17, -51, 12
Time1 Passage Comprehension as covariate						
Inferior occipital gyrus	R	19	-5.51	0.70	12	43, -72, 2
Angular gyrus	R	39	-5.08	0.66	30	46, -59, 34
Middle temporal gyrus	R	19/39	-5.07	0.66	13	49, -62, 18
Insula/ parahippocampal gyrus	R	13/21	6.06	0.74	28	34, -5, -9
Insula/ parahippocampal gyrus	L	21/13	5.91	0.73	28	-38, -8, -6
Inferior temporal gyrus	L	20	-4.43	0.60	33	-47, -12, -26
Thalamus	L		5.10	0.67	12	-11, -14, 2
Tone-symbols and Time1 Passage Comprehension as covariates						
Inferior occipital gyrus	R	19	-5.19	0.67	11	40, -75, -0
Angular gyrus	R	39	-4.88	0.65	31	46, -59, 34
Insula	L	13	6.00	0.73	20	-38, -5, -6
Thalamus	L		6.68	0.77	14	-11, -14, 2

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$. H = hemisphere, BA = Brodmann area, TLRC = Talaraich coordinates.

However, this cluster did not remain significant if pre-intervention levels of passage comprehension were added to the model. Two clusters of voxels were negatively correlated with growth in passage comprehension when pre-intervention levels of passage comprehension were included in the model along with the activation evoked by color-match trials. These clusters included the right inferior occipital gyrus (BA 19), and right angular gyrus (BA 39). In addition, clusters of voxels in the left insula (BA 13) and thalamus were positively correlated with growth in passage comprehension (see Figure 4.15).

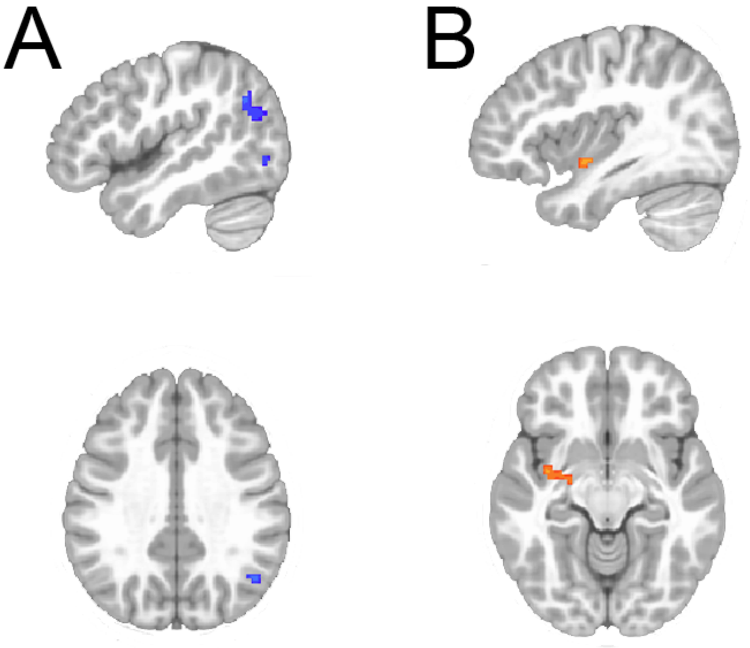

Figure 4.15. Clusters of phoneme-grapheme mapping task activation correlated with growth in passage comprehension. (A) Sagittal (x = 46) and axial (z = 34) images depicting the negative correlations and (B) sagittal (x = -37) and axial (z = -8) images depicting the positive correlations.

The amount of brain activation evoked by word-rhyme trials during the picture-word rhyming task was positively correlated with growth observed in passage comprehension across the intervention in a cluster of voxels in the left precentral/superior frontal gyrus (BA 6) at an uncorrected threshold of $p < 0.001$ that was spatially corrected to $p < 0.01$ (see Table 4.4). In addition to this cluster, there were also positive correlations with clusters in the right superior occipital gyrus (BA 17/18), left superior medial gyrus (BA 32) and left inferior frontal gyrus extending to the insula (BA 13/44) once activation evoked by color-match trials was included as a covariate of no interest.

Table 4.4. Voxelwise correlations of word-rhyme trial activation with growth in passage comprehension

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Word-rhyme trials						
Precentral/superior frontal gyrus	L	6	5.37	0.69	16	-38, -2, 56
Color-match as covariate						
Superior occipital gyrus/ Cuneus	R	17/18	4.96	0.65	10	22, -80, 21
Precentral/superior frontal gyrus	L	6	4.63	0.62	13	-38, -5, 56
Superior medial frontal gyrus	L	32	4.39	0.60	18	-5, 29, 38
Inferior frontal gyrus/insula	L	13/44	5.15	0.67	10	-35, 10, 14
Time 1 Passage Comprehension as covariate						
Lingual/inferior occipital gyrus	L	18/19	-4.62	0.62	15	-26, -81, -3
Posterior cingulate gyrus	L	30	-8.09	0.83	26	-20, -54, 15
Cingulate gyrus/corpus callosum	L	23	-7.07	0.79	26	-11, -24, 24
Fusiform gyrus	L	37	-6.12	0.74	30	-35, -63, -6
Middle temporal gyrus	L	37/21	-5.71	0.71	11	-55, -52, -2
Supramarginal gyrus/insula	L	13	-7.04	0.79	13	-38, -41, 25
Inferior temporal gyrus	L	20	4.45	0.60	26	-50, -12, -24
Medial frontal gyrus	L	32	5.77	0.72	18	-20, 17, 39
Color-match and Time1 Passage Comprehension as covariates						
Posterior cingulate gyrus	L	30/18	-8.86	0.86	21	-20, -54, 15
Cingulate gyrus/corpus callosum	L	23	-6.44	0.76	15	-14, -27, 27
Supramarginal gyrus	L	39	-6.96	0.79	10	-38, -41, 25
Fusiform gyrus	L	37	-5.74	0.72	21	-35, -63, -6
Inferior temporal gyrus	L	20	7.36	0.81	14	-50, -12, -19
Amygdala	L	34	8.00	0.83	22	-26, 3, -12
Medial frontal gyrus	L/R	10	-5.76	0.72	31	-11, 56, -10
Medial/superior frontal/cingulate gyrus	L	32	5.12	0.67	16	-20, 17, 39
Precentral/middle/superior frontal gyrus	L	4/6	4.48	0.61	17	-38, -5, 56
Precentral gyrus	L	4/6	8.35	0.84	10	-41, -5, 48
Anterior cingulate gyrus	L	24	7.40	0.81	10	-8, 22, 16
Inferior frontal gyrus/insula	L	13/44	4.51	0.61	28	-32, 19, 11
Insula/inferior frontal gyrus	L	44/13	5.24	0.68	12	-50, -2, 4
Inferior frontal gyrus	R	47	4.55	0.61	11	28, 36, 18
Lentiform nucleus/thalamus	L		5.28	0.68	12	-20, -5, 7
Thalamus/medial globus pallidus	R		6.09	0.74	19	16, -5, 4

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$. H = hemisphere, BA = Brodmann area, TLRC = Talaraich coordinates.

Only the cluster in the left inferior frontal gyrus/insula (BA 13/44) remained significant when pre-intervention passage comprehension was also added to the model. However, there were five additional clusters with negative correlations and eleven with positive correlations when both pre-intervention passage comprehension and activation evoked by color-match trials were included as covariates of no interest. The negative correlations were observed in the left fusiform (BA 37), supramarginal (BA 39), posterior cingulate (BA 30/18), and cingulate (BA 23) gyri and the left/right medial frontal gyrus (BA 10). Positive correlations included clusters of voxels in the right thalamus extending to the medial globus pallidus, and right inferior frontal gyrus (BA 47) as well as the left amygdala (BA 34), inferior temporal (BA 20), precentral/middle/superior frontal (BA 4/6), precentral (BA 4/6), superior frontal (BA 6), medial/superior frontal gyrus (BA 8/32), anterior cingulate (BA 24) gyri, the left insula extending to the left inferior frontal gyrus (BA 44/13), and left thalamus. Figure 4.16 depicts the pattern of positive correlations in frontal regions in orange (i.e., left precentral gyrus and insula) and negative correlations in posterior regions of the brain in blue (i.e., left supramarginal and fusiform gyri).

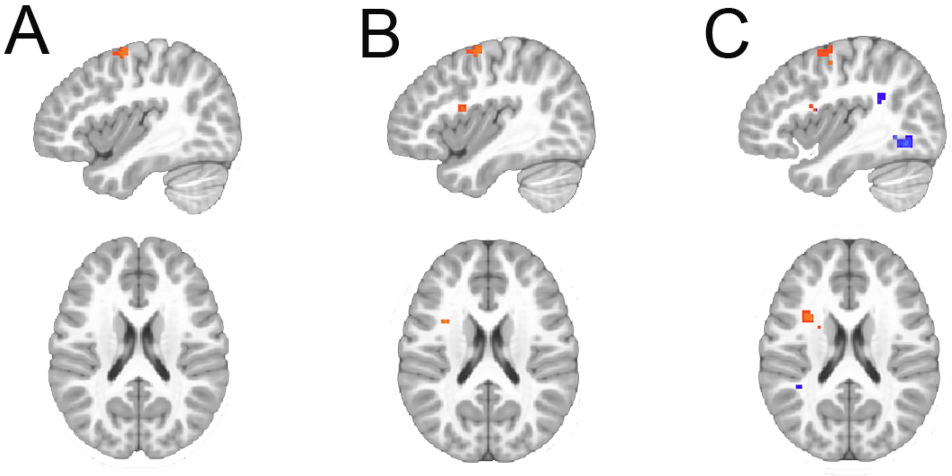

Figure 4.16. Sagittal (x = -39) and axial (z = 19) images depicting correlations between growth in passage comprehension and (A) word-rhyme activation, (B) word-rhyme activation controlling for color-match activation, and (C) word-rhyme activation controlling for color-match activation and time 1 passage comprehension.

In addition, two voxels in the left amygdala demonstrated an overlap between the correlations observed in the phoneme-grapheme mapping and color-word rhyming tasks once the corresponding control stimuli activation and pre-intervention levels of passage comprehension were included in the models.

4.2.2.3 GORT Comprehension

There were no clusters of voxels exhibiting a correlation between the amount of brain activation evoked by phoneme-grapheme trials during the phoneme-grapheme mapping task and growth observed in GORT comprehension across the intervention that survived an uncorrected threshold of $p < 0.001$ that was spatially corrected to $p < 0.01$. Furthermore, no clusters were large enough to survive these stringent criteria when activation evoked by tone-symbol trials and/or pre-intervention levels of GORT comprehension were added to the model. Thus, analyses were repeated at an uncorrected threshold of $p < 0.01$ that was spatially corrected to $p < 0.01$ (see Table 4.5). Thus, the correlations reported between phoneme-grapheme activation and growth in GORT comprehension exhibited medium to large effect sizes.

Table 4.5. Voxelwise correlations of phoneme-grapheme trial activation with growth in GORT comprehension.

