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/aba/ or */ada/*, that is the question:
Longitudinal investigation of letter-speech sound processing
in children with and without developmental dyslexia

Linda Romanovska

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of letter-speech sound processing in children with and
without developmental dyslexia

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General introduction

Based on

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Abstract

Reading acquisition reorganizes existing brain networks for speech and visual processing to form a reading network. This requires substantial cortical plasticity that is reflected in changes in brain activation and functional as well as structural connectivity between brain areas. The extent to which a child's brain can accommodate these changes will in turn affect interactions between the speech (dorsal) and visual (ventral) components of the reading network. The dynamic and idiosyncratic nature of these interactions may underlie the high variability in reading outcome in both, typical and dyslexic readers. In this review, we focus on reading-induced functional changes of the dorsal system in particular and discuss how its reciprocal interactions with the ventral reading system contributes to reading outcome. Finally, we discuss research paradigms best suited to investigate the intertwined development of the dorsal and ventral reading systems and elaborate on how these investigations could help further our understanding of individual differences in reading development and proficiency.

Introduction

Despite standardized curricula and teaching programs at school, children reach very different levels of reading fluency. Proficiency in reading determines personal achievement not only during primary and secondary education but also societal attainment later in life (Hudson, Price, & Gross, 2009; UNESCO, 2006). This especially affects those 5-10% of children with developmental dyslexia who struggle to acquire fluent reading skills despite adequate intellectual abilities and schooling opportunities (Blomert, Mitterer, & Paffen, 2004; Shaywitz & Shaywitz, 2008).

The acquisition of reading requires years of practice and is accompanied by a gradual re-shaping of existing brain networks for visual perception and spoken language into integrated ventral visual and dorsal language systems. Thus, when a child learns to read, striking changes occur in higher-order visual regions of the (left) ventral occipito-temporal cortex (vOTC) which becomes increasingly specialized in written text perception (Ben-Shachar, Dougherty, Deutsch, & Wandell, 2011; Brem et al., 2009; Dehaene-Lambertz, Monzalvo, & Dehaene, 2018; Maurer et al., 2006). Furthermore, auditory/speech sensitive regions in the posterior superior temporal cortex (pSTC) become linked to these higher-order visual regions and start responding to written text in addition

to spoken language (Brennan, Cao, Pedroarena-Leal, McNorgan, & Booth, 2013; Froyen, Bonte, van Atteveldt, & Blomert, 2009; Van Atteveldt, Formisano, Goebel, & Blomert, 2004). The emergence of these audio-visual response characteristics arguably reflects a form of neural plasticity that is central to reading acquisition, with reduced or less automatic text-induced audio-visual integration in dyslexic readers and illiterates (Blomert, 2011; Dehaene, Cohen, Morais, & Kolinsky, 2015). Individual differences in reading skills may thus scale with the capacity of the brain regions involved in auditory and visual perception to accommodate reading-induced changes. This may hold across largely different writing systems, with cultural variability mainly affecting the representational level at which written to spoken language associations are formed (phonemes, syllables, words; Feng et al., 2020; Perfetti, 2003; Rueckl et al., 2015).

Developmental dyslexia

Developmental dyslexia provides a good model for investigating the role of the dorsal and ventral reading systems in reading development and audio-visual integration as most dyslexic readers show difficulties in handling the sound structure of spoken language (phonological deficits, Goswami, 2003; Lyon, Shaywitz, & Shaywitz, 2003; Shaywitz et al., 1998; Snowling, 1980, 2013) and in forming associations between letters and speech sounds (Aravena, 2017; Blomert, 2011; Blomert & Willems, 2010; Kronschnabel, Brem, Maurer, & Brandeis, 2014, but see Clayton & Hulme, 2017; Nash et al., 2016). A major challenge in understanding this disorder lies in its highly heterogeneous behavioural manifestation. Suggested causes include - but are not limited to – deficits in letter-speech sound integration (Blomert, 2011; Snowling, 1980), poorly specified and/or less categorical speech representations (Serniclaes, Van Heghe, Mousty, Carré, & Sprenger-Charolles, 2004; Snowling, 1998), impaired access to speech representations (Ramus, 2003), impaired temporal sampling of speech (Goswami, 2011), inadequate implicit auditory regularity detection mechanisms (Ahissar, 2007), impaired processing of brief sounds (Tallal & Piercy, 1973), visual dysfunctions (Bosse et al., 2007), or more general deficits in magnocellular functions (Livingstone, Rosen, Drislane, & Galaburda, 1991), automation processes (Nicolson & Fawcett, 1999), or attentional mechanisms (Bosse, Tainturier, & Valdois, 2007; Lobier, Zoubrinetzky, & Valdois, 2012; Shaywitz & Shaywitz, 2008; Vidyasagar & Pammer, 2010). So far these different possibilities have been mostly studied in isolation and typically using cross-sectional experimental designs that may not have the sensitivity to reveal the underlying multifaceted and individually

General introduction

variable developmental dynamics. It is therefore promising that an increasing number of labs and research consortia have started longitudinal neuroimaging studies following children during different stages of reading development (e.g. Chyl et al., 2019; Dehaene-Lambertz et al., 2018; Lyytinen, Erskine, Hämäläinen, Torppa, & Ronimus, 2015; Moulton et al., 2019; van de Walle de Ghelcke, Rossion, Schiltz, & Lochy, 2020; Van Der Leij et al., 2013; Vanderauwera et al., 2018; Wang, Karipidis, Pleisch, Fraga-González, & Brem, 2020; Wang et al., 2017; Zuk et al., 2020). These studies are crucial to understanding how individual differences in reading trajectories and outcome can be positioned within the interactive development of the brain's spoken and written language systems (Pugh et al., 2001; Sandak, Mencl, Frost, & Pugh, 2004).

Individual variability in reading outcomes is likely rooted in genetic and environmental factors that interactively influence the dynamic structural and functional brain changes while children learn and develop (Nora Maria Raschle, Chang, & Gaab, 2011; Wang et al., 2017; Yu et al., 2020; Yu, Zuk, & Gaab, 2018; Zuk et al., 2020). While this variability is continuous in nature, dyslexia is typically diagnosed based on a specific cut-off, most commonly scoring 1,5 standard deviations below the age-group average on a battery of reading and/or spelling tests (American Psychiatric Association, 2013). Although in diagnostic practice, such an arbitrary cut-off criterion is currently unavoidable, recent research proposes a shift away from a dichotomous classification of reading as poor versus fluent and towards a multi-deficit spectral view of reading instead (Pennington, 2006; Peters & Ansari, 2019; Protopapas & Parrila, 2018). Here, reading fluency is represented on a spectrum ranging from poor to fluent, with dyslexia lying on one end of the spectrum rather than being defined as a qualitatively discontinuous condition (Peters & Ansari, 2019). This approach takes into account the variability in reading proficiency observed in both poor and fluent readers (Aravena, Snellings, Tijms, & van der Molen, 2013; Fraga-González et al., 2015; Žarić et al., 2014) as well as addressing the frequently reported comorbidity between learning disorders (Landerl & Moll, 2010; Peters & Ansari, 2019; van Bergen, van der Leij, & de Jong, 2014).

Speech perception and speech sensitivity in the auditory cortex

By the time children start to learn to read, neural functions for speech perception and production have already gone through several years of functional refinement. Spoken language functions thus form a linguistic basis for reading acquisition both from a phylogenetic and an ontogenetic

perspective (Dehaene et al., 2015). Since the first neuroimaging findings in the 1990s, numerous studies have been designed with the aim to delineate the brain's spoken language system. One of the first pioneering studies in this domain showed that listening to speech elicits extensive and bilateral activation in the superior temporal cortex (STC), including primary areas on Heschl's gyrus (HG), the planum temporale (PT), and along the superior temporal gyrus (STG) and superior temporal sulcus (STS) (see Figure 1; Binder et al., 1994). Building on this earlier work, advances in research methodology have enabled delineating a more fine-grained functional architecture of speech sound representations in the superior temporal cortex (Chang et al., 2010; Leonard, Baud, Sjerps, & Chang, 2016; Mesgarani, Cheung, Johnson, & Chang, 2014). One relevant new insight emerging from this work is the finding that the auditory representations of speech along the posterior and lateral STG are not restricted to low-level acoustic-phonetic speech features (Jäncke, Wüstenberg, Scheich, & Heinze, 2002; Obleser & Eisner, 2009), but include higher-order perceptual levels of representation that are strongly modulated by a listener's behavioural goals, learning and contextual information. Examples of different observed levels of abstraction are speech representations that are robust to speaker changes (Formisano, De Martino, Bonte, & Goebel, 2008; Mesgarani & Chang, 2012), categorically encode vowel sounds (Levy & Wilson, 2020), and are modulated by context and task demands (Bonte, Hausfeld, Scharke, Valente, & Formisano, 2014; Rutten, Santoro, Hervais-Adelman, Formisano, & Golestani, 2019; Yi, Leonard, & Chang, 2019). Most interesting with respect to reading development is the observation of plastic changes in auditory cortical speech representations in the context of multisensory information (Kilian-Hütten, Valente, Vroomen, & Formisano, 2011; Ozker, Schepers, Magnotti, Yoshor, & Beauchamp, 2017; Ozker, Yoshor, & Beauchamp, 2018), including visual presentation of text (Bonte, Correia, Keetels, Vroomen, & Formisano, 2017). Although it remains debated whether and how learning to read changes the representation of speech (Dehaene et al., 2015; Mitterer & Reinisch, 2015), the modulatory effect of audio-visual mappings between text and spoken language (Bonte et al., 2017) suggests a specific role of the auditory cortex in reading-induced plasticity.

