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Gray matter volume changes following reading intervention in dyslexic children

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ABSTRACT

Studies in children and adults with the reading disability developmental dyslexia have shown behavioral improvements after reading intervention. In another line of work, it has been shown that intensive training in a variety of cognitive and sensorimotor skills can result in changes in gray matter volume (GMV). This study examined changes in GMV following intensive reading intervention in children with dyslexia using voxel-based morphometry (VBM). Eleven dyslexic children underwent an eight week training focused on mental imagery, articulation and tracing of letters, groups of letters and words, which resulted in significant gains in reading skills. This was followed by an eight week null period (control) where no intervention was administered and no further significant gains in reading were observed. Structural scans were obtained before the intervention, after the intervention and after the null period. GMV increases between the first two time points were found in the left anterior fusiform gyrus/hippocampus, left precuneus, right hippocampus and right anterior cerebellum. However these areas did not change between time points two and three (control period), suggesting that the changes were specific to the intervention period. These results demonstrate for the first time that (1) training-induced changes in GMV can be observed in a pediatric sample and (2) reading improvements induced by intervention are accompanied by GMV changes.

Introduction

Developmental dyslexia is a neurobiologically-based learning disability in which individuals have difficulty with word decoding, word recognition and spelling and these in turn may negatively impact other reading abilities such as reading comprehension and vocabulary growth (Lyon et al., 2003). These deficits exist even though the individual has the intelligence, educational opportunity and motivation to learn to read (Lyon et al., 2003; Eckert, 2004; Vellutino et al., 2004). Dyslexia is more commonly observed in males than females and estimated to affect between 5.3% and 11.8% of school aged children (Katusic et al., 2001). Given this high incidence of dyslexia and the critical role of reading in the acquisition of knowledge and successful academic outcome, improving reading abilities in these children is an important priority for educators, policy makers and scientists. Over the past decade there has been increased interest amongst neuroscientists to quantify and characterize changes in brain structure, usually gray matter volume (GMV) following controlled learning experiences. These efforts, especially those focusing on the relationship between changes in brain structure and academic achievement in a formal learning environment (Draganski et al., 2006), have important implications for better understanding learning and skill acquisition in the classroom, especially in those children who encounter challenges in their efforts to acquire literacy. To date, no attempts have been made to measure changes in the brain's gray matter in children with dyslexia following a formal, structured learning experience. Here we address this gap and make the connection between behavioral intervention for reading disabilities and measures of brain morphometry, to inquire about the nature of GMV changes following intensive tutoring of children with dyslexia. The results, in conjunction with current understanding of brain-behavioral relationships, will help inform both educators and researchers in an effort to better understand the neural basis for successful reading intervention and potentially to develop programs to best help children who have trouble reading.

There exists now a significant corpus of work characterizing the neuroanatomical profile of dyslexia (for a review see Eckert, 2004). This research includes post mortem studies (Galaburda et al., 1985) and *in vivo* magnetic resonance imaging (MRI) research comparing dyslexic with non-dyslexic populations. The initial MRI research involved manual tracing of a variety of brain regions implicated in language and reading, however more recent research has quantified the neuroanatomical differences in dyslexic children and adults by using a technique known as voxel-based morphometry (VBM) (Ashburner and Friston, 2000). Using this automated method, a

Abbreviations: VBM, voxel based morphometry; GMV, gray matter volume; fMRI, functional MRI; PET, positron emission tomography; ALE, activation likelihood estimate; FA, fractional anisotropy; MRS, magnetic resonance spectroscopy.

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variety of brain structures have been shown to have smaller gray matter volume (GMV) in dyslexics as compared to controls. VBM studies comparing adult dyslexic to age matched control groups shave shown less left temporal GMV (Brown et al., 2001; Vinckenbosch et al., 2005) and less bilateral temporal GMV for the dyslexic groups (Brambati et al., 2004; Steinbrink et al., 2008). Brambati et al. (2004) found less bilateral GMV for dyslexics in the cerebellar nuclei and Brown et al. (2001) also found less left inferior frontal and right cerebellar GMV in the dyslexics. The only two studies of children with dyslexia employing VBM have shown less GMV in bilateral inferior parietal lobule and temporal gyri and left inferior frontal gyrus (Hoeft et al., 2007) and less bilateral lingual gyrus GMV compared to controls as well as left supramarginal gyrus and left posterior cerebellar lobe (Eckert et al., 2005). These regions are consistent with those implicated in studies using other structural analysis methods as described in Eckert (2004).

In parallel, functional brain imaging technologies (functional magnetic resonance imaging: fMRI; positron emission tomography: PET) have been used to investigate reading and language processing in the dyslexic brain. From these Pugh et al. (2001) has proposed a model describing the neural circuitry for reading in normal and disabled readers (2001). The model proposes that three left hemisphere regions are relied upon for typical reading: an inferior frontal region involved in phonological output, a temporo-parietal region involved in rule-based orthographic to phonological processing as well as semantic analysis, and an occipito-temporal region involved in single word identification. These areas are commonly found to be less activated in individuals with dyslexia during paradigms involving reading or reading-related skills. Specifically, temporo-parietal and occipito-temporal regions consistently show hypoactivation for children and adults with dyslexia compared to normal readers in phonologically demanding (real and pseudoword reading) tasks; the inferior frontal cortex is sometimes hyperactive in dyslexics compared to controls on similar tasks (Shaywitz and Shaywitz, 2008). A recent activation likelihood estimate (ALE) meta-analysis of predominantly adult studies of functional brain imaging in dyslexics compared to controls found left hemisphere temporal and parietal areas were most likely to be less active in dyslexics than controls, although support for inferior frontal hyperactivation was not found (Maisog et al., 2008).

