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Abnormal subcortical components of the corticostriatal system in young adults with DLI: A combined structural MRI and DTI study

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ABSTRACT

Developmental Language Impairment (DLI) is a neurodevelopmental disorder affecting 12% to 14% of the school-age children in the United States. While substantial studies have shown a wide range of linguistic and non-linguistic difficulty in individuals with DLI, very little is known about the neuroanatomical mechanisms underlying this disorder. In the current study, we examined the subcortical components of the corticostriatal system in young adults with DLI, including the caudate nucleus, the putamen, the nucleus accumbens, the globus pallidus, and the thalamus. Additionally, the four cerebral lobes and the hippocampus were also comprised for an exploratory analysis. We used conventional magnetic resonance imaging (MRI) to measure regional brain volumes, as well as diffusion tensor imaging (DTI) to assess water diffusion anisotropy as quantified by fractional anisotropy (FA). Two groups of participants, one with DLI ($n=12$) and the other without ($n=12$), were recruited from a prior behavioral study, and all were matched on age, gender, and handedness. Volumetric analyses revealed region-specific abnormalities in individuals with DLI, showing pathological enlargement bilaterally in the putamen and the nucleus accumbens, and unilaterally in the right globus pallidus after the intracranial volumes were controlled. Regarding the DTI findings, the DLI group showed decreased FA values in the globus pallidus and the thalamus but these significant differences disappeared after controlling for the whole-brain FA value, indicating that microstructural abnormality is diffuse and affects other regions of the brain. Taken together, these results suggest region-specific corticostriatal abnormalities in DLI at the macrostructural level, but corticostriatal abnormalities at the microstructural level may be a part of a diffuse pattern of brain development. Future work is suggested to investigate the relationship between corticostriatal connectivity and individual differences in language development.

1. Introduction

Developmental Language Impairment (DLI) is a neurodevelopmental disorder, which occurs in 12% to 14% of the school-age children in the United States (Tomblin et al., 1997). This common childhood disorder is characterized by difficulty acquiring and using language, in particular the morphosyntactic components of language, without identifiable causes (Leonard, 1997). A range of different terms has been used to describe this population, and *Specific Language Impairment* (SLI) is the most common usage in the literature. In the current study, we use the term DLI to acknowledge that deficits in individuals with DLI are not confined to language alone, but include general cognitive functioning, such as procedural memory (Ullman & Pierpont, 2005), phonological working memory (Archibald & Gathercole, 2006), reinforcement learning (Lee & Tomblin, 2012), statistical learning (Evans, Saffran, & Robe-Torres, 2009), and executive function (Henry, Messer, & Nash, 2011).

1.1. A domain-general approach: Corticostriatal system as one of the neuroanatomical mechanisms underlying DLI

It has been widely accepted that DLI is a multifactorial disorder involving both biological and environmental factors. However, there is no consensus to date on what these might be. Numerous studies have examined the linguistic characteristics of DLI, along with studies of plausible perceptual and cognitive factors. We have joined others in exploring the hypothesis that language development and disorders are grounded in general purpose learning systems (e.g., Ullman & Pierpont, 2005; Lum, Conti-Ramsden, Page, & Ullman, 2012). We are particularly interested in the procedural learning system and the closely related reinforcement learning system, and have found empirical support for their

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possible involvement in DLI (Tomblin, Mainela-Arnold, & Zhang, 2007; Lee & Tomblin, 2012, under review).

In the literature, both procedural learning and reinforcement learning are strongly mediated by the corticostriatal system. With respect to procedural learning, different types of procedural learning (e.g., motor skill learning, sequential learning) rely on different components of the corticostriatal system. For example, some studies showed a positive correlation between motor skill learning and neural activity of the motor corticostriatal loop (e.g., Grafton, Woods, & Tyszka, 1994), while others reported a significant right-lateralized activation in both the anterior putamen and the head of the caudate nucleus in sequential learning (e.g., Kim et al., 2004; Rauch et al., 1997). Despite different types of procedural learning, all findings indicate that the corticostriatal system, particularly the caudate and the putamen, plays an important role in supporting procedural learning (Seger, 2006). Concerning reinforcement learning, the basal ganglia function as a reinforcement learning center, learning about consequences of one′s actions, and then conveying prediction error signals (i.e., discrepancy between actual results and expected results) to guide action selection (Badre & Frank, 2012; Daw & Doya, 2006; Daw & Shohamy, 2008; Doya, 1999; Frank & Badre, 2012; Niv & Schoenbaum, 2008). In other words, the basal ganglia modulate activations in the cortex based on learned reinforcement history. Imaging findings support this view, showing that individual differences in performance on reinforcement learning are highly correlated with striatal blood oxygen-level dependent (BOLD) activities (Schonberg, Daw, Joel, & O′Doherty, 2007), and moreover, the occurrence of predication errors is closely related to increased activity in the nucleus accumbens and the putamen (Berns, McClure, Pagnoni, & Montague, 2001; McClure, Daw, & Montague, 2003; O′Doherty, Dayan, Friston, Critchley, & Dolan, 2003).

