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# Altered hemispheric lateralization of white matter pathways in developmental dyslexia: Evidence from spherical deconvolution tractography

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ABSTRACT

This study examines the structural integrity and the hemispheric lateralization patterns of four major association fiber pathways in a group of French dyslexic children and age-matched controls (from 9 to 14 years), using high angular diffusion imaging combined with spherical deconvolution tractography. Compared with age-matched controls, dyslexic children show increased hindrance-modulated oriented anisotropy (HMOA) in the right superior longitudinal fasciculus (SLF). They also show a reduced leftward asymmetry of the inferior fronto-occipital fasciculus (IFOF) and an increased rightward asymmetry of the second branch of the SLF (SLF II). The lateralization pattern of IFOF and SLF II also accounts for individual differences in dyslexic children's reading abilities. These data provide evidence for an abnormal lateralization of occipito-frontal and parieto-frontal pathways in developmental dyslexia.



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## 1. Introduction

Developmental dyslexia is a learning disability affecting the acquisition of fluent reading skills despite normal intelligence and schooling (Lyon, Shaywitz, & Shaywitz, 2003), with prevalence estimated around 3–7% of the population (Lindgren, Derenzi, & Richman, 1985). It is increasingly acknowledged to be a genetically influenced disorder with a neurological basis, which in turn engenders cognitive deficits affecting reading acquisition (Butterworth & Kovas, 2013; Darki, Peyrard-Janvid, Matsson, Kere, & Klingberg, 2012). Nevertheless, a full understanding of the pathophysiology of developmental dyslexia and of its links with cognitive deficits and possible genetic factors remains an important challenge (Giraud & Ramus, 2013).

Developmental dyslexia is often characterized as a disconnection syndrome, implicating weaker functional connections between reading-related cortical regions, notably left inferior frontal cortex, ventral occipito-temporal cortex and the temporo-parietal junction (Boets et al., 2013; Horwitz, Rumsey, & Donohue, 1998; Paulesu et al., 1996; Pugh et al., 2000). A recent meta-analysis of PET and fMRI activation studies of dyslexia has further suggested that dyslexia might be related to multiple dysfunctional systems in the left hemisphere reflected by i) reduced involvement in distributed left hemispheric regions across inferior frontal, premotor, supramarginal and occipito-temporal cortices, which might be associated with reading and the visual-to-phonology processes, and ii) less engagement in a more dorsal fronto-parietal network (left parietal and premotor cortices), which could be associated with motor or visuo-spatial perception/attention (Paulesu, Danelli, & Berlingeri, 2014). These results are partly supported by diffusion tensor imaging (DTI) studies showing reduced white matter connectivity in some portions of temporo-parietal and frontal white matter pathways (Deutsch et al., 2005; Klingberg et al., 2000; Rimrodt, Peterson, Denckla, Kaufmann, & Cutting, 2010; Vandermosten, Boets, Poelmans, et al., 2012; for a review see Vandermosten, Boets, Wouters, & Ghesquiere, 2012).

However, standard DTI models used in previous studies showed limitations in fiber-crossing regions, spuriously yielding reduced fractional anisotropy (FA) where highly directional fibers may cross, and leading tractography algorithms astray (Vanderauwera, Vandermosten, Dell'Acqua, Wouters, & Ghesquière, 2015; Wandell & Yeatman, 2013). For instance, it is not clear whether reduced FA reported in dyslexic individuals in the fronto-parietal region reflects a reduced connectivity or myelination, or an increase of fiber orientations, as several bundles cross in that region. Another limitation of standard tractography algorithms is that they typically do not allow distinguishing between neighboring tracts such as the arcuate and the superior longitudinal fasciculi. Thus previous studies on dyslexia have attributed some FA differences to the arcuate fasciculus (AF), sometimes solely on the basis of probabilistic atlases (Carter et al., 2009; Deutsch et al., 2005; Klingberg et al., 2000; Niogi and McCandliss, 2006; Odegard, Farris, Ring, McColl, & Black, 2009; Steinbrink et al., 2008), sometimes on the basis of an actual reconstruction of the AF (Saygin et al., 2013; Vandermosten, Boets, Poelmans, et al., 2012; Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012, Yeatman et al., 2011), but without concurrent consideration of the superior longitudinal fasciculus (SLF). This is important as these pathways connect different cerebral regions and their involvement in dyslexia may have different interpretations.

Developmental dyslexia has also been associated with atypical cerebral asymmetry, as suggested by clinical studies (Orton, 1937; Witelson, 1977), functional imaging (Lehongre, Morillon, Giraud, & Ramus, 2013; Lehongre, Ramus, Villiermet, Schwartz, & Giraud, 2011; Richlan, Kronbichler, & Wimmer, 2011) and anatomical dissection and imaging of specific cortical regions (Altarelli et al., 2014; Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985). Plausibly, a deviant hemispheric lateralization of cortical regions should be associated with similarly deviant lateralization of white matter pathways. Surprisingly, this hypothesis has only been tested for the AF in dyslexic adults (Vandermosten, Poelmans, Sunaert, Ghesquiere, & Wouters, 2013). Whether other white matter pathways such as the ventral pathways [i.e., the inferior fronto-occipital fasciculus (IFOF) and the inferior longitudinal fasciculus (ILF)] that are shown to be relevant to reading skills (e.g., Vandermosten, Boets, Poelmans, et al., 2012; Yeatman et al., 2012) also involve abnormal asymmetric patterns in dyslexia requires further testing.

In the present study, we attempt to systematically investigate the connectivity and lateralization patterns of major pathways related to reading and dyslexia (the arcuate fasciculus: AF, the superior longitudinal fasciculus: SLF, the inferior fronto-occipital fasciculus: IFOF and the inferior longitudinal fasciculus: ILF) (Rimrodt et al., 2010; Saygin et al., 2013; Vandermosten, Boets, Wouters, et al., 2012; Yeatman et al., 2011; Yeatman et al., 2012), by using optimized diffusion sequence parameters and tractography algorithms that overcome the limitations of standard DTI. Our goals were twofold: i) to evaluate whether the group differences that were found between dyslexic and normal readers in white matter pathways using standard DTI algorithms can be replicated with advanced tractography methods, and ii) to further examine whether dyslexic children show any deviation of hemispheric lateralization patterns compared with their age-matched controls.

## 2. Materials and methods

### 2.1. *Participants*

Thirty-two dyslexic and 32 typically developing children participated in this study. Children's age ranged from 109 to 169 months (9–14 years). All children were native French speakers with normal vision and hearing abilities. Dyslexic children were referred by a clinic for reading and language disabilities. No child was diagnosed with a history of brain damage, psychiatric, or any other cognitive disorder. For inclusion, dyslexic children had to present a delay greater than 18 months on text reading age [based on accuracy and speed of the Alouette test (Lefavrais, 1967)] while control children had to be no more than 12 months behind. Two dyslexic children were removed from the tractography analysis due to