In a study of dyslexic children, different results were found in comparisons with reading matched vs. age matched controls. When compared to both control groups the posterior network hypoactivation was found for dyslexics, however the hyperactivation in the frontal network was only found when compared to age matched controls, suggesting that the posterior hypoactivation represents a functional deficit of dyslexia, while the frontal hyperactivation is more representative of reading ability (Hoeft et al., 2007). Together these studies in children and adults point to a left hemisphere network that is impacted by an individual's reading disability. Notably these brain regions overlap with those that have demonstrated anatomical differences, as described above.

Most recently these functional brain imaging methodologies have been used to investigate whether the differences observed between dyslexic and normal readers change when the investigators intervene and improve reading ability in dyslexic individuals. Intervention studies in dyslexic children have shown changes in behavioral measures (i.e. increased performance in reading) and physiological changes measured using fMRI (Shaywitz et al., 2004; Aylward et al., 2003, Temple et al., 2003). While different types of interventions were given in these studies, similar patterns of increased activity were observed in bilateral frontal and temporo-parietal regions. An intervention study in adult dyslexics showed increases in activation in bilateral temporal and parietal areas as well as the right inferior frontal gyrus (Eden et al., 2004).

While these studies speak to physiological changes in brain function following intensive training regimens focused on reading, it is not yet known if there are parallel changes in cortical anatomy. Several longitudinal studies using VBM analysis have shown changes in subjects' GMV after training. Draganski et al. (2004) followed a group of adults who were scanned before and after learning to juggle, and after not juggling for 3 months. An increase in GMV in area V5/MT (known to be integral to visual motion processing) was observed following the training, yet after the third scan, following a period of no training, there appeared to be a reversal of this pattern in the form of GMV decrease (although it was not significant over the time observed). Other longitudinal VBM studies have examined GMV change after a variety of tasks including more juggling tasks (Driemeyer et al., 2008; Boyke et al., 2008; Scholz et al., 2009), medical students studying for an exam (Draganski et al., 2006), mirror reading (Ilg et al., 2008), as well as repetitive transcranial magnetic stimulation (rTMS) on the left superior temporal gyrus (May et al., 2007), cognitive behavioral therapy (CBT) in a chronic fatigue syndrome population (de Lange et al., 2008) and pharmacological (quetiapine) treatment of a schizophrenic population (Stip et al., 2009).

Taken together, this literature has provides insight into the plasticity of the adult brain during learning. Increases in gray matter density seen early on (i.e. within one week after onset of training) (Driemeyer et al., 2008), suggest changes in spine/synapse density or cell body increases rather than neuronal or glial genesis. Longer term increases in hippocampal gray matter (Draganski et al., 2006) are more likely to reflect this slower process of neurogenesis. Anatomical changes after training have been observed in adults ranging from their early 20's (Draganski et al., 2004) to early 60's (Boyke et al., 2008), but has yet to be studied in a pediatric population.

To this point, changes in GMV after reading intervention have not been shown in children or adults with dyslexia. However, the above studies of training-induced changes in GMV and the fact that brain anatomy varies as a function of reading status (as shown for dyslexic versus non-dyslexic comparisons as well as in studies of illiterates; Castro-Caldas et al., 1998), suggest the possibility that such changes in the cortex might be measurable.

The current study was designed to investigate whether children with dyslexia who receive a reading intervention over an eight week period show changes in GMV. A longitudinal VBM analysis comparing GMV before the intervention, after the intervention and after an equal time period of non-intervention was performed to examine if any changes in gray matter could be observed as a result of the training. This three time point design follows the original Draganski et al. (2004) juggling studies. Based on the anatomical differences known to distinguish dyslexics from non-dyslexics (Eckert, 2004), the physiological changes previously reported following successful reading interventions (Aylward et al., 2003; Shaywitz et al., 2004; Eden et al., 2004) and the nature of the intervention used in the current study (visual imagery of words, multisensory integration and development of the sound representation of words) areas for which GMV changes were predicted included left hemisphere ventral visual, parietal and frontal cortices.

Materials and Methods

Subjects

The eleven dyslexic children (8 male, 3 female) whose data were submitted to this analysis were recruited as part of a larger study from a private school specializing in students with dyslexia. The school records were used to identify students with Woodcock-Johnson III Letter-Word Identification (W-J WID; Woodcock et al., 2001) scores less than 92. Average age of the eleven subjects was 9.1 years (Range 7 yrs 5 months-11 yrs 11 months). IQ scores were obtained prior to the intervention using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) which measures verbal (VIQ), performance (PIQ) and full scale (FSIQ) IQ. To be included in the study subjects had