Given that individuals with DLI demonstrate impaired procedural and reinforcement learning that rely on the corticostriatal system, the basal ganglia in particular, this neuroanatomical system has become a good candidate for further study in the etiology of DLI. To the best of our knowledge, no studies have directly examined brain structures in DLI with an a priori hypothesis of structural abnormalities in the corticostriatal system.

1.2. *Previous studies of brain structure in DLI*

Very few researchers examined brain structures in DLI per se, and the findings are inconsistent. Most investigations focused on volume and asymmetry of classic cortical language areas in DLI. Results include atypical patterns of asymmetry, as well as reduced volumes of the perisylvian regions, the frontal regions (e.g., Broca′s area and pars triangularis), and the parietal lobes (Badcock, Bishop, Hardiman, Barry, & Watkins, 2012; De Fosse et al., 2004; Herbert et al., 2005; Jernigan, Hesselink, Sowell, & Tallal, 1991; Plante, Swisher, Vance, & Rapcsak, 1991), although non-significant structural differences between individuals with and without DLI were also reported (e.g., Gauger, Lombardino, & Leonard, 1997; Preis, Jancke, Schittler, Huang, & Steinmetz, 1998). It should be noted that the classic language areas were derived from adult patient studies (e.g., Broca, 1865; Wernicke, 1874). Given that DLI is a *developmental* language disorder, its anatomical correlates may not fully conform to the focal neuroanatomical basis of language that was built upon *acquired* language disorders (Johnson, Halit, Grice, & Karmiloff-Smith, 2002).

There were limited findings regarding global brain abnormalities in DLI. By using the conventional MRI, some researchers showed decreased white matter volumes in both motor- and language-related cortex of individuals with DLI (Jancke, Siegenthaler, Preis, & Steinmetz, 2007), whereas others showed global increases in total brain volumes driven by white matter enlargement (Herbert et al., 2004). Soriano-Mas et al. (2009) further pointed out that global volumetric increases in white and gray matter were more prominent in young children with DLI than in older children with DLI, indicating a trend toward normalization with age.

Kim et al. (2006) was the first to use diffusion tensor imaging (DTI) to examine white matter pathways in DLI. They found decreased anisotropy in the genu of corpus callosum of children with DLI whose brains looked normal on the magnetic resonance imaging (MRI) scans. This finding indicates a poor integrity of the corpus callosum in DLI, which may lead to abnormal integration of information between the left and right hemispheres. In addition, it also suggests that individuals with DLI may have structural brain abnormalities at the microstructural level, which cannot be observed by conventional MRI. DTI, on the other hand, provides microstructural information based upon the movement of water molecules in the brain (Basser, Mattiello, & Le Bihan, 1994; Basser & Pierpaoli, 1996), and therefore can be a promising method to identify abnormal brain regions in DLI at a microscopic scale.

1.3. *The current study*

The aim of the current study was to examine the subcortical components of the corticostriatal system in young adults with DLI by using a combined volumetry and DTI method. The subcortical structures of the corticostriatal system included the caudate nucleus, the putamen, the nucleus accumbens, the globus pallidus, and the thalamus. In addition, we also looked into the structures of the four cerebral lobes and the hippocampus for an exploratory analysis.

In this study, we used a combination of anatomical and diffusion tensor imaging, along with language measurements, to develop a deeper knowledge of the brain-behavior relationship in DLI. Conventional MRI measures tissue volumes of anatomical structures, while DTI measures motions of water molecules in the brain (i.e., brain water diffusivity) to highlight subtle alterations in the tissue microstructure. These two techniques provide complementary information of volumetric and microstructural changes within the subcortical areas. Although DTI has been used to investigate regional white matter changes and connectivity of white matter, it can be also utilized to highlight microstructural alterations of subcortical gray matter, as demonstrated by previous studies on psychiatric disorders (e.g., Spoletini et al., 2011), neurodegenerative disorders (e.g., Cherubini et al., 2010; Magnotta et al., 2009), and neurodevelopmental disorders (e.g., Makki, Behen, Bhatt, Wilson, & Chugani, 2008; Neuner et al., 2011). Hence, by combining the study of abnormalities in MR volumetry with the potential of DTI in highlighting microstructural alterations, it should be possible to describe in detail subcortical abnormalities in DLI.

2. Methods

2.1. *Participants*

Participants were recruited from prior participation in another behavioral study (Lee & Tomblin, 2012), wherein their language and nonverbal IQ scores were obtained (see Section 2.2). The original sample included 48 participants (DLI: $n=25$; Control: $n=23$). We paired them on age and gender, and excluded those who (1) were left-handed, (2) were pregnant, and (3) moved to other states and could not come back for participation. In the end, 24 participants, 12 from the DLI group and 12 from the control group, joined the current study. There was no significant difference in gender ratio (male: female=4: 8) or in age, $t(22)=.15$, $p=.89$, between the two groups (see Table 1).

This research was approved by the institutional review board (IRB) at the University of Iowa. All participants provided consent in accord with the Declaration of Helsinki after having been informed of the study procedures and purpose. All participants were compensated for their time.