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Phoneme-grapheme trials						
Inferior occipital gyrus	R	19	-3.34	0.46	12	37, -78, 2
Inferior occipital gyrus	L	19/18	-3.06	0.42	38	-32, -75, -0
Lingual gyrus	R/L	18	-3.29	0.45	17	1, -80, 5
Middle occipital gyrus	L	18	-3.33	0.46	13	-23, -89, 8
Inferior occipital/fusiform gyrus	L	19/18	-3.29	0.45	12	-35, -69, -3
Middle temporal gyrus	L	21/22	4.92	0.65	10	-61, -46, 1
Middle temporal gyrus	R	21	-3.36	0.47	29	49, -31, -5
Middle temporal gyrus	L	21	3.18	0.44	20	-55, -14, -11
Anterior cingulate/medial frontal gyrus	L	10/11	4.16	0.57	13	-8, 38, -14
Middle orbital/inferior frontal gyrus	L	10/46	3.13	0.43	16	-41, 50, -4
Tone-symbols as covariate						
Inferior occipital gyrus	L	19/18	-4.16	0.57	25	-32, -75, 2
Posterior cingulate gyrus	R	30	-4.14	0.57	10	22, -54, 12
Posterior cingulate/ parahippocampal gyrus	L	30	-3.07	0.42	16	-26, -54, 6
Middle temporal gyrus	L	21	3.18	0.44	24	-55, -14, -11
Precentral gyrus	L	4	3.20	0.44	11	-38, -8, 51
Inferior frontal gyrus	L	46	3.08	0.42	17	-47, 45, -1
Time1 GORT Comprehension as covariate						
Middle occipital gyrus	L	19	-3.92	0.54	22	-32, -75, 2
Parahippocampal/ calcarine gyrus	R	30/19	-3.77	0.52	26	25, -48, 6

Table 4.5 - *Continued*

Parahippocampal gyrus/hippocampus	R	36	-3.92	0.54	17	31, -29, -13
Posterior cingulate gyrus	R	29	3.40	0.47	14	4, -45, 6
Superior temporal gyrus	R	22/39	3.37	0.47	71	54, -51, 15
Middle temporal gyrus	L	21	3.30	0.46	23	-55, -17, -11
Middle temporal gyrus	L	21/22	3.22	0.44	13	-61, -49, 1
Middle/inferior temporal gyrus	L	21	3.67	0.51	12	-55, -3, -22
Postcentral gyrus/insula	R	43	-3.62	0.50	14	51, -13, 15
Superior frontal gyrus	R	10	-3.63	0.50	29	25, 50, -12
Postcentral gyrus/insula	L	43	-4.18	0.57	33	-58, -13, 15
Middle/inferior frontal gyrus	R	9	-3.82	0.53	52	43, 28, 24
Inferior frontal gyrus	L	44/9	-3.41	0.47	15	-38, 11, 25
Tone-symbols and Time1 GORT Comprehension as covariates						
Middle occipital gyrus	L	19	-5.22	0.68	15	-32, -72, 5
Parahippocampal gyrus	L	30	-4.30	0.59	13	-29, -54, 9
Parahippocampal gyrus	R	30	-3.56	0.49	19	25, -48, 6
Precuneus	L	7	3.23	0.44	17	-11, -52, 56
Posterior cingulate gyrus	R	29	3.77	0.52	10	7, -42, 9
Middle temporal gyrus	L	21	3.81	0.53	13	-55, -3, -22
Middle temporal gyrus	L	21	3.14	0.43	28	-55, -17, -11
Middle temporal gyrus	L	21/22	4.01	0.55	11	-61, -46, 1
Superior frontal gyrus	R	10	-3.33	0.46	26	22, 50, -12
Middle frontal gyrus	R	9	-3.97	0.55	43	43, 28, 24
Middle frontal gyrus	R	45/46	-4.06	0.56	19	46, 34, 13
Inferior frontal gyrus	L	46/10	3.15	0.43	11	-47, 45, -1

Note. Critical $t(13) = 3.014$, uncorrected $p < 0.01$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$. H = hemisphere, BA = Brodmann area, TLRC = Talaraich coordinates.

Analyses revealed six clusters of voxels with negative correlations between activation evoked by phoneme-grapheme trials and growth in GORT comprehension. These clusters included the left middle occipital (BA 18), inferior occipital (BA 19/18), and inferior occipital gyrus extending to the fusiform gyrus (BA 19/18), as well as an area of the lingual gyrus that crossed from the right to the left hemisphere (BA 18), the right inferior occipital gyrus (BA 19), and the right middle temporal gyrus (BA 21). Positive correlations were observed in clusters in the left anterior middle temporal gyrus (BA 21/22). There were also positive correlations in clusters in the left middle orbital (BA 10/46) and medial frontal (BA 10/11) gyri. Only the clusters in the left inferior occipital (BA 19/18), left middle temporal (BA 21/22), and left inferior frontal (BA 46) gyri remained significant when activation evoked by tone-symbol trials was added as a covariate of no interest.

In addition, new clusters of negative correlations in the left and right posterior cingulate gyrus (BA 30), and positive correlations in the left inferior frontal gyrus (BA 9), and left precentral gyrus (BA 4) emerged when activation evoked by tone-symbol trials was included. These new clusters were not large enough to survive the statistical thresholds once pre-intervention levels of GORT comprehension were added to the model with the exception of the cluster in the left posterior cingulate/parahippocampal gyrus (BA 30). The original clusters in the left middle temporal gyrus (BA 21/22), left middle occipital (BA 19), and left inferior frontal (BA 46/10) gyri remained significant with both control stimuli activation and pre-intervention GORT comprehension in the model.

However, when activation evoked by tone-symbol trials and pre-intervention levels of GORT comprehension were included as covariates of no interest eight additional clusters emerged. These clusters included negative correlations in the right posterior parahippocampal (BA 30), superior frontal (BA 10), and middle frontal (BA 9; BA 45/46) gyri. Positive correlations were observed in clusters in the right posterior middle temporal (BA 37/21/22), and posterior cingulate (BA 29) gyri as well as the left precuneus (BA 7). As depicted in Figure 4.17, the negative correlation in the left inferior occipital gyrus (depicted in blue), and positive correlations in the left middle orbital and middle temporal gyri (depicted in orange) remained significant regardless of whether the covariates were included in the model.

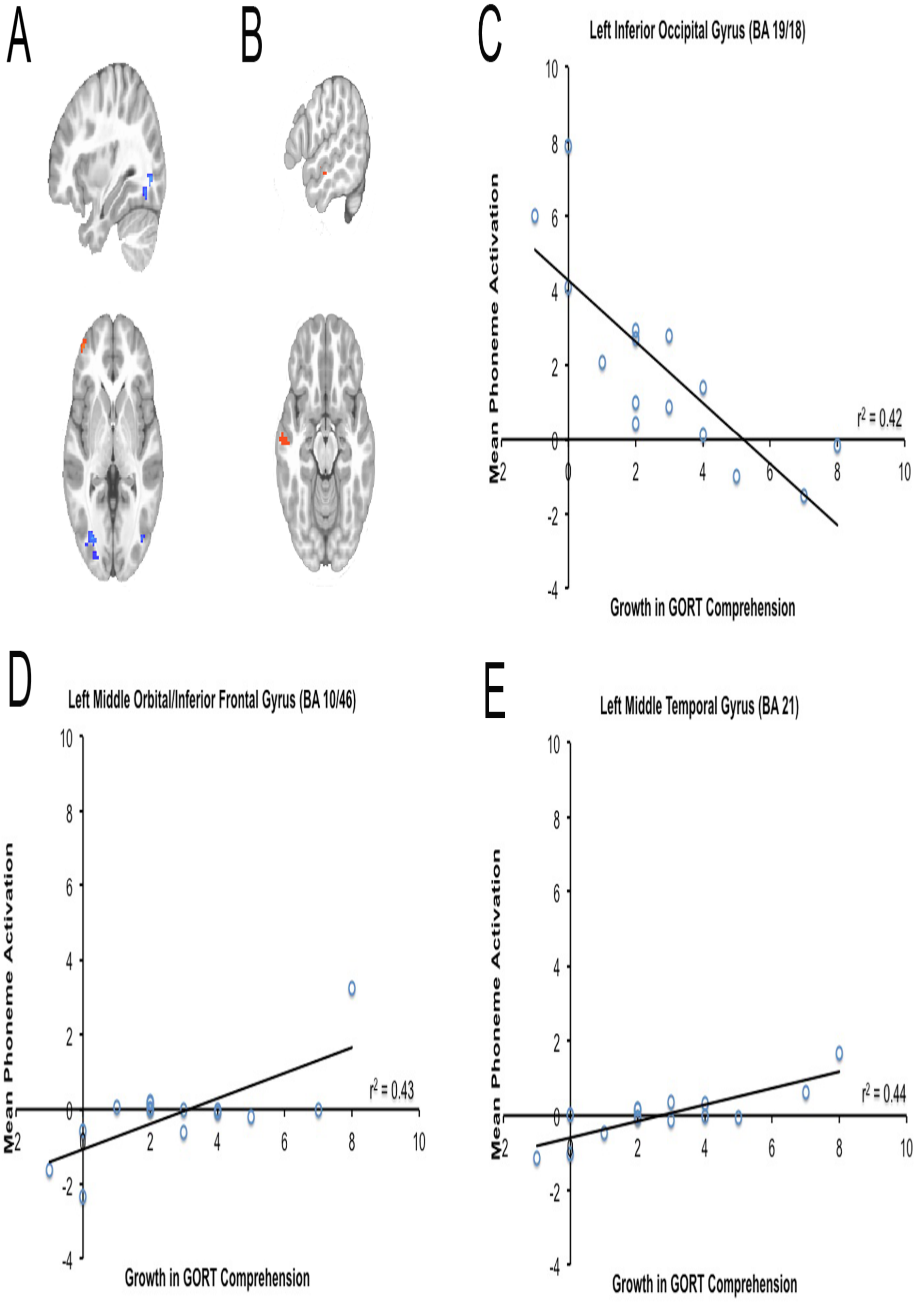

Figure 4.17. Clusters of phoneme-grapheme mapping task activation correlated with growth in GORT comprehension depicted with (A) sagittal (x = -32) and axial (z = 4) and (B) sagittal (x = -54) and axial (z = -11) images. Scatterplots of the clusters in the (C) left occipital, (D) left inferior frontal, and (E) left middle temporal gyri.

Positive correlations were observed in the right superior occipital (BA 7/19), right middle temporal (BA 22), and left middle frontal (BA 6) gyri between activation evoked by word-rhyme trials during the picture-word rhyming task and changes in GORT comprehension throughout the intervention at an uncorrected threshold of $p < 0.001$ that was spatially corrected to $p < 0.01$ (see Table 4.6).

Table 4.6. Voxelwise correlations of word-rhyme trial activation with growth in GORT comprehension

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Word-rhyme trials						
Superior occipital gyrus/ precuneus	R	7/19	4.66	0.63	12	25, -67, 43
Middle temporal gyrus	R	22	4.55	0.61	16	57, -40, 6
Middle frontal gyrus	L	6	5.41	0.69	18	-38, 18, 47
Color-match as covariate						
Precuneus	R	7	4.99	0.66	57	4, -64, 48
Middle temporal gyrus	R	22	4.33	0.59	13	57, -40, 6
Middle/superior temporal gyrus	R	41/42	5.07	0.66	10	60, -25, 8
Superior temporal gyrus	R	13/21	5.56	0.70	31	46, 0, -14
Superior middle temporal gyrus	L	22/39	6.65	0.77	25	-55, -51, 15
Medial frontal gyrus	L	6	5.05	0.66	12	-2, -10, 65
Insula	L	43	4.64	0.62	18	-50, -16, 13
Time1 GORT Comprehension as covariate						
Parahippocampal gyrus/ hippocampus	R	35/36	5.89	0.73	52	34, -17, -18
Parahippocampal gyrus/ hippocampus	L	35/36	5.89	0.75	44	-32, -26, -13
Superior temporal gyrus	R	38/22	5.38	0.69	24	51, 3, -12
Precuneus	L/R	7	4.93	0.65	10	-2, -55, 53
Postcentral gyrus	R	2	5.29	0.68	10	51, -21, 32
Middle frontal gyrus	L	6/8	5.45	0.70	27	-44, 15, 39
Lentiform nucleus/insula	L	13	4.62	0.62	11	-32, -7, 10
Insula/inferior frontal gyrus	L	13/44	4.43	0.60	53	-44, -16, 10
Color-match and Time1 GORT Comprehension as covariates						
Superior temporal gyrus	L	22/39	6.38	0.76	21	-55, -48, 14
Precuneus	R	7	4.94	0.65	12	1, -58, 51
Postcenteral gyrus/inferior parietal lobule	R	40	4.64	0.62	35	57, -24, 24
Parahippocampal gyrus/ hippocampus	R	35/36	5.78	0.72	23	31, -17, -18
Parahippocampal gyrus/ hippocampus	L	35/36	5.90	0.73	19	-32, -26, -13
Hippocampus	L	36	6.30	0.75	12	-32, -20, -18
Superior temporal gyrus	R	21/22	4.85	0.64	12	60, -22, -3
Superior temporal gyrus/insula	R	13/22	4.69	0.63	65	49, 9, -10
Superior frontal gyrus /supplementary motor area	L	6	6.48	0.76	11	-11, -5, 65

Table 4.6 - *Continued*

Middle frontal gyrus	L	6	5.17	0.67	25	-44, 15, 39
Insula	R	13	5.13	0.67	14	37, -4, 15
Insula	L	13	4.52	0.61	19	-32, -16, 16
Insula	L	13/44	5.08	0.67	48	-41, 4, 6
Thalamus	L		5.59	0.71	12	-8, -13, 10

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$. H = hemisphere, BA = Brodmann area, TLRC = Talaraich coordinates.

The clusters in the right middle temporal (BA 22; see Figure 4.18) and left middle frontal (BA 6) gyri remained significant, whereas the cluster in the right superior occipital (BA 7/19) was no longer significant when activation evoked by color-match trials was added to the model as a covariate of no interest.