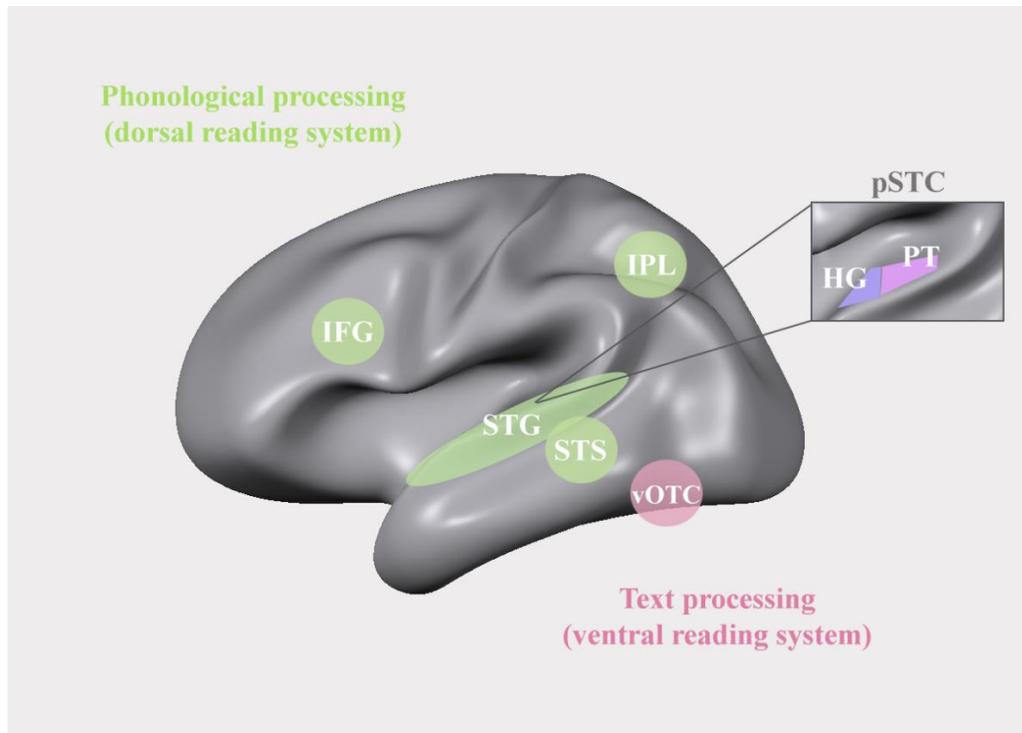


Figure 1: A representation of the dorsal (green) and ventral (pink) reading systems of the brain's audio-visual reading network. IFG = inferior frontal gyrus; IPL = inferior parietal lobe; STG = superior temporal gyrus; STS = superior temporal sulcus; vOTC = ventral occipito-temporal cortex; pSTC = posterior superior temporal cortex; HG = Heschl's gyrus; PT = planum temporale.

Auditory cortical development and reading

Further support for a key role of the superior temporal cortex in learning to read comes from developmental neuroimaging studies showing that the strength and/or extent of speech evoked responses in this region is associated with reading level (Brennan et al., 2013; Conant, Liebenthal, Desai, & Binder, 2014; Parviainen, Helenius, Poskiparta, Niemi, & Salmelin, 2011), and phonological skills (Bonte, Ley, Scharke, & Formisano, 2016; Conant et al., 2014; Randazzo, Greenspon, Booth, & Mcnorgan, 2019; Turkeltaub, Gareau, Flowers, Zeffiro, & Eden, 2003). Moreover, children with dyslexia (Bonte & Blomert, 2004; Schulte-Körne, Deimel, Bartling, & Remschmidt, 1998), or at familial risk for developing dyslexia (Vandermosten et al., 2019) may show reduced or less discriminable auditory cortical responses to speech. Such functional changes may result from less efficient speech sound learning during early development. Indeed, less efficient tuning to statistical regularities in speech sound structures has been observed in adults (Noordenbos, Segers, Mitterer, Serniclaes, & Verhoeven, 2013; Schmalz, Altoè, & Mulatti, 2017;

Zhang et al., submitted) and children (Bonte, Poelmans, & Blomert, 2007; Gabay, Thiessen, & Holt, 2015) with dyslexia.

Next to these more recent studies on functional characteristics of the superior temporal cortex that relate to reading skills, there is a long tradition of relating morphological variability of the PT in particular to inter-individual variability in auditory and language skills (e.g. Golestani, Price, & Scott, 2011), and to language dysfunctions in dyslexia (Galaburda, 1989; Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Geschwind & Levitsky, 1968; Leonard, Eckert, Given, Virginia, & Eden, 2006). However, there is no unequivocal evidence linking the morphological aspects of the PT to its functional characteristics and to individual children's language skills (Altarelli et al., 2014; Beelen, Vanderauwera, Wouters, Vandermosten, & Ghesquière, 2019; Ramus, Altarelli, Jednoróg, Zhao, & Scotto di Covella, 2018; Vanderauwera, Altarelli, et al., 2018). Nevertheless, reading related characteristics of the superior temporal cortex can be located within a more general pattern of protracted developmental changes in pSTC morphology, which have been observed to continue well into the third decade of life, particularly in the left hemisphere (Giedd et al., 1999; Gogtay et al., 2004; Sowell et al., 2003). Similarly, while the global signature of speech evoked STC responses is in place in infancy (Dehaene-Lambertz & Pena, 2001), its functional characteristics continue to change well beyond primary school years (Bonte & Blomert, 2004; Bonte et al., 2013; Brauer, Neumann, & Friederici, 2008; Chyl et al., 2017; Pang & Taylor, 2000; Sharma, Kraus, McGee, & Nicol, 1997). Such an extended developmental time course may allow a prolonged process of functional specialization during which auditory and visual language input contributes to the shaping and fine tuning of relevant brain circuitry (Johnson, 2001, 2011; Werker & Hensch, 2015).

The audio-visual reading network: dorsal and ventral systems

The audio-visual reading network can be sub-divided into an anterior and posterior dorsal system and a ventral system. The continued functional and morphological development of the pSTC in the posterior dorsal system may be key to the gradual build-up of neural associations between visual symbols (letters, words) and corresponding spoken language representations (phonemes, words) and on a more general level, the strong bi-directional influences between reading and spoken language development (Blomert, 2011; Morais, Cary, Alegria, & Bertelson, 1979; Perfetti,

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Beck, Bell, & Hughes, 1987; Rueckl et al., 2015; Sandak et al., 2004). Suggestive evidence for a direct influence of visual text processing on auditory cortical processing of speech comes from the observation that activation in pSTC increases in response to matching (congruent) compared to non-matching (incongruent) letter-speech sound pairs (Karipidis et al., 2017; Raij, Uutela, & Hari, 2000; Van Atteveldt et al., 2004; van Atteveldt, Blau, Blomert, & Goebel, 2010). Accordingly, these cross modal modulations in the STC were found to scale with phonological skills (McNorgan, Randazzo-Wagner, & Booth, 2013) and reading experience (McNorgan, Awati, Desroches, & Booth, 2014) in typical readers, and to be reduced in dyslexic readers (Blau et al., 2010; Blau, van Atteveldt, Ekkebus, Goebel, & Blomert, 2009; Kronschnabel et al., 2014; Ye, Rüsseler, Gerth, & Münte, 2017a). Evidence of a gradual strengthening of audio-visual associations throughout the first years of reading development – extending well beyond the initial phase of learning to map letter(s) to their corresponding speech sound(s) – comes from EEG studies employing audio-visual oddball paradigms. These studies have found that the neural time-window of audio-visual integration changes from later to earlier (Froyen et al., 2009; Žarić et al., 2014) and becomes narrower/more time-sensitive (Žarić et al., 2014) over the course of (reading) development. Moreover, the latency of integrative letter-speech sound responses has been found to deviate in dyslexic compared to typical readers (Froyen, Willems, & Blomert, 2011; Jones, Kuipers, & Thierry, 2016; Moll, Hasko, Groth, Bartling, & Schulte-Körne, 2016; Žarić et al., 2014) with a speeding up of these responses after 6 months of intensive letter-speech sound training in dyslexic children (Žarić et al., 2015).

