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Dyslexic children lack word selectivity gradients in occipito-temporal and inferior frontal cortex

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ABSTRACT

fMRI studies using a region-of-interest approach have revealed that the ventral portion of the left occipito-temporal cortex, which is specialized for orthographic processing of visually presented words (and includes the so-called “visual word form area”, VWFA), is characterized by a posterior-to-anterior gradient of increasing selectivity for words in typically reading adults, adolescents, and children (e.g. Brem et al., 2006, 2009). Similarly, the left inferior frontal cortex (IFC) has been shown to exhibit a medial-to-lateral gradient of print selectivity in typically reading adults (Vinckier et al., 2007). Functional brain imaging studies of dyslexia have reported relative underactivity in left hemisphere occipito-temporal and inferior frontal regions using whole-brain analyses during word processing tasks. Hence, the question arises whether gradient sensitivities in these regions are altered in dyslexia. Indeed, a region-of-interest analysis revealed the gradient-specific functional specialization in the occipito-temporal cortex to be disrupted in dyslexic children (van der Mark et al., 2009). Building on these studies, we here (1) investigate if a word-selective gradient exists in the inferior frontal cortex in addition to the occipito-temporal cortex in normally reading children, (2) compare typically reading with dyslexic children, and (3) examine functional connections between these regions in both groups. We replicated the previously reported anterior-to-posterior gradient of increasing selectivity for words in the left occipito-temporal cortex in typically reading children, and its absence in the dyslexic children. Our novel finding is the detection of a pattern of increasing selectivity for words along the medial-to-lateral axis of the left inferior frontal cortex in typically reading children and evidence of functional connectivity between the most lateral aspect of this area and the anterior aspects of the occipito-temporal cortex. We report absence of an IFC gradient and connectivity between the lateral aspect of the IFC and the anterior occipito-temporal cortex in the dyslexic children. Together, our results provide insights into the source of the anomalies reported in previous studies of dyslexia and add to the growing evidence of an orthographic role of IFC in reading.

1. Introduction

Developmental dyslexia is a common learning disability characterized by impaired reading accuracy and/or fluency. It is often accompanied by difficulties in spelling, and because of reduced reading experience, usually leads to a limited sight word vocabulary and poor reading comprehension (Lyon et al., 2003). Dyslexia is prevalent in many cultures, even though the formal diagnosis and some of the cardinal features vary depending on the language and the orthography used. For instance, while reading accuracy is often the preferred diagnostic measure for dyslexia in English-speaking countries, the rate of reading as well as spelling skills are often used to characterize dyslexia in languages with a shallow orthography such as German (see Erickson and Sachse, 2010). Importantly, independent of the spoken languages and writing systems used, it has now been shown that dyslexia exists worldwide, has a neurobiological origin, and is highly heritable (Peterson and Pennington, 2012).

Evidence from behavioral studies of dyslexia has demonstrated that weaknesses in phonological processing represent the core deficit of the reading difficulties (Wagner and Torgesen, 1987; Bruck, 1992; Stanovich and Siegel, 1994; Morris et al., 1998). In the last two decades, neuroimaging studies comparing dyslexic and typical readers have revealed differences in brain activity in left hemisphere language regions; some of these have been posited to be involved in phonological processing, including inferior frontal and parieto-temporal cortices (for reviews, see Pugh et al., 2001; Démonet et al., 2004; Maisog et al., 2008; Richlan et al., 2009; Richlan et al., 2013; Richlan, 2012). Most of these studies have also identified between-group differences in the left ventral occipito-temporal cortex (OTC) (Salmelin et al., 1996; Rumsey

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et al., 1997; Brunswick et al., 1999; Paulesu, 2001; Shaywitz et al., 2002; Cao et al., 2006; Maurer et al., 2007; Olulade et al., 2012; Richlan et al., 2011). This region has been of considerable interest in reading research because it encompasses the so-called "visual word form area" (VWFA (Cohen et al., 2000; Cohen et al., 2002; McCandliss et al., 2003; Cohen and Dehaene, 2004)). The VWFA is thought to be involved in fast orthographic processing of visually presented familiar words or letter strings (Salmelin et al., 1996; Cohen et al., 2002; Petersen et al., 1990; Tarkiainen et al., 1999; Dehaene et al., 2004; Maurer et al., 2006; Baker et al., 2007). It has been suggested that differences observed in the VWFA between dyslexics and controls are secondary in their developmental onset to the phonological weakness attributed to altered parieto-temporal and inferior frontal function (Pugh et al., 2001; McCandliss and Noble, 2003). However, a recent study reported the OTC as the only area underactivated in dyslexics compared with non-dyslexics in meta-analyses conducted in children as well as in adults. This indicates early and persistent involvement of the OTC in dyslexia (Richlan et al., 2011). Further, in a study combining dyslexic groups of participants from three countries, the left OTC was identified as the only region to be underactivated when compared with the control groups (Paulesu, 2001).