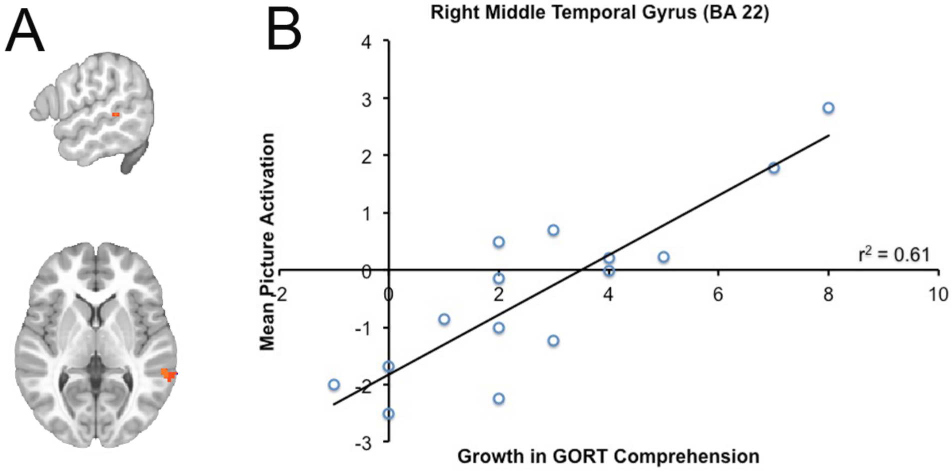

Figure 4.18. Cluster in the right middle temporal gyrus exhibiting a positive correlation between word-rhyme activation and growth in GORT comprehension. (A) sagittal (x = 57) and axial (z = 6) images. (B) scatterplot.

Additional clusters with positive correlations were observed in the right precuneus (BA 7), middle temporal (BA 22), middle to superior temporal (BA 41/42), superior temporal (BA 13/21), and middle frontal (BA 6) gyri as well as the left superior middle temporal (BA 22/36), medial frontal (BA 6), and middle frontal (BA 6) gyri and the left insula (BA 43).

The clusters in the right middle to superior temporal (BA 41/42), superior temporal (BA 13/21), and left medial frontal (BA 6) gyri were no longer significant when pre-intervention levels of GORT comprehension were also added to the model. However, new clusters of positive correlations emerged when activation evoked by color-match trials and pre-intervention levels of GORT comprehension were included as covariates of no interest. These clusters included areas of the right inferior parietal lobule (BA 40), right and left parahippocampal gyrus extending to the hippocampus (BA 35/36; see Figure 4.19), right insula (BA 13), and left thalamus.

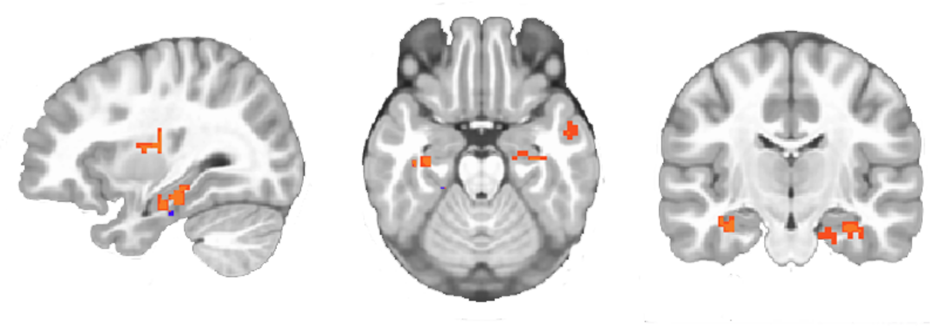

Figure 4.19. Sagittal (x = -31; left), axial (z = -18; center) and coronal (y = -17; right) images depicting the clusters of positive correlation between word-rhyme activation and growth in GORT comprehension in the bilateral parahippocampal gyrus.

There was no overlap in the significant clusters associated with growth in GORT comprehension across the phoneme-grapheme mapping and picture-word rhyming fMRI tasks.

4.2.2.4 Summary of Functional Neuroimaging Measures

My hypothesis was that pre-intervention measures of children with dyslexia's brain activation evoked by phonological tasks would be associated with changes observed in phonological decoding and reading comprehension throughout a 2-year multisensory reading intervention. The hypothesis was supported and a general pattern emerged across all three reading skills and both fMRI tasks. Negative correlations were more likely to be observed in occipito-temporal regions, whereas positive correlations were more likely to be observed in anterior temporal and prefrontal regions. However, differences occurred in the specific brain regions associated with growth in phonological decoding and each measure of reading comprehension across both fMRI tasks. The relevance of brain regions that should be included in future functional neuroimaging models to component processes of reading and the specific growth measures is briefly discussed below.

Phonological decoding is measured by having children read isolated novel pseudowords (Woodcock, 1998). Growth in phonological decoding was negatively correlated with activation in extrastriate regions across both the phoneme-grapheme mapping and picture-word rhyming tasks even after controlling for pre-intervention phonological decoding scores. These clusters extended to the fusiform gyrus such that the left hemisphere exhibited correlations with growth in phonological decoding across both tasks, whereas right hemisphere correlations were only present during the phoneme-grapheme mapping task. Specifically, it was the fusiform gyrus activation that remained significant after controlling for pre-intervention phonological decoding scores. Activation of extrastriate regions including bilateral inferior occipital gryi is associated with orthographic processing (Pugh et al., 1996) and activation of the left posterior fusiform gyrus is specialized for processing and identifying written words as part of the ventral stream, which directly maps words to their meaning (Coltheart et al., 2001; Devlin, Jamison, Gonnerman, & Matthews, 2006; McCandliss et al., 2003; McCandliss & Noble, 2003; Saur et al., 2008; Simos et al., 2002; Vigneau et al., 2005). Furthermore, Odegard et al. (2008) observed equivalent activation of the left fusiform gyrus during the same phoneme-grapheme mapping task across their groups of participants who differed in their phonological decoding and single word reading abilities. Additionally, dyslexic adults demonstrate less left and more right activation in the fusiform gyrus during reading tasks than adults with typical reading abilities. In regards to changes in reading skills, McNorgan et al. (2011) observed small improvements in pseuodoword reading efficiency (i.e., reading pseudowords under time pressure) over a 3—5 year period to be negatively correlated with left fusiform gyrus activation during a word rhyming task in 13—15 year-old children with typical reading skills.

One explanation for the negative correlation in the right fusiform gyrus is that children with dyslexia who exhibit brain activation commonly observed in struggling adult readers are less likely to exhibit improvements in their own reading skills. However, this logic suggests that if any correlations are found in the left fusiform gyrus, then they should be positive because left fusiform activation is observed in good readers. Yet, the correlations with the left fusiform gyrus observed in the present study were negative. The fusiform gyrus is part of the ventral pathway to reading, but in order to successfully read pseudowords a child needs to engage phonological processes through the dorsal pathway, which involves superior temporal and inferior parietal activation instead of fusiform activation (Coltheart et al., 2001; Seghier et al., 2008). Thus, children who rely primarily on the lexicosemantic ventral processing stream are less likely to exhibit growth in a more phonologically based process of reading novel pseudowords.

Greater left insula activation during the picture-word rhyming task, which requires phonological awareness abilities, was associated with more growth in phonological decoding. Left inferior frontal and insular regions are associated with phonological processing (Pugh et al., 1996) and activation is frequently seen in children with dyslexia as well as non-impaired readers during phonological tasks, including our phoneme-grapheme mapping task (Odegard et al., 2008) and other word rhyming tasks (e.g., Cao et al., 2006; Hoeft, Meyler et al., 2007; Shaywitz et al., 1998). In addition, the children in the present study exhibited left inferior frontal activation during the picture-word rhyming task (see Table B.2). Thus, activation of the left insula occurs in individuals with average reading skills and engaging this region pre-intervention is associated with dyslexic children improving phonological decoding skills that were deficient before the intervention.

Passage comprehension requires a child to provide the correct word based on the context of a sentence that she has read (Woodcock, 1998). Across both fMRI tasks positive correlations were observed between activation in the left insula and growth in passage comprehension. Not only has activation in the left insula and nearby left inferior frontal gyrus been associated with phonological processing during tasks similar to the ones in the present study, but left inferior frontal activation has also been associated with semantic processes, such as judging if an item belongs to a specific category (Pugh et al., 1996; Pugh et al., 2000). Specifically, posterior inferior frontal gyrus activation encompassing BA 44 is associated with phonological processes and anterior inferior frontal gyrus activation encompassing BA 45 and 47 is associated with semantic processes (Bokde et al., 2001; Saur et al., 2008; Simos et al., 2002; Vigneau et al., 2011).

Additionally, word-rhyme activation in a more anterior region of the right inferior frontal gyrus (BA 47) was also positively correlated with growth in passage comprehension. Children with dyslexia who have responded well to intervention and exhibited improvements in their reading skills frequently exhibit right inferior frontal activation (Odegard et al., 2008; Shaywitz et al., 1998). Furthermore, bilateral inferior frontal activation occurs in typical readers during difficult reading tasks, such as making rhyme judgments when words are not orthographically similar (Cao et al., 2006). Moreover, in the present study right inferior frontal gryus activation occurred during the picture-word rhyming task (see Table B.2). Thus, pre-intervention activation of bilateral inferior frontal gyrus and insular regions predicts that the children with dyslexia will exhibit improvements in comprehension, which itself relies on semantic and phonological processes.

Furthermore, positive correlations were also observed between growth in passage comprehension and activation evoked by word-rhyme trials in the left superior frontal and precentral gyrus and the left inferior temporal gyrus. Non-reading impaired children exhibit greater activation in left medial and superior frontal gyri compared to children with dyslexia when activation between difficult rhyming trials where orthography and phonology are inconsistent with one another is contrasted with activation during simple rhyming trials where orthography and phonology match. Additionally, non-reading impaired children exhibited greater activation in the anterior left inferior temporal gyrus, an area that is responsive to both auditory and visual word forms, during the difficult rhyming trials in comparison to the children with dyslexia (Cao et al., 2006). In the present study, the children with dyslexia who had greater activation in these regions exhibited more growth in passage comprehension that was perhaps due to an enhanced ability to use top-down processes engaged by anterior brain regions to modulate posterior regions (Cao et al., 2008).

Additional clusters of activation associated with growth in passage comprehension during the phoneme-grapheme mapping task included posterior regions of the right hemisphere, specifically the inferior occipital and angular gyri. Although the angular gyrus is associated with mapping phonemes and graphemes as well as semantic processes, this activation is primarily seen in the left hemisphere for non-impaired readers (Price et al., 2003; Shaywitz et al., 1998). Furthermore, Shaywitz et al. (1998) observed right angular gyrus activation to be greater in dyslexic adults than adults with average reading skills. In the present study, children who exhibited greater activation of the right angular gyrus, analogous to that seen in adults with dyslexia, were less likely to exhibit growth in the higher-order skill of reading comprehension.

In contrast, negative correlations between growth in passage comprehension and picture-word rhyming task activation occurred in left posterior regions including the fusiform gyrus, supramarginal gyrus, and posterior cingulate gyrus. The left fusiform gyrus is involved in rapidly identifying words, whereas the left supramarginal gyrus is associated with single word reading as well as the storage and manipulation of verbal information in working memory (McCandliss et al., 2003; Vigneau et al., 2011; Wise et al., 1991). Activation in medial extrastriate areas, encompassing the posterior cingulate gyrus, is associated with semantic processing (Pugh et al., 1996). Although the picture-word rhyming task involves phonological processing to determine if the words rhyme, there is also a memory component, as the child must recall the words represented by the pictures. Thus, it seems reasonable that this task would be more likely to engage semantic processing and working memory areas of the brain than the phoneme-grapheme mapping task. Yet, children with dyslexia often exhibit under activation of left posterior regions including the fusiform, supramarginal, and superior temporal gyri. As indicated in Table B.2 of Appendix B, the children in the present study did not exhibit activation in these brain regions at levels that would survive the stringent statistical thresholds used in my other analyses. In this regard, prior to intervention, children with dyslexia who exhibit greater activation in the left supramarginal gyrus, even though this activation may not be significantly above baseline, are less likely to exhibit large changes in their passage comprehension scores. These children are already exhibiting activation in a brain region more commonly activated by typical than by dyslexic readers. As such any deficits the children with dyslexia have in passage comprehension may not be as severe as their other deficits, or the deficits may be due to differences in the activation of other brain regions.

Growth in reading comprehension was also measured through GORT comprehension, which requires a child to respond to multiple-choice questions about stories that she has read aloud (Wiederholt & Bryant, 2001). Similar to analyses of passage comprehension, positive correlations were observed between growth in GORT comprehension and activation in left frontal regions across both fMRI tasks. The left frontal cluster was in more anterior and medial regions (BA 46/10) for the phoneme-grapheme mapping task, and in more insular regions (BA 43) for the picture-word rhyming task. During a word rhyming task that is very similar to the one in the present study because it also used line drawings to represent words, adult dyslexics with average skills, who are considered to be compensated readers, have been observed to exhibit left frontal activation that extends more medially and superiorly than activation in adults who never experienced reading problems (Macsweeney et al., 2009). This result helps to explain the positive correlations with growth in reading skills in the present study by providing further evidence that extensive left frontal activation in children with dyslexia may be a form of compensation.