Another brain region crucial for combining letters and speech sounds in the posterior dorsal network is the inferior parietal lobe (IPL). It has been proposed to be involved in letter-speech sound mapping, as well as semantic processing (Bonte et al., 2017; Paz-Alonso et al., 2018; Shaywitz & Shaywitz, 2008) and visual attention (Raman Vidyasagar, 1999; Saalman, Pigarev, & Vidyasagar, 2007). Similarly to pSTC, activation in the IPL has been found to increase with reading experience (Yu, Raney, et al., 2018) and to be decreased in dyslexic readers (Hoeft et al., 2007; Paz-Alonso et al., 2018; Richlan, Kronbichler, & Wimmer, 2009, 2011). The former finding is suggested to reflect a fine tuning of grapheme-phoneme mappings in early reading development (Yu, Raney, et al., 2018). Based on observations of a subsequent reduction of IPL involvement with continued reading development (Dehaene-Lambertz et al., 2018; Moulton et al., 2019) it may be speculated that the IPL is especially relevant for establishing new audio-visual associations (see

also e.g. Bonte et al., 2017), followed by the formation of more solidly integrated representations in the pSTC (Blau et al., 2010; Van Atteveldt et al., 2004).

The anterior part of the dorsal network houses the IFG which is increasingly recruited while beginning readers improve their reading ability and phonological skills (Turkeltaub et al., 2003). Functional connectivity between IFG and IPL has been associated with phonological processing skills during early reading development (Yu, Raney, et al., 2018), while functional connectivity between IFG and STG has been found to correlate with reading fluency and to be reduced in dyslexic readers (Figure 2 right panel; Schurz et al., 2015). Within the developing reading network, the IFG may be involved in the learning of novel audio-visual associations (Hein et al., 2007), phonologic-orthographic regularity of words (Pugh et al., 1997) and semantic and phonological processing of written and spoken words (Booth et al., 2001; Burton, 2001; Fiez, 1997; Poldrack et al., 1999; Sandak et al., 2004; Turkeltaub et al., 2003). One relevant domain of further investigation is the possible relevance of the (right) IFG in compensatory, alternative reading strategies in dyslexic readers (e.g. Hoeft et al., 2011; Žarić et al., 2015).

A core area for developing fluent reading in the ventral reading system is the putative visual word form area (VWFA) within the left ventral occipito-temporal cortex. This area has been shown to become increasingly specialized for text over the course of reading development (Ben-Shachar et al., 2011; Brem et al., 2009; Dehaene-Lambertz et al., 2018; Maurer et al., 2006) and to be less active in dyslexic readers (Figure 2 left panel; Dehaene & Cohen, 2011; Hoeft et al., 2007; Paulesu, 2001; Richlan et al., 2009; Wimmer et al., 2010). The central function of this specific occipito-temporal region in written text processing most likely relates to its close functional interactions with regions in the dorsal language network, including IFG, STS, pSTG, and IPL (Monzalvo, Fluss, Billard, Dehaene, & Dehaene-Lambertz, 2012; Richlan, 2012; Schurz et al., 2015; Yu, Raney, et al., 2018). Accordingly, the functional specialization of the VWFA is thought to be shaped by white matter connections to these key speech processing areas (Hannagan, Amedi, Cohen, Dehaene-Lambertz, & Dehaene, 2015; Moulton et al., 2019; Saygin et al., 2016).

One important open question is the extent to which the commonly observed reduced recruitment of regions within the dorsal and ventral reading systems in dyslexic readers constitutes a causal or (familial) risk factor in the aetiology of dyslexia. That is, a child of a parent with dyslexia has

about 40-60% chance of also developing dyslexia (Ozernov-Palchik & Gaab, 2016; Yu, Zuk, et al., 2018) but this familial risk does not necessarily lead to poor reading outcome (Pennington & Lefly, 2001; Ramus et al., 2018; Yu, Zuk, et al., 2018). Pre-readers categorized as high versus low-risk for developing dyslexia based on family history have been reported to show activation differences in similar regions as dyslexic versus typical readers (Figure 2 left panel). These include: activation differences in key spoken language and reading networks (Debska et al., 2016), VWFA (Karipidis et al., 2017; Plewko et al., 2018), left STC activation in response to letter-speech sound pairs (Maurer, Bucher, Brem, & Brandeis, 2003; Plewko et al., 2018) and during speech processing (Raschle, Zuk, & Gaab, 2012; Vandermosten et al., 2019), as well as reduced audio-visual modulations (Karipidis et al., 2017) and reduced distinctiveness of STC speech representations (Vandermosten et al., 2019). However, brain activation and connectivity patterns in the at-risk children who go on to develop typical reading skills does differ from those at risk children who develop reading difficulties, as well as typical readers with no family risk (e.g. Leppänen et al., 2011; Wang et al., 2017). Thus, whether a child develops dyslexia likely depends on a combination of risk and protective factors modulating the dynamic and individually variable development of the brain's reading network (Ozernov-Palchik & Gaab, 2016; Perry, Zorzi, & Ziegler, 2019; Zuk et al., 2020). Moreover, once a child has developed dyslexia, a history of reading problems will also affect the functional properties of this network and its associated cognitive perceptual functions (see e.g. Huettig, Lachmann, Reis, & Petersson, 2018). Any observed group differences should therefore be considered taking into account as many of these factors as possible. Longitudinal studies following the same children over the course of reading development are particularly well suited for investigations of changes in the dynamics of the dorsal and ventral reading systems as well as the contribution of risk/protective factors to reading outcome.

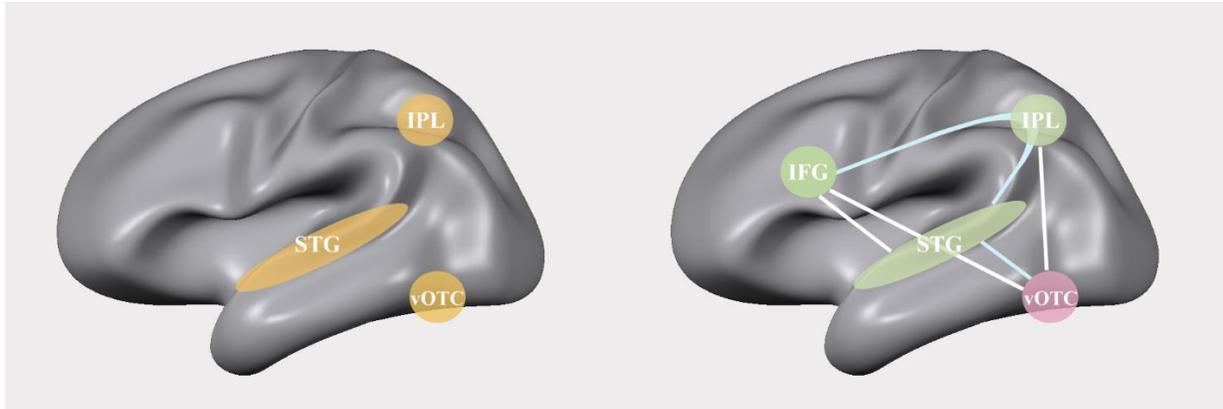


Figure 2: Left: Areas where aberrant cortical activation is often reported in readers with dyslexia; Right: Frequently observed differences in functional (white lines) and structural (light blue lines) connectivity between readers with and without dyslexia.

