Brain & Language 161 (2016) 45–56

Contents lists available at ScienceDirect

Brain & Language

journal homepage: www.elsevier.com/locate/b&l

White matter integrity of cerebellar-cortical tracts in reading impaired children: A probabilistic tractography study

Vindia G. Fernandez [a,*], Jenifer Juranek [b], Anna Romanowska-Pawliczek [b], Karla Stuebing [a], Victoria J. Williams [a], Jack M. Fletcher [a]

[a] *University of Houston, 4811 Calhoun Rd., 3rd Floor, Houston, TX 77204-6022, United States*
[b] *University of Texas Health Science Center, 6655 Travis, Houston, TX 77030-1312, United States*

ARTICLE INFO

Article history:
Received 1 January 2015
Revised 1 July 2015
Accepted 10 July 2015
Available online 22 August 2015

Keywords:
Cerebellum
DTI
Tractography
Dyslexia
Reading
Children

ABSTRACT

Little is known about the white matter integrity of cerebellar-cortical pathways in individuals with dyslexia. Building on previous findings of decreased volume in the anterior lobe of the cerebellum, we utilized novel cerebellar segmentation procedures and probabilistic tractography to examine tracts that connect the anterior lobe of the cerebellum and cortical regions typically associated with reading: the temporoparietal (TP), occipitotemporal (OT), and inferior frontal (IF) regions. The sample included 29 reading impaired children and 27 typical readers. We found *greater* fractional anisotropy (FA) for the poor readers in tracts connecting the cerebellum with TP and IF regions relative to typical readers. In the OT region, FA was greater for the older poor readers, but smaller for the younger ones. This study provides evidence for discrete, regionally-bound functions of the cerebellum and suggests that projections from the anterior cerebellum appear to have a regulatory effect on cortical pathways important for reading.

1. Introduction

Reports of structural differences, reduced functional activation, and atypical connectivity (functional and structural) in adults and children with dyslexia relative to typical readers have contributed to the idea of dyslexia as a "brain based" disorder with genetic and environmental components (Fletcher, Lyon, Fuchs, & Barnes, 2007; Gabrieli, 2009). Studies of children and adults with dyslexia have reliably documented the contributions of left hemisphere regions typically associated with language and sensory processing: temporoparietal (TP), occipitotemporal (OT), inferior frontal (IF), and to a lesser extent subregions of the corpus callosum, in accurate and fluent word reading (Fletcher et al., 2007; Pugh et al., 2010). Despite the growing body of literature on the role of the cerebellum in speech and language (Ackermann, 2013), and reports of regional structural differences in the cerebellum of children with dyslexia (Fernandez et al., 2013; Eckert et al., 2003, 2005; Kibby & Hynd, 2008; Leonard, Eckert, Given, Berninger, & Eden, 2006), very little is known about the integrity of cerebellar-cortical white matter in individuals with dyslexia relative to typical readers. The lack of empirical data is especially noteworthy because a cerebellar theory of dyslexia has been proposed (Nicolson & Fawcett, 2005). The present study examined cerebellar-cortical white matter pathways in children with dyslexia relative to typical readers to evaluate measures of white matter integrity which may help to explain the role of regional volumetric differences in the cerebellum.

1.1. Cerebellar theory of dyslexia

The cerebellar theory of dyslexia suggests that cerebellar abnormalities reduce the automaticity of decoding skills in children with dyslexia. Proponents of the theory argue that the cerebellum is active during early stages of skill acquisition (Nicolson & Fawcett, 2005, 2007), a process with which some children with dyslexia have difficulty (Reynolds, Nicolson, & Hambly, 2003). Theoretically, associated procedural learning deficits could prevent automatization of accurate word decoding and phonological processing in children with dyslexia.

This hypothesis has been evaluated behaviorally by comparing children with dyslexia and typically developing children on neuropsychological and cognitive tasks presumably associated with the cerebellum (Nicolson & Fawcett, 1994, 1999). There have been

* Corresponding author at: UCLA Semel Institute for Neuroscience & Human Behavior, 760 Westwood Plaza, 47-429A, Los Angeles, CA 90095-1795, United States.

E-mail addresses: vgfernandez@uh.edu (V.G. Fernandez), jenifer.juranek@uth.tmc.edu (J. Juranek), anna.m.pawliczek@uth.tmc.edu (A. Romanowska-Pawliczek), karla.stuebing@times.uh.edu (K. Stuebing), tori85@gmail.com (V.J. Williams), jack.fletcher@times.uh.edu (J.M. Fletcher).

http://dx.doi.org/10.1016/j.bandl.2015.07.006
0093-934X/

efforts to train the cerebellum through physical exercise, with claims that reading and cerebellar functions improved (Reynolds et al., 2003). However, these findings have been controversial because, among other issues, the children with dyslexia were defined in part by performance on these tasks (Bishop, 2007). In other studies, the same cerebellar tasks have not been strongly related to reading or to reading difficulties (Barth et al., 2010). Finally, it is not clear why the cerebellum would be involved in accurate decoding, a skill typically measured by untimed single-word reading tests without regard for efficiency, as opposed to problems with reading fluency, a skill that requires automaticity as proposed by the theory.

Despite these issues, there is evidence from postmortem studies and from quantitative MRI analyses for differences in cerebellar structure and volume between children and adults with dyslexia and typically developing comparison groups. To appreciate these differences, we will first review structural MRI studies of the cerebellum and then diffusion tensor imaging (DTI) studies of dyslexia more generally. Thus far, there are no published DTI studies of white matter integrity involving the cerebellum in individuals with dyslexia.