In contrast to the passage comprehension analyses, positive correlations with growth in GORT comprehension were also observed in the left and right middle temporal gyrus across both fMRI tasks. The left middle temporal gyrus is activated by both phonological and semantic processing tasks in individuals with average reading skills (Booth & Burman, 2005; Pugh et al., 1996; Pugh et al., 2000). Furthermore, non-reading impaired children have demonstrated greater left middle temporal gyrus activation than children with dyslexia (Shaywitz et al., 2002). Moreover, Hoeft Uueno et al. (2007) observed positive correlations between children's left middle temporal gyrus activation during a rhyming task and phonological decoding scores obtained one year later. In the present study, the children with dyslexia who exhibited greater left middle temporal gyrus activation pre-intervention were more likely to exhibit improvements in their GORT comprehension skills throughout the intervention. Positive correlations were also observed with right middle temporal activation even though previous studies reported right middle temporal activation to be greater in treatment non-responders than in children who responded positively to intervention or who did not have deficits in their reading skills (Odegard et al., 2008).

The phoneme-grapheme mapping task data also exhibited clusters in the left inferior occipital gyrus, right posterior parahippocampal/cingulate gyrus (BA 30), and right superior and middle frontal gyri that were negatively correlated with growth in GORT comprehension. The occipito-temporal regions are associated with phonological processing (Pugh et al., 1996) and right parahippocampal activation has been associated with reading false fonts (Turkeltaub et al., 2003). Furthermore, Shaywitz et al. (2002) observed right posterior cingulate activation during nonword rhyming tasks to increase with age in dyslexic readers. In the present study, the negative correlation between growth in GORT comprehension and activation of occipito-temporal regions in both hemispheres suggests that relying on primarily orthographic processing is not sufficient to lead to enhancements in comprehension.

Right middle frontal gyrus activation has been positively correlated with digit span performance, which provides a measure of verbal working memory (Turkeltaub et al., 2003). However, Hoeft Uueno et al. (2007) observed negative correlations between right middle frontal activation during a word rhyming task and phonological decoding scores obtained one year later. In the present study, right middle frontal gyrus activation while mapping phonemes and graphemes is associated with less growth in the ability to correctly answer multiple-choice questions about a story, therefore I replicated the results of Hoeft Uueno et al. (2007) and extended them to be able to predict changes in reading comprehension.

Correlations with growth in GORT comprehension that were only observed during the picture-word rhyming task occurred in the left posterior superior temporal gyrus, right precuneus and bilateral parahippocampal gyrus extending to the hippocampus. The left posterior superior temporal gyrus is associated with phonological processing and is frequently activated to a greater extent by non-impaired as compared to dyslexic readers (Hoeft Meyler et al., 2007; Shaywitz et al., 2002; Shaywitz et al., 1998). The precuneus and nearby superior parietal lobule are frequently activated during calculation and visual-spatial working memory tasks and are commonly associated with spatial attention processes (Dehaene et al., 2003). In regards to reading, Turkeltaub et al. (2003) observed decreased activation in the right precuneus with increasing age. However, Specht et al (2009) observed 5- to 8-year-old children without reading impairments to exhibit greater bilateral superior parietal lobule activation when presented with Norwegian words that had different levels of phoneme-grapheme correspondence in comparison to children who had a family history of reading problems and subsequently exhibited lower reading skills themselves. In the present study children who exhibited greater activation of the right precuneus were more likely to exhibit improvements in their GORT comprehension scores throughout the intervention.

Activation of the parahippocampal gyrus is associated with memory encoding for individual items (e.g., words, faces, and objects; Davachi & Wagner, 2002; Diana, Yonelinas, & Ranganath, 2007; Gonsalves et al., 2009; Ranganath et al., 2004) and activation of the hippocampus is involved in encoding associations between items (Addis & McAndrews, 2006; Bokde et al., 2001; Brown & Aggleton, 2001; Buckner, Kelley, & Petersen, 1999; Diana et al., 2007; Mayes, Montaldi, & Migo, 2007; Piekema, Kessels, Rijpkema, & Fernandez, 2009; Sperling et al., 2001; Sperling et al., 2003). GORT comprehension involves some memory processes as the child must be able to recall parts of the story in order to correctly respond to questions. The picture-word rhyming task taps memory processes as well because the child must be able to know the word that is represented by the picture in order to correctly make her rhyme or non-rhyme judgment. Thus, positive correlations between parahippocampal gyrus and hippocampus activation and growth in GORT comprehension suggest that children who exhibit greater activation of memory-related brain regions during a task requiring some implicit memory processing are more likely to also use their memory skills to refine their comprehension abilities throughout the intervention.

Although identifying how each of the brain regions discussed above are associated with component processes of reading can help us to interpret the results of the correlational analyses, it is difficult to understand the contribution of separate brain regions in isolation. Implications for how the brain regions associated with growth in phonological decoding and in reading comprehension may function as a distributed network are mentioned in the general discussion.

CHAPTER 5

GENERAL DISCUSSION

5.1 Proposed Goals and Review of Results

Behavioral and functional neuroimaging measures acquired at one time point can be used to predict later reading skills (Frijters et al., 2011; Hoeft Uueno et al., 2007; Maurer et al., 2008; McNorgan et al., 2011; Nelson et al., 2003). Other research has specifically focused on the ability to use initial assessments to predict the change that occurs in reading skills over time (i.e., Gantman, 2007; Hoeft et al., 2011), and this is the focus of the present dissertation. In past research, even though initial behavioral measures of a group of dyslexic children's' reading skills did not predict changes in single word reading abilities over a 2.5 year period, right inferior frontal gyrus activation was associated with growth in single word reading (Gantman, 2007; Hoeft et al., 2011). Supplementary analyses indicated similar patterns of results if changes over the 2.5 year period in passage comprehension or a composite measure of reading skills was used as the outcome variable (Hoeft et al., 2011). Yet, the mean performance of the children in these studies only exhibited an average increase of 5 standard scores over 2.5 years. Subsequently, a multivariate pattern analysis distinguishing between subgroups of these children with dyslexia who did and did not exhibit substantial gains in single word reading revealed differences in initial measures of brain activation. Specifically, greater activation in right inferior frontal gyrus, left inferior, middle, and superior frontal gyri, right lingual gyrus, and right precuneus occurred in children whose skills increased. Meanwhile, greater activation was observed in the left insula, left precentral gyrus, left inferior parietal lobule, left posterior cingulate gyrus, left middle and superior occipital gyri, and right fusiform gyrus in children whose reading skills did not improve (Hoeft et al., 2011).

The analyses in this dissertation extend prior research by tracking reading skills in a small group of children with developmental dyslexia as they completed a 2-year multisensory intervention. The children with dyslexia initially presented with deficits in several reading and reading-related skills (i.e., rapid naming, phonological decoding, single word reading, real word and pseudoword reading efficiency, reading fluency, and reading comprehension), but did not have standardized test scores that would qualify as being deficient in phonological memory or phonological awareness abilities. By the end of the intervention the majority of the children's reading skills had increased and were within average ranges. Although reading fluency was still below average, performance significantly increased during the intervention. In this regard, the data presented above provide compelling evidence that not only can behavioral and functional neuroimaging measures be used to predict changes in reading skills over a 2-year period, but also that those measures can predict changes associated with significant growth such that deficient abilities now qualify as being within the average range.

Three measures of reading skill were chosen in order to test hypotheses regarding the predictive ability of behavioral and functional neuroimaging measures. First, phonological decoding, which requires a child to be able to read unfamiliar pseudowords, was chosen as this ability is not only highly correlated with single word reading (Woodcock, 1998), but unlike single word reading, it is necessary for children to rely on phonological processes because prior exposure, and consequently, memory traces for pseudowords are almost guaranteed to be nonexistent. In contrast to previous analyses, the current study included a group of children enrolled in a specific intervention whose mean performance in phonological decoding exhibited an increase of approximately 10-12 standard scores by the end of the 2-year intervention.

The second outcome measure was passage comprehension, which was chosen to again attempt to replicate previous findings, but in a group of children whose standardized test scores improved substantially. Furthermore, the ultimate goal of reading is comprehension so analyses of factors predicting improvements in reading comprehension are of the upmost importance. The passage comprehension subtest from the WRMT requires children to provide an appropriate word based on sentence context (Woodcock, 1998) and in the present study the children with dyslexia's mean performance exhibited an increase of approximately 10 standard scores.

Third, a second measure of reading comprehension was also analyzed to potentially validate findings. GORT comprehension requires children to demonstrate knowledge about what occurred in a passage and children's mean performance increased by approximately 3 standard scores by the end of the intervention. Thus, this dissertation extends research investigating the ability to predict changes in reading skills in children with dyslexia through combinations of behavioral and fMRI measures to include predictions regarding phonological decoding and multiple reading comprehension measures. Moreover, this dissertation extends the choice of phonological processing tasks used to measure brain activation to include word rhyming judgments for stimuli presented as line drawings and the ability to map auditorily presented phonemes to visually presented graphemes.

5.1.1 Growth in Phonological Decoding

Negative correlations with growth in phonological decoding were observed between pre-intervention behavioral measures and brain activation across both fMRI tasks. However, the behavioral measures of single word reading and real word reading efficiency were no longer significantly related to changes in phonological decoding once initial time 1 measures of phonological decoding were controlled. Negative correlations with left inferior occipital gyrus remained significant for both fMRI tasks after time 1 phonological decoding was controlled. Furthermore, a positive correlation was observed between growth in phonological decoding and left insula activation during the picture-word rhyming task. Thus, the present results replicated prior research and extended it in two ways. First, behavioral measures were found to not significantly predict a measure of pseudoword as opposed to only real word reading. Second, clusters of brain activation associated with growth were observed in regions previously used to discriminate between children who did and did not experience gains in single word reading. Importantly, Hoeft et al. (2011) observed left occipital gyrus activation to be associated with children's test scores remaining the same and this region exhibited a negative correlation with growth in my study. Furthermore, extensive left prefrontal activation has been associated with children whose test scores improved (Shaywitz et al., 2004) and I observed this region to exhibit a positive correlation with growth.

However, my results did not extend the previous finding of a positive correlation between right inferior frontal gyrus activation and growth in single word reading to a measure of phonological decoding. Even when the correlational analyses were repeated controlling for the influence of age (see Tables A.1 and A.2), I still did not observe a significant cluster in the right inferior frontal gyrus. This is disconcerting because the right inferior frontal gyrus has been proposed as a marker of treatment response (Odegard et al., 2008; Pugh et al., 2000; Shaywitz & Shaywitz, 2004; Shaywitz et al., 1998, 2002). Furthermore, functional connections between the right and left inferior frontal gyri are observed in children who respond well to treatment as well as non-impaired readers, and may provide a means to recruit additional brain regions to aid in the performance of reading tasks (Farris et al., 2011).

Examination of the brain regions engaged by the fMRI tasks in the present study revealed that the right inferior frontal gyrus was not significantly activated above baseline during the phoneme-grapheme mapping task (see Table B.1), but activation was observed during the picture-word rhyming task (see Table B.2). An exploratory analysis with a less stringent statistical criteria of an uncorrected $p < 0.01$ revealed a positive correlation in the right insula during the picture-word rhyming task suggesting that with a larger sample size I may have been more likely to replicate the correlation in the right inferior frontal gyrus.

5.1.2 Growth in Passage Comprehension

The analyses with passage comprehension as the outcome measure also partially replicated previous findings, and extended the results to my group of children who exhibited significant improvement in their test performance. Once pre-intervention measures of passage comprehension were controlled, the negative correlation with phonological awareness remained significant and the correlation with single word reading reversed signs from analyses not including time 1 passage comprehension to now be positive. Both of these correlations had small effect sizes. Phonological awareness abilities have been positively associated with later reading comprehension performance as well as later single word reading scores (Torgesen, Wagner, Rashotte, Burgess, & Hecht, 1997). Furthermore, in an analysis of response to intervention using growth curve modeling, Frijters et al (2011) observed phonological awareness to discriminate between good and poor response to intervention when later single word reading and reading comprehension scores were treated as outcome measures. Additionally, single word reading abilities account for a large portion of the variance when reading comprehension is assessed through CLOZE-type probes as it is with the passage comprehension subtest (Cutting & Scarborough, 2006).

Thus, future research investigating the impact of single word reading on changes in reading comprehension may reveal explanations for why the correlations between phonological awareness and single word reading with growth in passage comprehension are in different directions in the present study. At first glance the explanation seems simple, children with lower scores on more basic measures (i.e., phonological awareness and single word reading) likely also have lower scores in higher-order abilities (i.e., passage comprehension), and thus more room to grow. Yet, controlling for initial passage comprehension scores reveals that this relationship is more complex and may be due to other underlying factors because the correlation with single word reading is now positive. Attention and working memory abilities have been proposed as neurocognitive factors that impact performance and growth of reading skills (Frijters et al., 2011; Gathercole, Alloway, Willis, & Adams, 2006; Vellutino, Tunmer, Jaccard, & Chen, 2007). Future research should continue to investigate the contributions of neurocognitive factors as well as the influence of changes in different reading outcome measures on each other.