Developmental dynamics of reading development and dyslexia

When learning to read, we initially rely mostly on the dorsal network (Figure 3 top row; Booth et al., 2001; Pugh et al., 2001; Sandak et al., 2004; Turkeltaub et al., 2003), employing the IPL in particular to map letters and eventually letter strings onto corresponding speech sounds (Blomert, 2011; Moulton et al., 2019). With continued practice, the dorsal network helps in developing phonological awareness and encoding relations between orthographic, phonological, and semantic features of words (Pugh et al., 2013). Effortful letter-for-letter reading and emerging phonological and orthographic knowledge create and strengthen functional (Dehaene et al., 2015; Moulton et al., 2019; Price & Devlin, 2011; Schlaggar & McCandliss, 2007; Yu, Raney, et al., 2018) and structural (Gullick & Booth, 2014; Moulton et al., 2019; Myers et al., 2014; Vandermosten, Boets, Wouters, & Ghesquière, 2012; Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012) links between the dorsal and ventral systems, gradually re-shaping dedicated areas in both, including the VWFA in particular (Aravena & Tijms, 2009; Gorka Fraga González et al., 2014; Gorka Fraga González, Zaric, Tijms, Bonte, & van der Molen, 2017; Pugh et al., 2001) but possibly also the STG (Bonte et al., 2017; Joo, Tavabi, & Yeatman, 2019). Once fluent reading is achieved, the ventral network ensures rapid and automatized recognition and processing of text and becomes the dominant system used for reading (Figure 3 bottom row; Cohen & Dehaene, 2009; McCandliss, Cohen, & Dehaene, 2003; Sandak et al., 2004; Shaywitz et al., 2002). While the contribution of the dorsal network to fluent reading at this stage may be reduced, areas within the network have

General introduction

been found to be automatically activated by text (Joo et al., 2019) and to be employed for reading difficult, irregular words or novel pseudo-words by fluent readers (Pugh et al., 2001; Simos, 2002).

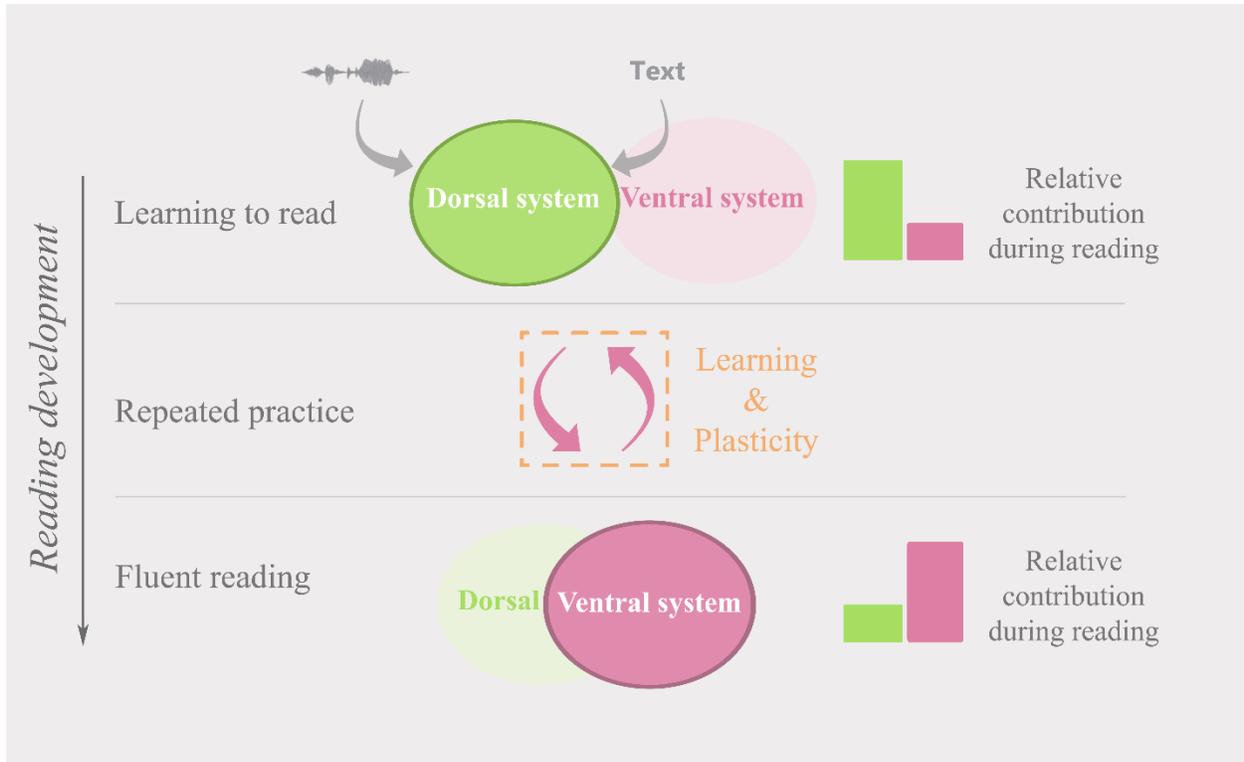


Figure 3: A representation of the relative dorsal (green) and ventral (pink) cortical reading network contribution over the course of reading development.

Based on longitudinal evidence, the strength of functional connectivity between the IPL and vOTC is suggested to be key to successful audio-visual integration of letters and speech sounds during initial reading development and to shaping the VWFA for automatized, fluent reading (Wise Younger, Tucker-Drob, & Booth, 2017; Yu, Raney, et al., 2018). Indeed, in line with the proposed shift to the ventral system in fluent readers, decreased connectivity between the areas has been associated with larger gains in reading fluency in 8-14 year old children (Wise Younger et al., 2017). Given the dynamic relationship between the dorsal and ventral systems in early reading development, an inverted-u-trajectory of connectivity patterns between these systems may be expected. When acquiring a new skill, children make use of both, active, explicit strategies as well as passive, statistical/associative learning (Shrager & Siegler, 1998; Siegler & Araya, 2005; Siegler, 2005). During the initial stages of learning, the active strategies are relied upon the most, helping to establish rules necessary to acquire a skill (e.g. mapping certain speech sounds to

specific letters). Continued practice serves as input for the passive learning mechanisms that are mainly used once a child has mastered the skill (e.g. become a fluent reader). These skill learning stages would correspond to less reliable connectivity at the onset of reading instruction (i.e. no robust associations between letters and speech sounds), an increase in connectivity strength with repeated practice and increased reading fluency, followed by less strong connectivity once reading has become fully automatized and mainly taken over by the ventral system.

The developmental changes in functional connectivity are paralleled by changes in diffusivity in the white matter tracts connecting the key nodes of the reading network (Myers et al., 2014; Vanderauwera, De Vos, et al., 2018; Yeatman et al., 2012), with structural differences reported in dyslexic readers (Figure 2 right panel; Cui, Xia, Su, Shu, & Gong, 2016; Rimrodt, Peterson, Denckla, Kaufmann, & Cutting, 2010; Steinbrink et al., 2008; Vandermosten, Boets, Poelmans, et al., 2012) and at-risk pre-readers (Langer et al., 2017; Vanderauwera, Wouters, Vandermosten, & Ghesquière, 2017; Vandermosten, Cuynen, Vanderauwera, Wouters, & Ghesquière, 2017; Vandermosten et al., 2015). Also the developmental changes in white matter diffusivity have been proposed to follow an inverted-u-trajectory over the course of reading development, with increases in diffusivity observed at the beginning of reading instruction, followed by decreased diffusivity with improved reading proficiency (Yeatman et al., 2012). However, the time it takes to become a fluent reader will inevitably differ per individual and will be influenced by (but not limited to) genetic (Friend, Defries, & Olson, 2008; Hawke, Wadsworth, & DeFries, 2006; Keenan, Betjemann, Wadsworth, Defries, & Olson, 2006) and socio-economic factors (Aikens & Barbarin, 2008; Noble, Farah, & McCandliss, 2006; Noble, Wolmetz, Ochs, Farah, & McCandliss, 2006). Especially individuals with (familial risk of) dyslexia may require an extended period for speech structure and audio-visual learning (Karipidis et al., 2018; Zhang et al., submitted). A longitudinal investigation of children with and without dyslexia showed delayed development of connections between vOTC and IFG between ages 6 to 8 in dyslexic compared to age-matched typical readers, reaching the same level of connectivity by age 12 (Morken, Helland, Hugdahl, & Specht, 2017). Aberrant connectivity between vOTC and the dorsal network has also been reported in cross sectional studies, with dyslexic children showing less robust connectivity between the VWFA, IFG and IPL (Figure 2 right panel; Finn et al., 2014; Schurz et al., 2015; van der Mark et al., 2011). The connectivity patterns in these studies reveal alternate connectivity between the vOTC and the dorsal system, as well as connectivity to right hemisphere areas. Whereas developmental changes

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in functional connectivity between the IPL and VWFA may be key for a successful switch to automatized, ventral processing of text in typical readers (Wise Younger et al., 2017), dyslexic readers may develop different connectivity patterns between the ventral and dorsal reading systems, potentially as a compensatory reaction to difficulties with quick, automatized text processing in the vOTC. Thus, children of the same age may be at different stages of reading and functional brain development, resulting in the observed high variability in neural and especially behavioural measures.