1.2. Structural MRI studies of the cerebellum

Structural imaging studies have been conducted that yielded findings concerning the cerebellum in children and adults with dyslexia. This area of research was influenced by early, small-sample postmortem studies (5 with dyslexia, 7 controls) in which abnormalities in the medial (Galaburda, Menard, & Rosen, 1994) and lateral geniculate nuclei (Livingstone, Rosen, Drislane, & Galaburda, 1991), auditory cortex (Galaburda & Kemper, 1979), and primary visual cortex (Eckert, 2004; Jenner, Rosen, & Galaburda, 1999) were identified.

Subsequent volumetric MRI studies of the cerebellum have yielded inconsistent findings in adult samples. Some have found differences in regional cerebellar volume between adults identified as having dyslexia (either by testing or history) and those without such problems (Brambati et al., 2004; Brown et al., 2001; Leonard et al., 2001; Rae et al., 2002). Other studies have found no differences in cerebellar volume using similar methods (Menghini et al., 2008; Pernet, Poline, Demonet, & Rousselet, 2009; ; Laylock et al., 2008). However, reduced volume in the right anterior lobe of the cerebellum has been more reliably identified in reading impaired children relative to typical readers (Eckert et al., 2003, 2005; Kibby & Hynd, 2008; Leonard et al., 2006).

Fernandez et al. (2013) investigated the role of regional variation in cerebellar anatomy in children with single-word decoding impairments ($N = 23$), children with impairment in fluency alone ($N = 8$), and typically developing children ($N = 16$). Children with single-word decoding impairments demonstrated no statistically significant differences in overall gray and white matter volumes or cerebellar asymmetry; however, reduced volume *bilaterally* in the anterior lobe of the cerebellum relative to typical readers was observed. These results supported previous findings in the child literature suggesting cerebellar involvement in dyslexia, and provided additional groundwork for the proposed study on the integrity of white matter connecting the cerebellum and cortical regions that are typically associated with reading impairment.

1.3. White matter integrity in adults and children with reading impairment

Fractional anisotropy (FA) is a complex measure of white matter structural integrity. It is a composite measure that expresses the proportion of the longest eigenvalue, λ_1, to the two shorter eigenvalues, λ_2 and λ_3, in an ellipsoid (Beaulieu, 2002). In the central nervous system, λ_1 represents the water diffusivity parallel to the axonal fibers and is referred to as the axial diffusivity (AD). The water diffusivities perpendicular to the axonal fibers, λ_2 and λ_3, are averaged and referred to the radial diffusivity (RD) (Basser, 1995; Basser, Pajevic, Pierpaoli, Duda, & Aldroubi, 2000; Song et al., 2002; Xue, van Zijl, Crain, Solaiyappan, & Mori, 1999). Changes in RD in the absence of changes in AD are typically associated with myelin abnormalities (Keller & Just, 2009; Beaulieu, 2002; Song et al., 2002, 2005) while changes in AD in the absence of changes in RD are typically associated with an increase in axon diameter (Keller & Just, 2009; Dougherty et al., 2007).

Studies of white matter integrity in adults and children with dyslexia have generally focused on regions typically associated with the language network and do not involve the cerebellum. In adults, DTI studies have identified differences in FA in the frontotemporal and TP regions important for language comprehension and articulatory processes (Fletcher et al., 2007; Klingberg et al., 2000; Pugh et al., 2010; Steinbrink et al., 2008). DTI studies of children with dyslexia have also implicated bilateral (Deutsch et al., 2005) and left TP regions (Niogi & McCandliss, 2006; Rimrodt, Peterson, Denkla, Kaufmann, & Cutting, 2010) and, more broadly, the left superior longitudinal fasciculus (Carter et al., 2009). Abnormal orientation of fibers (specifically an increase in superior–inferior oriented fibers in its TP projection that ordinarily runs anterior-laterally) in the right superior longitudinal fasciculus (Carter et al.) and *higher* FA in right frontal regions have also been described (Rimrodt et al., 2010). Taking a slightly different approach, longitudinal studies of children with dyslexia reported that left TP regions were significant predictors of reading outcomes (Hoeft et al., 2011; Meyers et al., 2014) while intensive intervention was associated with increases in FA in the left centrum semiovale (anterior to TP region) (Keller & Just, 2009).

In the only published DTI study which included the cerebellum, Richards et al. (2008) also conducted a whole-brain DTI study of fathers of children in a familial study of dyslexia, 14 with dyslexia and 7 without dyslexia. Typical readers had greater FA in language-related white matter tracts (28 bilateral frontal, temporal, parietal, and occipital areas as defined by Anatomical Automatic Labeling (AAL) atlas boundaries and an additional 7 by DTI atlas boundaries). Notably, 9 regions showed *greater* FA for the group with dyslexia, including the left and right cerebellum (using the AAL atlas) and middle cerebellar peduncle (using the DTI atlas boundaries). The presence of greater FA raises the question of whether the cerebellum is somehow over-compensating for a weak reading network (Richards et al., 2008).

In an effort to summarize DTI findings in white matter, Vandermosten, Boets, Wouters, and Ghesquiere (2012) conducted an activation likelihood estimation (ALE) analysis resulting in two clusters of significant ALE value: a region near the left TP region and the IF gyrus (Vandermosten, Boets, Wouters et al., 2012). The lack of reported cerebellar findings may reflect the fact that the cerebellum is rarely included in quantitative analyses. These studies are notable because they have continued to advance the notion that myelination, important for rapid conduction of action potentials, could disturb accurate decoding and the transmission of rapidly changing stimuli (Klingberg et al., 2000).

1.4. Rationale

Evidence of differences in white matter between adults and children with dyslexia and typically developing readers clearly demonstrates the importance of a neural networks approach to the study of dyslexia. However, because the cerebellum is rarely