In regards to correlations between growth in passage comprehension and brain activation, similar to the analyses of growth in phonological decoding, a positive correlation was observed in the left insula across both the phoneme-grapheme mapping and picture-word rhyming task. Furthermore, replicating prior research (i.e., Gantman, 2007; Hoeft et al., 2011) and extending it to a rhyming task with picture stimuli, a positive correlation was observed between right inferior frontal gyrus activation and growth. Additionally, negative correlations observed during either task occurred in occipito-temporal regions. The correlations with the phoneme-grapheme mapping task were in the right hemisphere, whereas correlations with the picture-word rhyming task were in the left hemisphere. Dyslexic readers characteristically exhibit hypoactivation of left posterior brain regions, and may be more likely to exhibit right hemisphere posterior activation than age-matched peers (Shaywitz et al., 2002; Shaywitz et al., 1998; Turkeltaub et al., 2003). Although explanations may be devised for the negative correlations with the left and right occipito-temporal regions in isolation, it is difficult to reconcile these findings when considering the full brain all at once. Previous research has investigated the directional influence of the connections between areas of the brain evoked by reading tasks and found many areas to have reciprocal connections with each other. However, children and adults with dyslexia tend to exhibit fewer modulatory connections between parieto-temporal and prefrontal brain regions than children without reading impairments (Bitan, Cheon, Lu, Burman, & Booth, 2009; Bitan et al., 2006; Cao et al., 2008; Horwitz et al., 1998; Levy et al., 2009; Seghier & Price, 2009). Future studies could extend this line of research to examine how differences in the direction of influence between brain regions can be used to predict changes in reading skills.

Moreover, it is important to keep in mind the different processing demands of the fMRI tasks used in the present study. Negative correlations in right occipito-temporal regions occurred during a phonics task that requires phonological and orthographic processing. Activation of right occipito-temporal regions is characteristic of younger children and individuals who continue to struggle with reading (Shaywitz et al., 1998; 2002; Turkeltaub et al., 2003). In this regard, the negative correlation suggests that when brain activation evoked by phonological processes occurs in areas that are not engaged by good readers, children are less likely to exhibit growth in a skill requiring phonological and semantic processing. The negative correlations in the left hemisphere occur during a task requiring phonological processing as well as some semantic processing. Activation of left occipito-temporal regions is associated with both types of processing and is more frequently observed in good readers (McCandliss et al., 2003; Shaywitz et al., 1998; 2002; Vigneau et al., 2011; Wise et al., 1991). In this regard, children who already exhibit activation of expected brain areas during phonological and semantic processing tasks are less likely to exhibit significant growth in a measure encompassing both of those processes.

Although previous research has examined differences in the activation evoked by a variety of tasks in children and adults who exhibit reading impairments as well as non-impaired readers (i.e., Cao et al., 2006; Price et al., 2003; Pugh et al., 2000; Pugh et al., 1996; Shaywitz et al., 1998; 2002), less research has focused on task related differences in the ability to predict changes in reading skills through brain activation. In fact this dissertation extends research on the ability to predict changes in reading skills through brain activation to two additional fMRI tasks. These tasks have identified differences in brain activation based on individual's reading abilities. Specifically, activation during the phoneme-grapheme mapping task discriminates between children who did and did not respond well to treatment (Odegard et al., 2008). Activation during another incarnation of the picture-word rhyming task discriminates between typically reading adults with and without a history of reading problems (MacSweeney et al., 2009) and between adult native and non-native sign language users and non-hearing impaired adults (MacSweeney, Waters, Brammer, Woll, & Goswami, 2008).

5.1.3 Growth in GORT Comprehension

The ability to predict changes in GORT comprehension was also investigated in the present study. Single word reading and real word reading efficiency abilities measured prior to intervention were negatively correlated with changes in GORT comprehension. Thus, across all of the chosen outcome measures the ability to read isolated words, even when there is time pressure, can predict changes in reading skills. Specifically, children who are better are reading isolated words prior to beginning the intervention exhibit less growth in the chosen outcome measures. A large portion of this relationship occurs due to the initial scores on the growth measures, yet in the case of GORT comprehension, real word reading efficiency could still predict growth after controlling for initial GORT comprehension performance. Furthermore, a small positive correlation with pre-intervention phonological awareness was significant when the influence of initial GORT comprehension performance was removed from the analysis. Performance on a measure of phonological awareness has previously been observed to discriminate between children based on how well they responded to intervention as measured by performance on a CLOZE-type probe comprehension task (Frijters et al., 2011). Thus, the results of this dissertation suggest that similar results may be observed if a comprehension measure requiring knowledge of the content of a story was used as an outcome measure.

In regards to brain activation, growth in GORT comprehension was positively correlated with activation of the left inferior frontal gryus across both fMRI tasks. Thus, left prefrontal regions were positively associated with growth in all three of the chosen outcome measures in this study. In addition, right insula activation evoked by the picture-word rhyming task was positively correlated with growth in GORT comprehension. Thus, extending previous results regarding the ability to predict changes in reading skills to a second measure of reading comprehension. Moreover, left middle temporal activation evoked by both fMRI tasks was also positively correlated with growth in GORT comprehension. Left middle temporal gyrus activation is evoked by word rhyming tasks and greater activation is observed in non-reading impaired children compared to children with dyslexia (Booth & Burman, 2005; Cao et al., 2006). Furthermore, phoneme-grapheme task activation in bilateral extrastriate areas exhibited negative correlations with growth in GORT comprehension and these results are similar to the ones previously discussed regarding growth in phonological decoding. Children with dyslexia who exhibit greater bilateral extrastriate activation prior to intervention, thus demonstrating activation frequently observed in young children or adult dyslexics (Shaywitz et al., 1998; Turkeltaub et al., 2003), exhibit less growth in both phonological decoding and GORT comprehension scores.

In contrast to the other outcome measures, changes in GORT comprehension were also positively correlated with brain activation in medial temporal lobe areas associated with memory processing. Specifically, growth in GORT comprehension was positively correlated with activation in bilateral parahippocampal gyrus and hippocampus during the picture-word rhyming task. These medial temporal lobe areas are not always included in discussions of brain regions associated with reading, however, the hippocampus and parahippocampal gyrus are associated with memory processes (Diana et al., 2007; Sperling et al., 2001; Sperling et al., 2003). Memory processes can include semantic as well as episodic information and help to provide a knowledge base for a child to be able to successfully respond to comprehension questions. Furthermore, a positive correlation was also observed in a cluster of voxels in the right precuneus and activation in this region is associated with working memory and spatial attention abilities (Dehaene et al., 2003). In this regard, changes in an outcome measure that requires the child to rely the most on information in memory was associated with activation of brain regions involved more specifically with memory processing.

Hence the goal of identifying behavioral and functional neuroimaging measures that could reliably predict changes in reading skills throughout the course of a 2-year multisensory intervention was met. The results of this dissertation indicate that single word reading abilities and real word reading efficiency performance prior to intervention can predict the amount of growth observed in phonological decoding and reading comprehension. Furthermore, phonological awareness is also associated with changes in reading comprehension. In regards to brain activation, left prefrontal regions, specifically including the insula and inferior frontal gyrus demonstrate greater activation across two independent fMRI tasks in children with dyslexia who exhibited greater gains in phonological decoding and reading comprehension. Additionally, right prefrontal activation evoked by the picture-word rhyming task was positively correlated with growth in both measures of reading comprehension. Bilateral parahippocampal gyrus and hippocampus activation was positively associated with growth in GORT comprehension. Furthermore, negative correlations were observed across all three measures of growth in reading and activation in bilateral occipito-temporal regions. Yet, it is important to critically evaluate the study in order to identify improvements that can be made in the future so that one day pre-intervention behavioral and functional neuroimaging measures can guide decisions about which intervention methods or additional training will be most likely to enable a child with dyslexia to learn to read.

5.2 Limitations

The results of this dissertation help to further our knowledge of the relationship between behavioral measures of reading skills, fMRI measures of brain activation and growth in phonological decoding and reading comprehension. However, the results should be interpreted with caution. There were only 15 children with dyslexia included in the sample and they may have comprised a homogenous group that is not representative of the general population of children with developmental dyslexia. It is also possible that the growth observed in these dyslexic children's reading skills was due to factors other than their participation in the intervention. Specifically, the changes in the children with dyslexia's reading and reading-related skills may be due to regression to the mean, a statistical phenomenon in which extreme scores appear closer to average values with repeated measurement over time (Barnett, van der Pols, & Dobson, 2005). The children with dyslexia exhibited below average reading and reading-related skills prior to intervention that were within the average range a year later, or by the end of the intervention.

One way to obtain objective evidence that changing reading skills are due to participation in an intervention is to include a sample of children with dyslexia who do not participate and are kept on a waiting list (i.e., wait list control). It is unethical to deny a child the opportunity to receive treatment, yet a child may be treated as her own demographically matched wait list control if sufficient time elapses between her initial assessment and the beginning of the intervention. A lack of differences between initial evaluation and pre-intervention assessments accompanied by significant differences between pre-intervention and middle or end of the intervention assessments suggest that any improvements in the child's test scores are due to the effects of the intervention, rather than regression towards the mean.

Take Flight is a 2-year program (Avrit et al., 2006) and new groups of students start at TSRHC at the same time every year, even though a child may be assessed, diagnosed, and admitted into the program throughout the entire year. Thus, the children with dyslexia in the present sample had to wait approximately 7 months from the time that they were initially assessed until the intervention began. These children were reassessed shortly before the beginning of the intervention and it is these scores that are reported as the prior to intervention measures. Comparisons between initial evaluation and pre-intervention performance on available measures are reported in the methods section and revealed that phonological awareness, rapid naming, and single word reading skills did not increase during this waiting period.

Second, evidence that changes in reading skills are associated with the intervention itself can be obtained by tracking changes in academic skills in another domain, such as mathematics. *Take* Flight was designed to enable children with dyslexia to read more accurately and efficiently, and with better understanding (Avrit et al., 2006). It was not specifically designed to lead to significant improvements in unrelated domains, such as mathematics, except for improvements that are primarily due to enhanced reading abilities. If growth in reading skills is due to participation in the intervention, then any changes observed will be larger in the reading than the mathematics domain. The children in the present study completed an assessment of numerical operations at each time point. Although numerical operations skills increased over the first year of the intervention, the size of this effect was smaller than that reported with the improvements in the individual reading skills.

Third, an age- and gender-matched group of children without reading impairments was included as a control group. In the present study the control group also did not differ from the children with dyslexia in regards to socioeconomic status as measured by their parents' education level. However, due to random sampling error, the control group included a large portion of children who performed above average on many of the measured reading and reading-related skills. Comparing the performance of these non-reading impaired children to the children with dyslexia answers questions about differences in the size of the any observed skill increases and whether the children with dyslexia were able to perform at levels comparable to a group of peers who did not have learning disabilities. In the present study, changes observed in reading skills over time were larger in the children with dyslexia than those observed in the non-reading impaired children and, for the most part, the children with dyslexia continued to exhibit lower scores than the non-reading impaired children. Consequently, three lines of evidence (i.e., self wait list control, mathematics skill change, and non-reading impaired control group) suggest that the changes observed in the reading skills of the children with dyslexia were not due to regression towards the mean.

Another limitation of the study is the possibility that the children with dyslexia represented a homogenous group with a restricted range of reading skills. When performance on a measure of interest is very similar across a sample it is possible that the sample will not be representative of the entire population, and this is especially a concern in cases of small sample size, such as the present study. Range restriction can bias statistical analyses such that correlations between different measures or predicting changes across measures are attenuated and null results are more likely to be found (Stoolmiller, 1998; 1999). If normed-referenced instruments are used, then the amount of range restriction in a sample can be calculated by examining the ratio of the sample variance to the normative variance on an instrument of interest. This ratio can be converted to represent the percentage of range restriction in the sample by subtracting the ratio from 1 and then multiplying by 100 (Stoolmiller, 1999). In the present study, the pre-intervention phonological decoding, single word reading, real word and pseudoword reading efficiency and reading comprehension test scores of the children with dyslexia exhibited 43 – 74% range restriction. Thus, it is plausible that many of the results were attenuated.

On one hand, the restricted range suggests that any effects that were observed, even if they were accompanied with a small measure of effect size, are reliable. On the other hand, the knowledge of the range restriction in the current sample raises questions about possible range restriction in prior research. Range restriction is an issue that has not been prominently discussed in studies of response to intervention in children with dyslexia and future research investigating the presence and potential impact of range restriction is needed.

Consequently, I examined whether range restriction may have attenuated results in other studies examining response to intervention in children with dyslexia with neuroimaging measures. I only examined the range restriction ratio for a group of studies that used the same assessment instruments as I did and that used behavioral and neuroimaging measures to assess response to intervention. As can be seen in Table 5.1, pre-intervention assessments of phonological decoding, single word reading, real word and pseudoword reading efficiency, and reading comprehension varied from 40 – 95% restriction across a group of 7 studies and 9 subgroups of children. Thus, it appears that even though my sample size was smaller, my study may not have been affected by range restriction any more so than prior studies in this area.