Investigating text-speech sound learning mechanisms

In line with the idea that the brain's reading network relies on the integration of dorsal phonological and ventral visual systems, difficulties in letter-speech sound mapping and automatization are one of the proposed core deficits of developmental dyslexia (Aravena, 2017; Blomert, 2011; Blomert & Willems, 2010; Kronschnabel et al., 2014, but see Clayton & Hulme, 2017; Nash et al., 2016). Studies investigating dyslexia intervention targeting letter-speech sound automatization, have shown improvements in reading outcome and in brain responses associated with letter-speech sound integration following intervention (Fraga González et al., 2016; Fraga González et al., 2017; Žarić et al., 2015). However, typically used 'static' or outcome measures of letter-speech sound integration (e.g. (in)congruency effects of learnt associations) yield variable results in dyslexic readers/pre-readers at high family risk compared to typically reading children/children with low family risk (Blau et al., 2010; Karipidis et al., 2018; Plewko et al., 2018; Richlan et al., 2011). It is difficult to capture the dynamics of individual children's learning trajectories in these paradigms in a way that is not biased by context variables such as task strategies and (self-beliefs regarding) the ability to perform the experimental task.

A promising platform to investigate audio-visual learning mechanisms underlying letter-speech sound coupling and the dynamic involvement of the dorsal and ventral reading systems can be found in artificial letter training and phonetic recalibration paradigms. Artificial letter training involves mapping known speech sounds onto novel visual symbols, thus directly targeting letter-speech sound integration mechanisms. Intriguingly, no group differences in the overall ability to learn novel letter-speech sound pairs have been observed between children with dyslexia (Aravena et al., 2013; Aravena, Tijms, Snellings, & van der Molen, 2018; Law, 2018) and at-risk pre-readers

(Karipidis et al., 2018) compared to their age-matched peers. Group differences did emerge under time constraints (i.e. rapid naming of the letter-speech sound pairs; Aravena et al., 2013, 2018; but see Law, 2018) and when the newly learnt letter-speech sound mappings need to be applied to another task (e.g. reading names of familiar objects using the artificial script; Aravena et al., 2013, 2018; Karipidis et al., 2018; Law, 2018). These findings point to difficulties in automatizing letter-speech sound mappings rather than struggling to create these mappings in the first place (Blomert, 2011; Blomert & Willems, 2010; Kronschnabel et al., 2014).

Text-based recalibration paradigm

Another interesting type of paradigm that enables examining perceptual mechanisms associated with short-term audio-visual learning is phonetic recalibration (also ‘perceptual learning’, Samuel & Kraljic, 2009; Vroomen & Baart, 2012). Recalibration refers to a shift in an individual’s perception of ambiguous speech induced by the presentation of disambiguating visual input such as lip-read speech (Bertelson, Vroomen, & De Gelder, 2003; Vroomen & Baart, 2012), spoken word context (Norris, McQueen, & Cutler, 2003), overt speech articulation (Scott, 2016a) or text (Bonte et al., 2017; Keetels, Bonte, & Vroomen, 2018; Keetels, Schakel, Bonte, & Vroomen, 2016; Romanovska, Janssen, & Bonte, 2019). In the classical paradigm, an ambiguous speech sound /a?a/ midway between /aba/ and /ada/ is combined with a disambiguating video of a speaker articulating ‘aba’ or ‘ada’. The perception of the ambiguous speech sound is temporarily biased in the direction of the video – i.e. it will be perceived as /aba/ following an ‘aba’ video and as /ada/ following an ‘ada’ video. This perceptual shift leads to a measurable shift in fMRI activation patterns in early and higher-order auditory cortex (Kilian-Hütten et al., 2011), indicating that the same ambiguous /a?a/ sound is perceived differently depending on the disambiguating video it has been coupled with. This shift indicates that the two modalities have been successfully combined and a new audio-visual association created.

In the research reported in this dissertation, an alternative to the classical recalibration paradigm – text-based recalibration – is employed (Figure 4). Here, text is used as the disambiguating visual information, tapping into the mechanisms underlying letter-speech sound mapping that relies on the interplay between the dorsal and ventral reading systems. An fMRI study exploring text-based recalibration in typically reading adults found that text-induced changes in auditory cortical

General introduction

representations of speech might be mediated by the bilateral IPL (Bonte et al., 2017). Behavioural evidence has further suggested an absence of this text-induced perceptual shift in adult dyslexic readers (Keetels et al., 2018) while lip-read information was found to yield similar shifts in dyslexic and fluent readers (Baart, De Boer-Schellekens, & Vroomen, 2012; Keetels et al., 2018). Eight year-old dyslexic children instead were found to show comparable text-based recalibration to their typically reading peers (Romanovska et al., 2019; Chapter 2), emphasizing the importance of studying the same reading functions across multiple age groups.

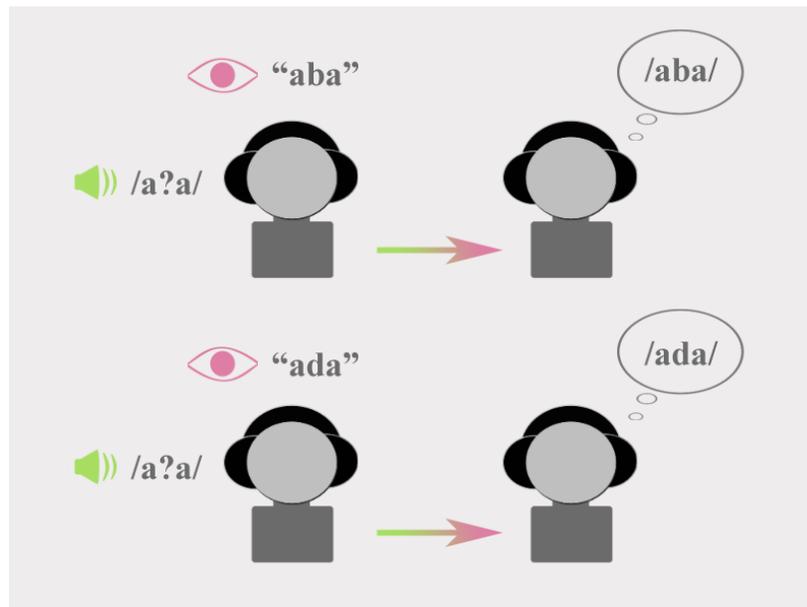


Figure 4: The text-based recalibration paradigm. /a?a/ = ambiguous speech sound mid-way between /aba/ and /ada/.

Developmental research has indicated a relatively late emergence of the recalibration effect, with pre-literate children not showing the effect and the first reliable recalibration effects emerging in 8-year-olds (van Linden & Vroomen, 2008). During the first years of reading instruction, children are still refining the connections and interplay between the dorsal and ventral reading systems (Wise Younger et al., 2017; Yu, Raney, et al., 2018) and are beginning to make a switch from more effortful, dorsal system engagement in reading to increasingly automatized text processing relying on the ventral system. Thus, behaviourally, comparable text-based recalibration effects can be observed in both typical and dyslexic readers while the two groups of children may rely on different brain areas/networks to perform the task (Chapter 3). Once a more fixed and mature connectivity pattern has been established, group differences may emerge as a result of discrepant interactions between the dorsal and ventral systems in dyslexic adults (Finn et al., 2014; Schurz et

al., 2015; van der Mark et al., 2011). Furthermore, in future research, it is particularly important to consider the mediating role protective and risk factors play in shaping these interactions, ideally employing longitudinal designs.