Most neuroimaging studies published to date have searched for the most salient differences between groups of dyslexics and their typically reading counterparts by conducting whole-brain analysis to identify activity underlying reading or reading-related skills, then reporting on between-group differences. However, other experimental and analytic approaches have been used to understand the functional neuroanatomy of reading and reading disability. One notable approach has been to examine in detail pre-specified regions of the brain using a region-of-interest (ROI) analysis, and to examine gradient patterns (i.e. differential task activations) amongst a series of ROIs. Specifically, the ventral OTC, often referred to as the "visual word form system" (VWFS), has been shown to demonstrate a posterior-to-anterior gradient of increasing word selectivity in typical readers. That is, in French-speaking adults (Vinckier et al., 2007) and in Swiss–German-speaking adults, adolescents (Brem et al., 2006; Brem et al., 2009), and children (Brem et al., 2009; van der Mark et al., 2009), as well as English-speaking adults and children (Olulade et al., 2013), investigators have observed a relative signal increase for word stimuli compared to false-font/symbol-string stimuli along the posterior-to-anterior axis in the medial aspect of the left OTC, with the absence of this pattern reported in the right hemisphere homologue. These results demonstrate the presence of hierarchical specialization in a region of the brain that is important for orthographic processing of visually presented words and automatic word recognition in individuals with typical reading skills. In a recent report (Olulade et al., 2013), we demonstrated developmental differences between children and adults in the nature of this gradient, providing evidence of fine-tuning of functional specialization in the VWFS with age-dependent reading experience.

A critical question is whether this word-sensitive architecture in the ventral OTC is altered in individuals with dyslexia. This was addressed by van der Mark et al. (2009), who employed a region-of-interest analysis involving a series of spheres within the left ventral OTC to examine activation in response to pseudoword, pseudohomophone, and real-word stimuli contrasted with false-font strings. The typically reading children exhibited significantly greater activation for false fonts relative to real words in the most posterior region, and significantly greater activation for real words relative to false fonts in an anterior region, thereby confirming the previously reported posterior-to-anterior gradient for proficient readers. Similar findings were observed for pseudowords, which yielded significantly greater activation than false fonts in the three most anterior regions. By contrast, the dyslexic children did not show this gradient of word selectivity. By moving beyond the simple observation of hypoactivity in the occipito-temporal region, this approach has uncovered the complex nature of the differences that exist in dyslexia.

Several questions, however, remain unanswered. First, does the lack of a gradient in dyslexia in the VWFS also exist in children who read in English? The answer to this question is important to our understanding of the universal versus orthography-specific aspects of dyslexia, as well as the role of the VWFS in reading generally. Based on current models of reading in different orthographies, one would anticipate disruption of the gradient in dyslexic readers of English. Specifically, it has been suggested that for orthographies where there is less (e.g. English) or no (e.g. Chinese) grapheme–phoneme correspondence, there is greater reliance on the OTC and IFC (Richlan, 2014). Research in alphabetic languages indicates greater engagement of the OTC and the inferior frontal gyrus (IFG) by readers of English, which has a "deep" orthography, whereas readers of Italian, which is "shallow," preferentially engage the posterior superior temporal gyrus (Paulesu et al., 2000). For shallow languages, which includes German, the mapping between graphemes and phonemes is one-to-one, while reading in English requires more words to be recognized by sight (i.e. words with irregular spelling), placing greater reliance on the VWFA. We therefore fully expected to replicate the OTC disruption in dyslexic readers of English. A second question concerns the role of the IFG, which traditionally has been considered a contributor to phonological assembly and articulatory planning (Pugh et al., 2001). As such, it is surprising that Vinckier and colleagues found a gradient of increasing word selectivity not only in the OTC in typically reading adults, but also in Broca's area (Vinckier et al., 2007). This inferior frontal gradient occurred along the transverse axis, with selectivity for words increasing from medial to lateral ROIs. The authors postulated that co-occurrence of gradients of word selectivity in the left inferior frontal cortex (IFC) region and in the VWFS may be a result of neuronal connections between left hemisphere posterior visual (occipito-temporal) and anterior language regions, but did not test this hypothesis directly. Replication of a topographical organization in the left IFC, this time in a group of younger readers, would be important to establish whether there is a more direct orthographic role for the IFC in print processing, making it similar in function to the VWFA (Paulesu, 2001). In addition to examining the IFC in normally reading children, we also tested the integrity of this area in children with dyslexia. This builds on a body of literature that, generally speaking, has been mixed, with some reporting underactivity in the dyslexic group compared to the control group in the IFC (Cao et al., 2006; Brambati et al., 2006; Booth et al., 2007; Schulz et al., 2008) but others not (Brunswick et al., 1999; Shaywitz et al., 1998; Georgiewa et al., 2002). As such, a more focused examination of the IFC region involving gradient sensitivity can shed light on this issue. Finally, we examined functional connectivity between the left IFC and ventral OTC with the expectation that, as suggested by Vinckier et al. (2007), they are functionally connected in typical readers. In studies of dyslexia, several investigators have reported altered connectivity between brain regions involved in the various aspects of word processing (Horwitz et al., 1998; Pugh et al., 2000; Stanberry et al., 2006; Cao et al., 2008; Ligges et al., 2010; van der Mark et al., 2011; Vourkas et al., 2011), including an observation of weaker connectivity between the VWFA and the IFG reported by van der Mark et al., (2011). Together, the results should advance our understanding of the roles of the VWFA and IFG in readers of English, their interrelationship, and their functionality in children with dyslexia.

2. Materials and methods

2.1. Participants

All subjects were monolingual native speakers of English without prior diagnosis of developmental disability or psychiatric disorder. Subjects underwent a battery of behavioral tests to measure intelligence, reading proficiency, and skills known to support reading. The Wechsler Abbreviated Scale of Intelligence (WASI) was used to measure Verbal and Performance IQ (Wechsler, 1999). To be eligible for the study all