Table 5.1. Range restriction in longitudinal dyslexia intervention studies with neuroimaging components.

	Phonological Decoding	Single Word Reading	Reading Efficiency		Comprehension	
			Real word	Pseudoword	Passage	GORT
Present Study Dyslexic (n = 15)						
Time 1	0.26	0.25	0.38	0.16	0.41	0.57
Time 3	0.27	0.23	0.34	0.24	0.20	0.46
Gantman (2007) Dyslexic (n = 22)						
Time 1		0.20				0.49
Time 2		0.30				0.69
Hoeft Uueno et al (2007) Diverse Reading (n = 64)						
Time 1	0.50	0.44			0.60	
Time 2	0.51	0.35			0.35	
Hoeft et al (2011) Dyslexic gain (n = 13)						
Time 1	0.27	0.19	0.27	0.41	0.53	1.00
Time 2	0.56	0.21	0.33	0.37	0.68	0.28
Hoeft et al (2011) Dyslexic no gain (n = 12)						
Time 1	0.31	0.21	0.42	0.28	0.41	0.61
Time 2	1.38	0.30	0.29	0.27	0.55	0.34
McNorgan et al (2011) Younger 9 – 11 years (n = 14)						
Time 1	0.04	0.04	0.35	0.05		
Time 2	0.53	0.67	0.05	0.07		
McNorgan et al (2011) Older 13 – 15 years (n = 12)						
Time 1	0.03	0.03	0.02	0.01		
Time 2	0.38	0.53	0.02	0.01		
Meyler et al (2008) Poor readers (n = 23)						
Time1		0.32	0.42			
Time 2		0.45	0.42			
Time 3 (n = 18)		0.25	0.37			
Shaywitz et al (2002) Dyslexic (n = 70)						
Time 1	0.54	0.51				
Simos et al (2007b) Dyslexic (n = 15)						
Time 1	0.31		0.34			
Time 3	0.24		0.31			

Note. Range restriction indicated with the ratio of sample variance to normative variance for each measure. Normative variance is 225, except for GORT comprehension where this value is 9.

A third limitation also associated with characteristics of the sample in the present study is the amount of comorbid attention problems in the children with dyslexia. The sample was limited to one cohort of children attending the Dyslexia Lab School at TSRHC. Although the presence of comorbid attention problems makes the children more representative of the general population of children with learning disabilities, it also impedes the interpretation of the results as relating specifically to reading deficits. Thankfully, reported attention problems did not differ between the children with dyslexia who did and did not have a comorbid diagnosis of attention problems suggesting that attention problems did not have a large impact in the present study. As a byproduct of increasing the sample size in future studies it may be possible to examine subgroups of children with developmental dyslexia based on the presence of comorbid conditions. Estimates suggest that up to 40% of children with developmental dyslexia also exhibit comorbid mathematics disabilities and a significant portion of these children may also exhibit underlying attention problems (Lyytinen & Rasanen, 1994; Rubinsten & Henik, 2006; Tressoldi, Rosati, & Lucangeli, 2007). Thus, it would be beneficial if future research could rely on a sample that is significantly larger than the present study so that potential differences between subgroups of children based on comorbid conditions can be more fully investigated.

5.3 Conclusions and Future Directions

In spite of the above limitations, and the use of stringent statistical criteria, behavioral and functional neuroimaging measures were associated with growth in phonological decoding and reading comprehension. Specifically, pre-intervention phonological awareness, single word reading, and real word reading efficiency measures were associated with changes exhibited by children with dyslexia in phonological decoding and reading comprehension throughout the 2-year multisensory intervention. Higher initial scores were associated with less growth in the chosen outcome measures. Furthermore, the initial performance on measures of phonological decoding and reading comprehension accounted for much of the relationship between other reading measures and growth in phonological decoding and reading comprehension. Consequently, it appears as though information other than children's reading skill performance may be needed to more accurately predict which child will positively respond to reading interventions. In this regard, information about brain activation during phonological processing tasks obtained prior to intervention may be useful in predicting response to intervention (Hoeft Uueno et al., 2007).

In the present study, activation evoked by both fMRI tasks in many areas of the reading brain network, as well as some homologues to these areas, were correlated with growth in phonological decoding and reading comprehension. The direction of the correlations between reading growth and pre-intervention brain activation was primarily negative in posterior occipito-temporal brain regions. Children with dyslexia frequently exhibit less activation in these areas than children without reading impairments, and activation in left parieto-temporal regions increases in response to intervention (Cao et al., 2006; Hoeft Meyler et al., 2007; Shaywitz et al., 2002; Simos et al., 2007b). Therefore, greater activation in occipito-temporal regions prior to intervention, especially in the left hemisphere, may indicate that a child with dyslexia is already able to engage the reading network in a manner exhibited by a typical reader and is less likely to exhibit large changes in her reading skills.

In contrast, positive correlations between growth in reading skills and brain activation were more likely to occur in left and right prefrontal regions. Bilateral inferior frontal activation occurs in individuals without reading impairments when reading tasks are difficult, and is observed in individuals with dyslexia who have increased reading skills after completing intervention programs (Cao et al., 2006; Odegard et al., 2008; Pugh et al., 2000; Shaywitz & Shaywitz, 2004; Shaywitz et al., 1998, 2002). Consequently, greater activation in left and right prefrontal regions prior to intervention may indicate that a child with dyslexia is able to engage portions of phonological and semantic processing networks used by typical readers and is more likely to exhibit large changes in her reading skills.

Although the implications for the positive and negative correlations with growth in reading skills work in isolation, they appear to be in direct contrast with one another. When children with dyslexia engage some parts of the reading network (i.e., left parieto-temporal regions) prior to intervention they are less likely to exhibit changes in their skills, but engaging other parts of the reading network (i.e., bilateral inferior frontal regions) lead to changes in reading skills. Such discrepancies provide further support for research focused on understanding how distributed parts of the brain function as a network.

The structural connections between the parts of the reading network have been investigated using diffusion tensor imaging (DTI), which is a magnetic resonance imaging technique that is used to measure the impact of white matter on the nonrandom (i.e., anisotropic) diffusion of water within the brain (for a review see, Beaulieu, 2002). Significant correlations between phonological decoding and word reading abilities and left temporo-parietal areas including portions of the superior longitudinal fasciculus, and inferior fronto-occipital fasciculus as well as the left superior corona radiata and posterior corpus callosum have been observed in children and adults with a diverse range of reading abilities (e.g., Beaulieu et al., 2005; Ben-Shacher, Dougherty, & Wandell, 2007; Deutsch et al., 2005; Dougherty et al., 2007; Klingberg et al., 2000; Niogi & McCandliss, 2006; Odegard, Farris, Ring, McColl, & Black, 2009). Furthermore, Farris et al. (2011) observed a positive correlation between a measure of the integrity of the anterior corpus callosum and a measure of the degree of functional connectivity between the left and right inferior frontal lobes during the phoneme-grapheme mapping task.

Other investigations have focused more exclusively on the functional connectivity, or temporal synchrony (Friston et al., 1997), of activation in reading network brain regions. Functional connections during reading tasks have been observed between the left and right inferior frontal lobes and between left inferior frontal and left parieto-temporal and left occipito-temporal regions. Furthermore, as compared to individuals without reading impairments, children and adults with dyslexia exhibit functional connectivity disruptions that coincide with deficits in the activation of posterior regions in the left hemisphere (Bitan et al., 2006; Cao et al., 2008; Farris et al., 2011; Horwitz et al., 1998; Richards & Berninger, 2008; Seghier & Price, 2010; Stanberry et al., 2006). Moreover, dynamic causal modeling (for a review see Friston, 2009) has been used to understand the direction of influence in the functional connections between reading brain areas. Children with dyslexia exhibit weaker modulation of left posterior brain regions from the left inferior frontal gyrus (Bitan et al., 2006; Cao et al., 2008).

It would be invaluable to be able to merge the research focused on predicting response to intervention through functional neuroimaging, such as that reported in this study, with investigations of the functional connections and consequently the modulatory influence of reading network brain areas on each other. It is anticipated that such an enterprise would help to explain the seemingly contradictory findings when the direction of the correlations between brain activation and reading growth in the current study are considered. Perhaps positive correlations were observed with activation in left frontal regions because this area exerts top-down processing on posterior brain regions (Bitan et al., 2006). Thus, when the left frontal regions are engaged prior to intervention the benefits a child receives from her specialized training may help her to use these frontal lobe driven modulatory processes to engage posterior brain regions more effectively. If the child already exhibits activation in the left posterior regions she may have higher reading skills to being with, or the training during the intervention allows for changes in other connections within the reading network. Greater knowledge of how changes in reading skills relate to the influences that brain regions have on one another during reading tasks may increase the ability to predict which child will respond to intervention.

Yet, it is crucial to also consider how to help the child who does not display factors associated with a likely positive response to intervention. One possibility is to look at the child's pre-intervention profile and identify which factors associated with growth in reading skills are absent. Then, additional training on those particular skills or processes could be added to the child's treatment plan in hopes of obtaining a more positive response to intervention. A second possibility is to consider factors other than behavioral test performance and neuroimaging measures.

As evidenced by the literature and analyses discussed in this dissertation, a great deal is known about the cognitive aspects of dyslexia, yet less is known about the impact of potential negative emotions that may be fostered in these children as a result of the frustration they experience when trying to read. Children in grades 1-3 who struggle to read have more negative attitudes towards reading for recreation and academic purposes than children without reading deficits (McKenna, Kear, & Ellsworth, 1995). Furthermore, children diagnosed with a reading disability, who were receiving special education instruction, exhibited more negative attitudes towards reading during grades 1-3 than average readers (Lazarus & Callahan, 2000). Thus, during the grades when children are being taught to read, the children who need to exert the most effort in these endeavors (i.e., those diagnosed with learning disabilities) have the most negative attitudes towards reading. The negative attitudes held by children with dyslexia may affect their ability to exert the extra effort needed to respond to interventions designed to help them with their reading difficulties.

Children’s attitudes towards reading are influenced by their home literacy environment (Greaney, 1986; Shaywitz, 2003). Parents identifying pleasure as a reason for reading and the child taking an active role in learning to read can be used as predictors for the child’s level of reading motivation (Baker & Scher, 2002). However, it is likely that the home environment of children with dyslexia is qualitatively different from that of children without reading impairments. As indicated in the family history information for the present sample, when a parent has a childhood history of reading problems, or continues to exhibit difficulties in reading, their child has a greater likelihood of developing her own reading problems (Gilger, Hanebuth, Smith, & Pennington, 1996). The relatively negative attitudes held by these parents who themselves struggled or continue to struggle with reading could result in a home environment that would not be as conducive to reading and reading education.

For example, parents of dyslexic children who themselves have low reading skills as adults, a majority of whom also had childhood reading problems, reported engaging in less reading for pleasure than parents with average reading skills (Scarborough et al., 1991). Furthermore, a parent’s history of reading difficulties as well as her current reading habits are associated with poorer orthographic processing and less positive perceptions of reading competence in her children (Conlon, Zimmer-Gembeck, Creed, & Tucker, 2006). Further research is needed to investigate the extent to which parents’ own reading attitudes foster or hinder the ability of children with dyslexia to overcome their reading problems when provided with targeted interventions aimed at remediating reading abilities.

In conclusion, substantial gains have been made in understanding the deficits associated with dyslexia on both a behavioral and neurobiological level. Factors at both of these levels associated with changes in reading skills have also been identified. Yet, there is still work to be done in order for this knowledge to be put to use so that interventions can be modified in order to better serve each child who presents with reading problems.

APPENDIX A

FUNCTIONAL NEUROIMAGING MEASURES INCLUDING AGE

Although in the present sample of children with dyslexia age was not significantly related to changes in behavioral measures of reading, brain development continues to occur across childhood (i.e., Turkeltaub et al., 2003). Thus, analyses of the correlations between brain activation during the fMRI tasks and growth in phonological decoding and reading comprehension were also ran with age at scanning as a covariate of no interest. The following results should be interpreted with caution as adding variables to the analyses further decreases the amount of statistical power and increases the possibility of finding spurious results.

The amount of brain activation evoked by phoneme-grapheme trials was correlated with growth in phonological decoding in many of the same areas as reported earlier after age at scanning had been added as a covariate of no interest. Specifically, a cluster in the right fusiform gyrus still exhibited negative correlations between task activation and growth in phonological decoding. This cluster was significant even when the previously analyzed covariates of tone-symbol (i.e., control task stimuli) activation and time 1 phonological decoding were included in the model. The addition of age at scanning resulted in an additional cluster in the right thalamus also exhibiting a negative correlation (see Table A.1).

Table A.1. Voxelwise correlations of phoneme-grapheme trial activation with growth in phonological decoding with age.