Conclusions

Reading development is a highly dynamic and individually variable process illustrating an impressive capacity of the brain to accommodate the requirements of a culturally acquired skill. These changes are shaped around the formation of solid associations between the dorsal spoken language system and the ventral visual system, which specializes for written language. Over the last decades, research has started to delineate the establishment of functional and anatomical links between the areas of both systems. Relating these findings to reading outcome across the reading spectrum would help elucidate the currently often mixed findings across studies and provide much needed insight into the mechanisms underlying (a)typical reading development. Part of the variability in these studies stems from problems inherent to the prevalent approach of cross-sectional group comparisons, including variability in dyslexia selection criteria (Peters & Ansari, 2019), and group composition in terms of e.g. age, gender, socio-economic background and language environment. It is therefore important for future studies to take into account as many factors contributing to the mixed findings as possible, including the integration of risk and protective factors into research designs in order to disentangle risk factors, compensatory mechanisms and potential consequences of dyslexia.

One essential but challenging way of addressing the heterogeneity in reading research can be found in longitudinal studies. Exploring the individual variability in functional and structural connectivity between the reading systems using paradigms that tap into the mechanisms underlying letter-speech sound mapping could help delineate the dynamic changes taking place during this sensitive learning period. While current research paradigms mainly focus on learning outcomes (e.g. employ well-established letter-speech sound pairs), learning paradigms in particular can provide an important means of exploring developmental trajectories, as they rely on the same mechanisms involved in successful mapping and automatization of letter-speech sound pairs that are used when learning to read.

Outline of the dissertation

Cross-sectional studies employing congruency manipulation paradigms have yielded mixed findings regarding cortical activation associated with letter-speech sound processing in children with and without dyslexia. The aim of the current dissertation was to explore audio-visual processing of letters and speech sounds in 8 – 11 year-old children longitudinally over a three-year period encompassing three annual fMRI measurements, with an experimental paradigm combining text and ambiguous speech stimuli. The longitudinal design of the project allowed us to explore individual developmental changes in cortical activation and improve the reliability of the observed age-related effects, as all findings come from the same sample. We also investigated associations between children's brain activation and their reading and phonological skills. This constitutes an important part of developmental research that helps further our understanding of the relation between brain activation and behavioural outcomes. The ambiguous speech and text stimuli used in the text-based recalibration paradigm engage short term audio-visual learning mechanisms to map letters onto speech sounds. This allowed us to explore letter-speech sound processing in the brain without the confounding effects of over-learned letter-speech sound pairs that may be affected by additional cognitive/motivational factors, as is the case in congruency manipulation paradigms. Chapter 2 describes behavioural text-based recalibration findings in 8 year-old children with and without dyslexia. Somewhat surprisingly, no group differences in task performance were observed, all children showed a significant recalibration effect regardless of dyslexia diagnosis. The recalibration effect was however, associated with the opposite perceptual effect – adaptation – in dyslexic but not typical readers. When these findings were extended to a larger sample of only typically reading children, a positive correlation between the magnitude of the recalibration effect and children's phonological perception was observed. In chapter 3, we investigated brain activation underlying the recalibration task performance in children with and without dyslexia during the first longitudinal fMRI measurement. We specifically focused on the audio-visual exposure blocks when children are presented with text and ambiguous speech sounds to investigate letter and speech sound processing in the brain. The behavioural results were in line with those of chapter 2 insofar as no significant difference in text-based recalibration was observed between groups. However, group differences in cortical activation of a left fusiform region were observed, with dyslexic children showing less activation compared to their typically reading peers. The activation within this region was furthermore associated with reading fluency and phonological

skills across participants. Additional correlations between letter-speech sound identification fluency and bilateral activation of superior temporal gyri regions was found across participants. The longitudinal comparisons of changes in brain activation across three annual fMRI measurement sessions in typically reading children are reported in chapter 4. We observed a significant difference in cortical activation in a left hemisphere superior temporal gyrus region between the first two sessions. A closer investigation of activation within this region across all three measurements revealed an inverted-u-pattern of activation that was driven by age. More specifically, a peak in activation within this area was observed in children aged 9 during the second measurement. Finally, chapter 5 contains the summary and general discussion of the dissertation findings in the broader framework of reading development.

2

Exploring text-based recalibration behaviourally in typically reading and dyslexic children

Based on

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Abstract

One of the proposed mechanisms underlying reading difficulties observed in developmental dyslexia is impaired mapping of visual to auditory speech representations. We investigate these mappings in 20 typically reading and 20 children with dyslexia aged 8-10 years using text-based recalibration. In this paradigm, the pairing of visual text and ambiguous speech sounds shifts (recalibrates) the participant's perception of the ambiguous speech in subsequent auditory-only post-test trials. Recent research in adults demonstrated this text-induced perceptual shift in typical, but not in dyslexic readers. Our current results instead show significant text-induced recalibration in both typically reading children and children with dyslexia. The strength of this effect was significantly linked to the strength of perceptual adaptation effects in children with dyslexia but not typically reading children. Furthermore, additional analyses in a sample of typically reading children of various reading levels revealed a significant link between recalibration and phoneme categorization. Taken together, our study highlights the importance of considering dynamic developmental changes in reading, letter-speech sound coupling and speech perception when investigating group differences between typical and dyslexic readers.

Introduction

Reading is a complex cognitive skill most of us learn within the first decade of life. While there is some variability in how smoothly this learning process goes, most children learn to correctly associate corresponding letters and speech-sounds after 1 year of reading instruction (Blomert, 2011) and continue refining the newly acquired skill over a protracted period throughout primary school (Ben-Shachar et al., 2011; Brem et al., 2009; Froyen et al., 2009; Maurer et al., 2006). However, 5-10% of children show particular difficulties in learning to read and are diagnosed with developmental dyslexia, a learning difficulty characterized by impaired reading fluency and spelling despite adequate intelligence, motivation and schooling (Lyon et al., 2003).

A number of theories have been proposed to describe the underlying mechanisms of developmental dyslexia, ranging from phonological (Lyon et al., 2003; Shaywitz et al., 1998; Snowling, 1980), to audio-visual (Aravena, 2017; Blomert, 2011; Kronschnabel et al., 2014), visual (Bosse et al., 2007; Vidyasagar & Pammer, 2010), auditory (Tallal, 2004; Vandermosten et al., 2010), magnocellular

(Ramus, 2003) and cerebellar (Fawcett & Nicolson, 1999) deficits. However, most theories converge in acknowledging that dyslexic readers typically exhibit difficulties in phonological processing and that the formation of robust letter-speech sound mappings is essential to fluent reading acquisition. Here we explore letter-speech sound mappings in typically reading children and children with dyslexia using a newly developed short-term audio-visual learning paradigm called text-based recalibration.

Support for a deficit in letter-speech sound integration in dyslexic readers largely comes from studies comparing the processing of congruent versus incongruent letter-speech sound stimuli. Indeed, both behavioural (Aravena et al., 2013; Blomert & Willems, 2010; Snowling, 1980) and brain activity studies (Blau et al., 2009, 2010; Froyen et al., 2011; Jones et al., 2016; Moll et al., 2016; Žarić et al., 2014, 2015) have shown that children and adults with dyslexia process letter speech sound pairs differently from typical readers (but see Clayton & Hulme, 2017; Nash et al., 2016). In a series of EEG studies in the relatively transparent Dutch orthography, these differences were observed in audio-visual mismatch negativity (MMN) and late negativity (LN) responses at a 100-200 ms and 600-750 ms latency following an audio-visual deviant stimulus in a sequence of standards (Froyen et al., 2009, 2011; Žarić et al., 2014). The audio-visual MMN and LN responses can be seen as an indirect measure of letter-speech sound integration, for only if the auditory and visual modalities have been properly processed and integrated, they will yield a mismatch response. Studies by Froyen and Žarić and colleagues have revealed that children with dyslexia show a reduced audio-visual MMN and/or LN response compared to typically reading children, pointing to a reduced integration of letters and speech sounds. Furthermore, the latency of these responses has been found to scale with reading fluency and remediation respectively (Žarić et al., 2015, 2014). Concordantly, in functional magnetic resonance imaging (fMRI) studies, superior temporal cortical (STC) activity of children (Blau et al., 2010) and adults (Blau et al., 2009) with dyslexia, as well as pre-readers at familial risk of dyslexia (Karipidis et al., 2017), has been found to show less sensitivity to letter-speech sound (in)congruency compared to typical readers. Taken together these findings indicate deviant letter-speech sound processing and integration processes in dyslexic readers.