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Age as covariate						
Fusiform gyrus	R	37	-5.27	0.68	16	40, -58, -14
Thalamus	R		-4.95	0.65	17	13, -28, -3
Tone-symbol and age as covariates						
Fusiform gyrus	R	37	-5.88	0.73	16	40, -58, -14
Age and Time1 Phonological Decoding as covariates						
Fusiform gyrus	R	19/37	-5.26	0.68	22	40, -72, -8
Thalamus	R		-4.94	0.65	13	13, -28, -3
Tone-symbols, age, and Time1 Phonological Decoding as covariates						
Fusiform gyrus	R	19/37	-5.52	0.70	24	40, -72, -8

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$.

The amount of activation evoked by word-rhyme trials during the picture-word rhyming task was significantly correlated with changes in phonological decoding. Adding age at scanning eliminated the clusters in the left fusiform and inferior occipital gyrus that had originally been identified. The cluster in the left insula that exhibited a positive correlation when both color-match activation and time 1 phonological decoding were controlled was significant when age was added to the model. In addition, new clusters emerged in the left middle frontal gyrus and right middle occipital gyrus (see Table A.2).

Table A.2. Voxelwise correlations of word-rhyme trial activation with growth in phonological decoding with age.

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Age as covariate						
No significant clusters						
Color-match and age as covariate						
No significant clusters						
Age and Time1 Phonological Decoding as covariates						
Middle/ superior occipital gyrus	R	19/39	-5.88	0.73	26	40, -76, 30
Fusiform gyrus	L	37	-4.76	0.64	11	-41, -66, -8
Subcallosal/inferior frontal gyrus	R	47	4.52	0.61	10	13, 12, -17
Color-match, age, and Time1 Phonological Decoding as covariates						
Middle/superior occipital gyrus	R	19/39	-6.22	0.75	21	40, -76, 30
Middle frontal gyrus	L	6	4.96	0.65	10	-32, 0, 40
Insula	L	13	5.89	0.73	16	-29, 13, 17

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$.

The addition of age at scanning to analyses of the relationship between phoneme-grapheme activation and growth in passage comprehension resulted in some clusters remaining significant, while new clusters also emerged (see Table A.3). The negative correlation in the right angular gyrus, and positive correlations in the left insula and thalamus remained significant when age at scanning was included in the model that already controlled for tone-symbol activation and time 1 passage comprehension. A new cluster was also observed in the right middle temporal gyrus.

Table A.3. Voxelwise correlations of phoneme-grapheme trial activation with growth in passage comprehension with age.

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Age as covariate						
Middle temporal gyrus	R	39/19	-4.41	0.60	11	51, -59, 18
Tone-symbol and age as covariate						

Table A.3 - *Continued*

Posterior cingulate gyrus	L	30/18	-4.64	0.62	10	-17, -51, 12
Age and Time1 Passage Comprehension as covariates						
Inferior occipital gyrus	R	19	-5.10	0.67	10	43, -72, 2
Angular gyrus	R	39	-4.70	0.63	29	46, -59, 34
Middle temporal gyrus	R	19/39	-5.34	0.69	23	49, -62, 18
Inferior temporal gyrus	L	20	-4.72	0.63	22	-47, -12, -26
Inferior frontal gyrus	L	44/45	-5.11	0.67	21	-52, 22, 8
Insula	L	13	6.14	0.74	17	-38, -8, -6
Insula/putamen	R	13	4.96	0.65	15	31, -5, -9
Medial globus pallidus	R		6.89	0.78	13	19. -8, -9
Tone-symbols, age, and Time1 Passage Comprehension as covariates						
Angular gyrus	R	39	-4.69	0.63	24	49, -58, 37
Middle temporal gyrus	R	19/39	-5.03	0.66	14	49, -62, 18
Inferior frontal gyrus	L	6/9	5.33	0.69	17	-35, 5, 28
Insula/putamen	L	13	5.76	0.72	12	-38, -5, -6
Thalamus	L		6.34	0.76	13	-11, -14, 2

Note. Critical *t*(13) = 4.217, uncorrected *p* < 0.001, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected *p* < 0.01.

When age was incorporated into analyses of word-rhyme activation and growth in passage comprehension many of the clusters previously identified after controlling for color-match activation and time 1 passage comprehension remained significant (see Table A.4). Importantly the positive correlations in left precentral gyrus and insula and the negative correlations in the left supramarginal and fusiform gyri depicted in Figure 4.16 remained significant. A new cluster in the right angular gyrus exhibited a negative correlation between picture-word rhyming task activation and growth in passage comprehension.

Table A.4. Voxelwise correlations of word-rhyme trial activation with growth in passage comprehension with age.

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Age as covariate						
Precentral/superior frontal gyrus	L	6	5.61	0.71	44	-38, -2, 56
Color-match and age as covariate						
Calcarine gyrus/cuneus	R	17	5.25	0.68	10	19, -80, 19
Precentral gyrus	L	4/6	5.63	0.71	15	-50, -3, 45
Superior medial/Cingulate gyrus	L	32	4.76	0.64	19	-5, 29, 35
Age and Time1 Passage Comprehension as covariates						
Middle occipital gyrus	L	19	4.74	0.63	10	-26, -94, 14
Superior temporal/angular gyrus	R	39	-8.44	0.85	113	49, -53, 26
Cingulate/posterior cingulate gyrus	L	23	-6.59	0.77	19	-11, -24, 24
Posterior cingulate gyrus	L	18/30	-5.39	0.69	35	-17, -54, 12
Fusiform gyrus	L	37	-5.64	0.71	25	-35, -63, -6
Middle temporal gyrus	L	37/21	-8.76	0.86	21	-55, -49, -2
Insula/transverse temporal gyrus	R	13/41	-4.56	0.61	13	31, -31, 11

Table A.4 - *Continued*

Medial frontal gyrus	R	10	-5.93	0.73	24	4, 50, -7
Medial/superior frontal gyrus	R	10	-6.77	0.78	15	19, 53, -2
Superior frontal gyrus	L	6/32	-8.21	0.84	19	-14, 32, 44
Superior frontal gyrus	R/L	6	5.30	0.68	18	1, 15, 55
Precentral/superior frontal gyrus	L	6	5.63	0.71	11	-35, -2, 56
Medial frontal gyrus	L	6/32	5.26	0.68	11	-20, 17, 39
Inferior frontal gyrus	L	44/45/46	-4.50	0.61	10	-50, 34, 10
Color-match, age, and Time1 Passage Comprehension as covariates						
Lingual gyrus	R/L	17/18	5.53	0.70	22	4, -9, 26
Angular/middle temporal gyrus	R	39	-4.72	0.63	60	43, -59, 26
Posterior cingulate gyrus	L	30/18	-5.41	0.69	26	-17, -54, 12
Middle temporal gyrus	L	37/26	-7.48	0.81	11	-55, -49, -2
Insula/supramarginal gyrus	L	13	-6.48	0.76	10	-38, -41, 25
Precentral gyrus	L	4/6	7.89	0.83	16	-41, -5, 48
Anterior cingulate/medial frontal gyrus	R	10/32	-5.73	0.72	14	4, 47 -12
Medial frontal gyrus	R	10	-8.05	0.83	13	16, 50, -4
Medial/superior frontal gyrus	L	32/6	4.73	0.63	12	-20, 17, 39
Superior frontal gyrus	L	6/8	-7.10	0.80	12	-14, 32, 44
Superior frontal gyrus	L	10	-6.73	0.78	17	-8, 56, -12
Thalamus/medial globus pallidus	R		5.79	0.72	22	16, -5, 4
Insula	L	13	5.25	0.68	25	-32, 19, 11
Inferior frontal gyrus/insula	L	44/13	5.37	0.69	21	-50, -2, 4
Amygdala/putamen/insula	L	13	9.05	0.86	10	-26, 3, -12

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$.

Analyses of phoneme-grapheme activation and growth in GORT comprehension including age revealed that the clusters in the left middle occipital gyrus remained significant. In addition, the positive correlation in the left middle temporal gyrus also remained significant. Controlling for age in addition to tone-symbol activation and time 1 GORT comprehension in the analyses also revealed new clusters of positive correlations in the right insula (see Table A.5).

Table A.5 Voxelwise correlations of phoneme-grapheme trial activation with growth in GORT comprehension with age.

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Age as covariate						
Inferior occipital gyrus	L	19/18	-3.67	0.51	11	-32, -75, 2
Inferior temporal/fusiform gyrus	R	37	-3.65	0.51	20	51, -58, -6
Precuneus	L	7	3.55	0.49	11	-11, -58, 51
Middle temporal gyrus	L	21	3.78	0.52	50	-44, -1, -32
Middle temporal gyrus	L	21	3.30	0.46	27	-55, -14, -11
Middle temporal gyrus	L	21	5.43	0.69	18	-61, -46, 1
Postcentral gyrus	R	3	4.02	0.55	26	22, -19, 63
Anterior cingulate/medial frontal gyrus	L	32/24	3.56	0.49	15	-5, 35, -14
Tone-symbols and age as covariates						

Table A.5 - *Continued*

Fusiform gyrus	R	37	-3.23	0.44	10	51, -63, -6
Precuneus	L	7	3.32	0.46	13	-11, -58, 51
Postcentral gyrus	R	3	3.38	0.47	20	22, -19, 63
Postcentral gyrus	L	3	4.84	0.64	20	-20, -25, 60
Middle temporal gyrus	L	21	3.23	0.45	12	-58, -3, -19
Middle temporal gyrus	L	21/22	5.46	0.70	15	-61, -46, 1
Middle temporal gyrus	L	21	3.45	0.48	10	-44, -1, -32
Anterior cingulate gyrus	L	10	3.26	0.45	12	-5, 41, -14
Insula/putamen	R	13	3.12	0.43	12	28, 6, -12
Age and Time1 GORT Comprehension as covariates						
Middle occipital gyrus	L	19	-4.99	0.66	14	-32, -72, 5
Posterior cingulate gyrus	R	29	4.82	0.64	10	10, -42, 9
Middle temporal gyrus	R	21/37	3.46	0.49	37	60, -54, 6
Middle temporal gyrus	R	21/22	3.18	0.44	27	63, -34, -5
Middle temporal/ parahippocampal gyrus	L	19	-3.18	0.44	12	-35, -51, 6
Middle temporal gyrus	L	21/22	4.05	0.56	26	-58, -14, -11
Middle temporal gyrus	L	21	3.33	0.46	21	-47, -1, -32
Middle temporal gyrus	L	21	3.31	0.46	19	-55, -3, -22
Middle temporal gyrus	L	21	4.73	0.63	10	-61, -46, 1
Precuneus	L	7	3.32	0.46	36	-8, -58, 51
Postcentral gyrus	R	2	-3.77	0.52	13	51, -21, 32
Postcentral gyrus/insula	L	43	-5.24	0.68	27	-61, -13, 18
Middle frontal gyrus	R	8	-3.29	0.45	11	28, 23, 41
Medial frontal gyrus	R	9	-3.99	0.55	12	4, 52, 20
Middle frontal gyrus	R	9	-3.51	0.67	38	40, 23, 27
Middle frontal gyrus	R	46	-3.33	0.46	10	46, 34, 10
Medial frontal gyrus	L	6	4.65	0.62	11	-8, -16, 65
Inferior frontal gyrus	L	9	-3.60	0.50	10	-38, 11, 25
Tone-symbols, age, and Time1 GORT Comprehension as covariates						
Middle occipital gyrus	L	19	-4.69	0.63	10	-32, -72, 5
Precuneus	L	7	3.17	0.44	35	-8, -58, 51
Middle temporal gyrus	R	22	3.75	0.52	13	60, -51, 6
Middle temporal/ parahippocampal gyrus	L	19	-3.80	0.53	15	-35, -48, 6
Middle temporal gyrus	L	21	3.53	0.49	18	-55, -3, -22
Middle temporal gyrus	L	21/22	3.36	0.46	18	-58, -14, -11
Middle temporal gyrus	L	21	4.80	0.64	12	-61, -46, 1
Anterior cingulate gyrus	R	25	-3.75	0.52	11	7, 15, -15
Superior frontal gyrus	R	10	-4.03	0.55	44	22, 50, -12
Middle frontal gyrus	R	9	-4.22	0.58	11	40, 19, 17
Medial frontal gyrus	R	9	-3.78	0.52	11	4, 52, 20
Middle frontal gyrus	R	9	-3.86	0.53	13	40, 23, 30
Insula	R	13	4.91	0.65	11	37, 9, -12
Inferior frontal gyrus	L	45/44	-3.24	0.45	10	-47, 22, 11

Note. Critical $t(13) = 3.014$, uncorrected $p < 0.01$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$.

Many of the correlations between word-rhyme activation and growth in GORT comprehension remained significant when age was controlled as well as when color-match activation and time 1 GORT comprehension were also included as covariates of no interest (see Table A.6). Positive correlations were observed in bilateral middle frontal and parahippocampal gyri, and bilateral insula as well as the right precuneus.