However, the manner in which stimulus (in)congruency is processed may be influenced by a number of factors, including individual differences in the level of reading skills (Plewko et al.,

2018), or phoneme perception (Basu Mallick, Magnotti, & Beauchamp, 2015), but also more general factors such as attentional focus (Talsma & Woldorff, 2005), task characteristics (Basu Mallick et al., 2015) or familial risk for dyslexia (Maurer et al., 2003). A complementary approach to investigate letter-speech sound coupling can be found in (phonetic) recalibration paradigms, in which the perceived identity of an ambiguous speech sound is biased in the direction of previously presented disambiguating context information. This context information can consist of lip-read speech (Bertelson et al., 2003; Vroomen & Baart, 2012), lexical (spoken word) context (Norris et al., 2003), overt or imagined speech articulation (Scott, 2016a), or, most relevant for our current study, visual text (Bonte et al., 2017; Keetels et al., 2018). In the classical recalibration paradigm an ambiguous speech sound /a?a/ midway between /aba/ and /ada/ is combined with a disambiguating video of a speaker articulating ‘aba’ or ‘ada’ to bias the perception of the ambiguous sound towards the video. Thus, repeated presentation of a speaker articulating ‘aba’ while playing the /a?a/ sound, shifts participants’ subsequent perception of this ambiguous sound towards /aba/. Similarly, a speaker articulating ‘ada’ shifts later perception towards /ada/. Recalibration thus involves an ‘attracting’ perceptual bias where participants perceive phoneme boundary shifts towards the visual information. The induced bias (recalibration) is typically described as a multi-sensory perceptual effect that has been found to be minimally influenced by higher-level task demands (Baart & Vroomen, 2010). In contrast, an opposite ‘repulsive’ perceptual bias (or auditory selective adaptation) is induced after repeated presentation of the same videos together with clear speech sounds. That is, after exposure to a speaker articulating ‘aba’ together with clear /aba/ speech sounds, the ambiguous /a?a/ sound is more likely to be perceived as /ada/ (and ‘ada’ articulation more often leads to /aba/ perception; Bertelson et al., 2003; Keetels et al., 2016; Vroomen et al., 2004). Phonetic recalibration with lip-read speech has been reliably shown in typically reading adults (Bertelson et al., 2003) and 8-year-old children but not in 5-year-old children, suggesting a developmental build-up of the effect. (van Linden & Vroomen, 2008). A similar but delayed developmental trend has been reported in the adaptation effect, with robust effects observed in adults (Baart & Vroomen, 2010; Bertelson et al., 2003; Vroomen et al., 2004, 2007) but not in 5-10 year-old children (Sussman, 1993; Sussman & Carney, 1989).

To investigate potential differences in letter speech-sound mappings between children with dyslexia and typically reading children, we use a recent modification of the recalibration paradigm which employs visual ‘aba’ or ‘ada’ text to bias the perception of ambiguous /a?a/ speech sounds

(Bonte et al., 2017; Keetels et al., 2018, 2016). Most interestingly, while both videos and text were recently shown to elicit significant recalibration effects in typically reading adults (Keetels et al., 2018), adults with dyslexia only showed significant recalibration with videos, but not with text (Keetels et al., 2018), suggesting a specific deficit in the audio-visual mapping of letters and speech sounds. Here, we use text-based recalibration to investigate letter-speech sound mapping in 8-10 year-old typically reading children and children with dyslexia. While the nature of the study was exploratory, as text-based recalibration has not been previously studied in children, we expected to replicate the findings of Keetels and colleagues (2018) and to observe significant recalibration effects only in typical readers. We also explored potential links between recalibration effects and individual differences in reading proficiency (accuracy and fluency) and in categorical speech perception (phoneme categorization slope). In addition, we employ an adaptation task with clear /aba/ and /ada/ stimuli providing both a baseline with respect to potential response strategies and a test for potential developmental changes in speech adaptation (van Linden & Vroomen, 2008).

Methods

Participants

Twenty children with dyslexia (mean age 8.5 ± 0.82 years; 9 females) were recruited from a specialized institute for dyslexia and reading problems, and fifty-six typically reading children (mean age 8.4 ± 0.94 years; 34 females) from local elementary schools. Parents gave written informed consent for participation in the study. To perform group comparisons and run statistical analyses, a subset of twenty typically reading children were matched for age, gender and scores on a non-verbal subtest (block design) of the Dutch version of the Wechsler Intelligence Scale for Children-III (WISC-III-NL; Kort et al., 2005) to the children with dyslexia, group characteristics and comparisons using one-way ANOVA are shown in Table 1. All children were native Dutch speakers with no reported hearing impairments, normal or corrected to normal vision, and no history of diagnosed neurological disorders. The dyslexia diagnosis was given by the institute based on the results of extensive cognitive psycho-diagnostic testing and results of standardized reading measures. Children received a small present as participation reward. The experiment was approved by the ethics committee of the Faculty of Psychology and Neuroscience, Maastricht University.

Table 1. Descriptive statistics of typical and dyslexic readers

	Dyslexic readers			Typical readers			Dyslexic vs Typical readers	
	N							
Age	20			20				
Gender ratio(m/f)	8.60 (0.94)			8.70 (1.13)			t(1,38)=-0.30, p=0.76	
	11:9			11:9				
	<i>M</i>	<i>SD</i>	Range	<i>M</i>	<i>SD</i>	Range	F(1,39)	p
Word reading – accuracy [%]								
3DM High frequency words	94.69	7.13	73-100	99.79	0.65	97-100	10.16	0.003
3DM Low frequency words	89.48	10.26	63-100	99.07	3.21	85-100	15.90	0.000
3DM Pseudo words	83.88	13.03	50-100	91.82	6.17	81-100	6.07	0.018
3DM Total	90.28	8.35	63-98	97.72	2.11	91-100	14.92	0.000
3DM Total words [T]	38.75	11.32	20-57	55.20	5.87	40-63	33.24	0.000
Word reading – fluency [T]								
3DM High frequency words	33.45	7.97	21-49	58.85	11.48	36-80	66.02	0.000
3DM Low frequency words	33.55	5.70	23-45	57.50	11.26	32-78	71.94	0.000
3DM Pseudo words	35.25	6.07	24-46	55.30	12.36	34-79	42.36	0.000
3DM Total words	33.10	6.15	22-45	57.95	11.96	33-80	68.20	0.000
IQ norm scores								
Verbal (similarities)	11.20	2.26	7-15	13.95	2.89	9-18	11.22	0.002
Non-verbal (block design)	11.15	3.45	5-18	12.50	3.57	7-19	1.47	0.232

Literacy skills

Each participant performed a computerized reading task of the 3DM (Dyslexia Differential Diagnosis; Blomert & Vaessen, 2009). The task comprised three subtasks including reading of high frequency words, low frequency words and pseudo words. Instructions of the reading task were simultaneously presented on the computer screen and aurally through over-ear headphones. The participant was asked to read the (pseudo)words as quickly and accurately as possible. For each subtask the participant had a time limit of 30 seconds to read. Reading accuracy was determined by calculating the proportion of correctly versus incorrectly read words within the given time limit. Reading fluency was calculated as the number of correctly read words within the given time limit for the whole task as well as per subtask.

Experimental design and procedure

Stimuli

The speech stimuli consisted of recordings of a native male Dutch speaker pronouncing the speech sounds /aba/ and /ada/ (see Bertelson et al., 2003 for a detailed description). Both speech sounds lasted 650 ms and were used to create a nine-token continuum (BD1-BD9) ranging from a clear /aba/ sound to a clear /ada/ sound by changing the second formant (F2) in eight steps of 39 Mel using PRAAT software (Boersma & Weenink, 2001). The visual stimuli consisted of the written

counter-parts of the speech sounds, namely ‘aba’ and ‘ada’ text presented in white at the centre of a black screen in ‘Times New Roman’ font (font size 50). The auditory and visual stimuli were presented using Presentation software (Version 17.2, Neurobehavioral Systems, Inc., Berkeley, CA).

All children completed the pre-test, recalibration and adaptation tasks. The children with dyslexia completed these tasks in a quiet room at the specialized dyslexia institute, whereas the typically reading children were tested in a quiet room at their school. All tasks were performed on a laptop computer with the auditory stimuli presented at a comfortable listening level over noise-cancelling headphones (SONY MDR-7509HD).

Pre-test

Prior to the main experimental tasks, all participants completed a pre-test in which all nine tokens of the /aba/ - /ada/ continuum were presented a total of 98 times in a randomized order. The children were instructed to listen to each sound carefully and to indicate which sound they heard by pressing the left (/aba/) or right (/ada/) shift button with the left or right index finger respectively following a response cue (Figure 1). The response cue consisted of ‘aba’ (left) and ‘ada’ (right) text held up by cartoon monsters created using the Monster Workshop content pack of the iClone 6 software (<https://www.reallusion.com/>). No emphasis was put on speed, and it was furthermore emphasized that there were no correct or incorrect responses. While the speech sounds were played, children viewed a black screen with a white fixation cross, which was followed by the response screen (cartoon monsters) after 1 s and terminated when children provided a response. The subsequent speech sound was presented 2 s after a response was given. The total duration of the pre-test was approximately 5 minutes.