Table A.6 Voxelwise correlations of word-rhyme trial activation with growth in GORT comprehension with age.

Region	H	BA	t-test	r^2	voxels	x, y, z (TLRC)
Age as covariate						
Middle temporal gyrus	R	22/21	4.94	0.65	10	60, -40, 6
Color-match and age as covariate						
Cuneus/ calcarine gyrus	L	23/18	6.43	0.76	34	-5, -74, 18
Precuneus	R	7	6.85	0.78	53	1, -64, 46
Parahippocampal gyrus	R	20/28	4.60	0.62	27	34, -15, -21
Superior temporal gyrus	R	21/38	5.15	0.67	11	51, 3, -12
Inferior temporal gyrus	L	20	5.63	0.71	15	-50, -9, -29
Precentral/inferior frontal gyrus	R	6/44	4.95	0.65	12	54, 1, 9
Inferior frontal gyrus	L	44/45	8.73	0.85	56	-41, 20, 22
Age, and Time1 GORT Comprehension as covariates						
Parahippocampal gyrus/ hippocampus	R	35/36	5.47	0.70	45	34, -17, -18
Parahippocampal gyrus/ hippocampus	L	35/36	6.72	0.78	35	-32, -26, -13
Superior temporal gyrus	R	38/22	4.90	0.65	15	51, 3, -12
Middle temporal gyrus	R	22	5.18	0.67	10	63, -40, 6
Cingulate gyrus	R	24	8.76	0.86	18	4, 6, 42
Middle/superior frontal gyrus	R	6	4.82	0.64	18	25, 10, 56
Precentral/middle frontal gyrus	L	6	5.86	0.73	12	-35, -0, 31
Middle frontal gyrus	L	6	5.13	0.67	21	-44, 15, 39
Insula/superior temporal gyrus	L	13/41	5.45	0.70	13	-47, -16, 10
Insula	L	13	4.62	0.62	17	-32, -13, 18
Insula	L	13	5.70	0.71	27	-41, 1, 6
Color-match, age, and Time1 GORT Comprehension as covariates						
Middle occipital/lingual gyrus	R	18	4.70	0.63	14	22, -89, 3
Inferior occipital gyrus	R	18	5.90	0.73	12	34, -78, -0
Cuneus	L	18	5.30	0.68	32	-5, -74, 21
Parahippocampal gyrus/ hippocampus	R	35/36	4.72	0.63	44	25, -12, -24
Parahippocampal gyrus/ hippocampus	L	35/36	6.29	0.75	18	-32, -26, -13
Parahippocampal gyrus/ hippocampus	L	35/36	5.83	0.72	11	-32, -20, -18
Superior temporal gyrus	R	22/143	4.59	0.62	35	49, 9, -10
Postcentral gyrus/inferior parietal lobule	R		4.62	0.62	16	54, -21, 32
Precuneus	R	7	6.33	0.76	17	1, -64, 46
Posterior superior temporal gyrus	L	22/21	5.36	0.69	11	-55, -45, 14
Cingulate gyrus	R	24	5.36	0.69	17	4, 9, 36
Middle/superior frontal gyrus	R	6	4.70	0.63	14	25, 10 56

Table A.6 - *Continued*

Middle frontal gyrus	L	6	4.91	0.65	14	-44, 15, 39
Middle frontal gyrus	L	9	7.30	0.80	10	-41, 20, 22
Insula	R	13	4.87	0.65	12	37, -4, 15
Insula	L	13	5.13	0.67	31	-32, -16, 16
Insula	L	13	5.64	0.71	27	-41, 1, 6
Inferior frontal gyrus	L	44/9	7.31	0.80	22	-41, 5, 28
Thalamus	R		6.44	0.76	27	4, -10, 12
Thalamus	L		6.19	0.75	17	-11, -13, 10

Note. Critical $t(13) = 4.217$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$.

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APPENDIX B

PHONEME-GRAPHEME MAPPING AND PICTURE-WORD RHYMING TASK ACTIVATION

The primary fMRI analyses in this dissertation investigate correlations between brain activation obtained pre-intervention and growth observed in reading skills throughout the 2-year multisensory intervention (i.e., *Take Flight*). In order to understand why activation of particular brain regions is negatively or positively correlated with growth in reading it is helpful to know if the children with dyslexia demonstrated significant activation in those regions during the fMRI tasks. Thus, clusters of significant activation evoked by phonological stimuli are reported for each of the fMRI tasks.

The phoneme-grapheme mapping task is a phonics tasks requiring children to map phonemes and graphemes. Activation and functional connectivity associated with this task has been previously investigated in a group of children who completed *Take Flight* and age- and gender-matched non-impaired readers (Farris et al., 2011; Odegard et al., 2008). However, activation evoked by this task has not been investigated prior to intervention. The children with dyslexia demonstrated activation in several left hemisphere areas in response to the phoneme-grapheme trials after controlling for activation evoked by the tone-symbol trials (see Table B.1).

Table B.1. Voxelwise activation evoked by the phoneme-grapheme mapping task

Region	H	BA	t-test	voxels	x, y, z (TLRC)
Phoneme-grapheme trials					
Middle occipital gyrus	L	19	4.45	19	-32, -82, 22
Fusiform/inferior occipital gyrus	L	19/37	4.35	48	-35, -66, -3
Fusiform/parahippocampal gyrus	L	37/20	4.36	16	-41, -40, -10
Superior frontal gyrus	L	6	4.53	30	-2, 6, 42
Cingulate gyrus	L	24	4.20	11	-47, -13, 18
Insula	L	13	4.23	11	-47, -13, 18
Tone-symbols as covariate					
Fusiform/inferior occipital gyrus	L	19/37	4.88	82	-35, -69, -3
Middle occipital gyrus	L	18	4.98	65	-23, -88, 22
Parahippocampal/fusiform gyrus	L	37	5.25	10	-32, -49, -7
Supramarginal/precentral gyrus	L	40/42	5.34	17	-58, -21, 21
Postcentral gyrus/inferior parietal lobule	R	40/13	4.91	31	54, -27, 22
Cingulate gyrus	R	24	4.48	17	1, 3, 37
Cingulate gyrus/corpus callosum	R		4.70	22	1, -7, 21
Cingulate gyrus	L	32/24	4.75	27	-5, 14, 36
Cingulate/superior frontal gyrus	L	6/24	4.73	32	-2, 6, 42
Medial globus pallidus	R		4.27	14	13, -2, -2
Caudate	L		5.58	19	-8, 10, 14
Inferior frontal gyrus	L	47	4.77	17	-50, 10, 0
Inferior frontal gyrus	L	9/6	4.75	38	-38, 8, 28

Table B.1 - *Continued*

Insula	L	13/43	5.51	64	-47, -13, 15
Tone-symbols and age as covariates					
Inferior occipital gyrus	R	19	4.92	19	43, -80, 2
Cuneus	L	18	4.52	16	-5, -77, 10
Cuneus/middle occipital gyrus	L	19/18	5.70	91	-11, -85, 22
Fusiform/inferior occipital gyrus	L	19/18	5.30	61	-35, -69, -3
Fusiform gyrus	R	19/37	4.94	12	37, -72, -8
Fusiform gyrus	L	37	7.22	61	-44, -52, -2
Inferior parietal lobule/insula/postcentral gyrus	R	40/13	5.87	27	54, -27, 22
Supramarginal/postcentral gyrus	L	40	5.16	30	-58, -21, 21
Cingulate gyrus/corpus callosum	R	23/24	4.54	19	1, -7, 21
Cingulate gyrus	R/L	24	4.32	11	1, 3, 37
Cingulate gyrus	L	32	4.59	23	-5, 14, 36
Cingulate/superior frontal gyrus	L	6	4.54	28	-2, 6, 42
Inferior frontal gyrus	L	47	4.58	13	-50, 10, 0
Inferior frontal gyrus	L	44	4.87	34	-38, 8, 28
Insula	L	13	5.37	50	-47, -13, 15
Caudate	L		5.39	14	-8, 10, 14

Note. Critical $t(14) = 4.116$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$.

These left hemisphere areas included the middle and inferior occipital and fusiform gyri (BA 19/37), fusiform/parahippocampal gyri (BA 37/20), anterior supramarginal gyrus (BA 40/42), inferior frontal gyrus (BA 9/6), insula (BA 13), and caudate. In addition activation was observed in the right cingulate gyrus (BA 24), medial globus pallidus, and inferior parietal lobule (BA 40/13). Once activation associated with age at scanning was added as a covariate of no interest an additional cluster was present in the right fusiform gyrus (BA 19/37).

The picture-word rhyming task requires the children to use phonological awareness skills to decide if the words represented by two pictures rhyme. The children with dyslexia demonstrated bilateral activation in several brain regions in response to word-rhyme trials after activation evoked by color-match trials was removed as a covariate of no interest. These regions included the bilateral middle occipital (BA 18/19), fusiform (BA 37), cingulate (BA 32/24), and inferior frontal (BA 13/44/45) gyri (see Table B.2). Furthermore, when activation associated with age at scanning was also included as a covariate of no interest additional clusters were observed in the right angular gyrus (BA 19/22) and right parahippocampal gyrus (BA 34) extending to the hippocampus.

Table B.2. Voxelwise activation evoked by the picture-word rhyming task

Region	H	BA	t-test	voxels	x, y, z (TLRC)
Word-rhyme trials					
Cuneus	R	18	4.92	39	7, -74, 16
Cuneus	L	18/17	4.43	10	-11, -83, 13
Cuneus/middle occipital gyrus	R	18/17	4.40	143	5, -77, 19
Lingual gyrus/cuneus	R	17/18	4.46	17	13, -89, 5
Middle/superior occipital gyrus	L	19/18	5.76	132	-35, -80, 8
Fusiform/parahippocampal gyrus	R	19/37	4.25	105	31, -63, -4
Fusiform/parahippocampal gyrus	L	37/19	4.77	187	-35, -69, -3
Cingulate/medial frontal gyrus	L/R	32/6	5.54	248	-2, 20, 36
Postcentral gyrus	L	3	5.28	12	-47, -20, 54
Insula/inferior frontal gyrus	R	13/46	4.25	18	34, 22, 11
Insula/inferior frontal gyrus	L	13/44/45	8.35	625	-32, 16, 6
Caudate/putamen	R		4.53	80	10, 7, 6
Thalamus	L		4.79	12	-14, -16, 16
Thalamus	L		5.69	10	-5, -10, 4
Color-match trials					
Lingual gyrus	R	18	4.25	11	22, -84, -3
Middle occipital gyrus/cuneus	L/R	18/19	4.24	1240	-8, -77, 10
Middle occipital/fusiform gyrus	R	19/37	4.51	134	40, -63, 1
Fusiform gyrus	R	37	4.28	28	28, -64, -9
Parahippocampal gyrus/hippocampus	R	34	6.31	26	-2, 47, -7
Anterior inferior temporal/fusiform gyrus	L	20	7.97	178	-47, -18, -26
Postcentral gyrus	L	3	5.79	26	-47, -20, 54
Precentral gyrus	R	4	5.35	47	37, -17, 52
Cingulate/superior medial gyrus	L	32	5.50	301	-2, 20, 36
Cingulate gyrus/thalamus	R	23/24	4.21	12	1, -7, 18
Middle frontal gyrus	R	8	6.35	11	46, 20, 36
Insula	R	13/45	5.65	31	34, 22, 11
Insula/inferior frontal gyrus	L	13/44/45	8.11	818	-32, 16, 6
Caudate/putamen	R		4.92	165	10, 7, 9
Color-match trials and age as covariates					
Lingual gyrus/cuneus	L	17/18	4.61	16	-23, -80, 10
Superior occipital gyrus/cuneus	L	19/18	4.32	28	-14, -91, 30
Middle occipital/fusiform gyrus	L/R	18/19/37	5.66	1679	-35, -69, -3
Middle temporal/angular gyrus	R	19/22	4.34	10	40, -56, 20
Parahippocampal gyrus/hippocampus	R	34	6.24	22	28, -8, -14
Cingulate gyrus	L/R	32	5.47	326	-2, 20, 36
Cingulate gyrus/corpus callosum	L/R	23	5.05	160	-2, -13, 21
Anterior inferior temporal/fusiform gyrus	L	20	7.68	174	-47, -18, -26
Postcentral gyrus	L	3	5.61	24	-47, -20, 54
Precentral gyrus	R	4	5.45	50	37, -17, 52
Insula/inferior frontal gyrus	R	13/45	5.44	24	34, 22, 11
Insula/inferior frontal gyrus	L	13/45/44	8.03	704	-32, 16, 6
Cingulate gyrus/caudate	L		4.88	21	-14, -12, 24

Note. Critical $t(14) = 4.116$, uncorrected $p < 0.001$, spatial clustering threshold set to 10 voxels (NN=1) resulting in spatially corrected $p < 0.01$.

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