The results of the pre-test were used to determine the most ambiguous speech sound for each participant. This was done based on the proportion of /aba/ responses to each token along the /aba/-/ada/ continuum and was identified as the sound with a response proportion of /aba/ versus /ada/ closest to 0.5. This individually determined most ambiguous sound was subsequently used in the audio-visual exposure blocks of the recalibration task as well as in the post-test trials of the

recalibration and adaptation tasks. In the post-trials, next to the most ambiguous sound, we also presented its flanking sounds /a?a/+1 and /a?a/-1 on the /aba/-/ada/ continuum.

The pre-test served two purposes: (1) to determine the most ambiguous sound for each participant, and (2) to allow for the investigation of the phoneme categorization slope in each group. Previous research has indicated that adult readers with dyslexia perceive speech sounds less categorically compared to normal readers (Ahissar, 2007; Baart et al., 2012). Thus, the results of the pre-test allow us to investigate whether these findings extend to our sample of children with dyslexia and typically reading children.

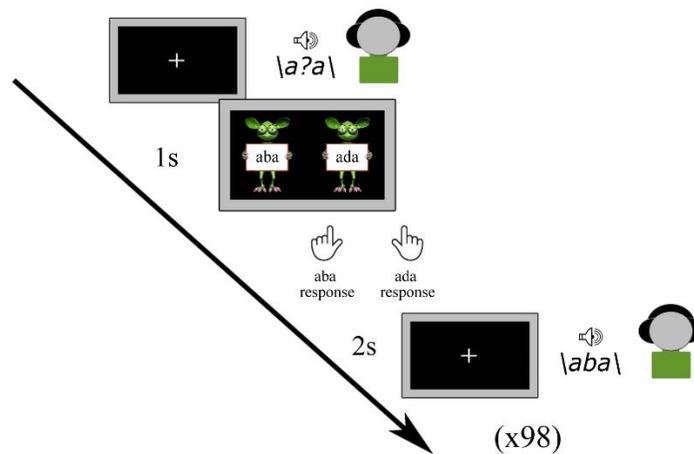


Figure 1: Pre-test

Recalibration task

The text-based recalibration paradigm is composed of audio-visual exposure blocks and subsequent auditory-only post-test trials (Figure 2). During each audio-visual exposure block, the children were presented with 8 repetitions of either the text ‘aba’ or ‘ada’, paired with the individually-determined ambiguous speech sound /a?a/. The speech sound and visual text were presented simultaneously (relative SOA of 0 ms) and auditory stimuli had a duration of 650 ms, while text was presented for 1 s. The inter-trial interval between subsequent audio-visual exposure trials was set to 2 s. During the audio-visual exposure blocks, children were instructed to pay close attention to the speech sounds and text without providing a response.

Each exposure block was followed by four auditory-only post-test trials. The four post-test sounds were presented in a randomized order with the individually-determined most ambiguous $/a?a/$ sound presented twice and each of its flanking sounds $/a?a+1/$ and $/a?a-1/$ on the $/aba/-/ada/$ continuum, presented once. Each post-test sound was followed by a response cue consisting of ‘aba’ and ‘ada’ texts held by cartoon monsters (Figure 2).

Children were instructed to listen to each sound carefully and to make forced-choice $/aba/-/ada/$ judgments by pressing the left/right shift button with the left/right index finger respectively once the cartoon monsters appeared. Identical to the pre-test, no emphasis was put on speed and it was further emphasized that there were no incorrect responses. All responses were self-paced. The onset of the response picture was jittered 1-2 s in relation to the post-test sound and was terminated upon the button-press. Post-test trials were presented with an inter-trial interval of 2 s after the participant had provided a response. The recalibration task was divided into 2 6-minute runs, both consisting of 10 ‘aba’ and 10 ‘ada’ exposure blocks, each followed by 4 post-test trials amounting to 40 post-test trials for each type of exposure block.

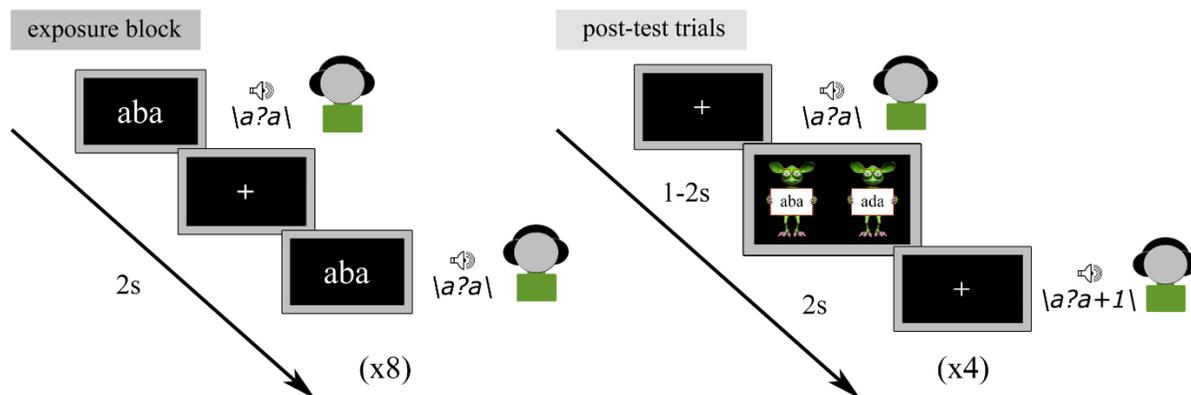


Figure 2: Text-based recalibration paradigm

Adaptation task

The adaptation task was identical to the recalibration task in all aspects except for the speech sounds used in the exposure blocks. Here, the clear /aba/ and /ada/ sounds were combined with the corresponding 'aba' and 'ada' text, creating congruent audio-visual stimuli in the exposure blocks. The task instructions and stimulus timings were all identical to those of the recalibration task. The adaptation task allowed us to explore auditory adaptation and served as a control for potential response strategies that children may employ.

All children performed the pre-test followed by 2 runs of the recalibration task and 2 runs of the adaptation task. The task order was kept constant across all participants. The reason for this fixed order instead of counterbalancing was threefold: (1) because we were interested in audio-visual learning, the recalibration blocks were of primary interest, with the adaptation blocks serving as a control, (2) this behavioural experiment served as a preparation of a longitudinal fMRI project where we only included text-based recalibration, and (3) initial pilot results suggested interference from adaptation blocks to subsequent recalibration blocks but not vice versa. This finding is in line with the observation of short-lived audio-visual recalibration effects compared to longer lasting adaptation effects (Vroomen & Baart, 2012).

Statistical analysis

The data were assessed for statistical significance using repeated measures ANOVA (SPSS version 24.0, IBM Corp., Armonk, NY, USA). The ANOVA model included the type of task (recalibration vs adaptation), type of exposure ('aba' text vs 'ada' text), post-test sounds (/a?a/, /a?a/ +1, /a?a/-1) as within subjects factors and group (dyslexic vs typically reading) as between subjects factor. The differences in average /aba/ versus /ada/ response proportions (aftereffects) following the two types of exposure blocks were further assessed using paired-samples t-tests. For the conditions in which the sphericity assumption was violated, the degrees of freedom were adjusted using the Greenhouse-Geisser correction.

The fit of the pre-test slopes was estimated using the Slope Fitting Tool in MATLAB 2016a (The MathWorks, Inc., Natick, Massachusetts, United States). Based on previous literature, a custom

logistic function (Function 1) was used to obtain partial R^2 values and evaluate the goodness of fit of individual as well as group-level categorization slopes (Ley et al., 2012; McMurray & Spivey, 2000). Subsequently, the non-linear least squares solver in MATLAB was employed to obtain the slope value (c in Function 1) that provided the best fit to the data and yielded the smallest sum of squares. To optimize the outcome, the results of the fitting procedure were restricted for each of the variables in Function 1 to $0 \leq a \leq 10$, $-10 \leq b \leq 10$, $-10 \leq c \leq 10$, $-9 \leq d \leq 18$. The best fit was determined by running 30 iterations of the slope fitting procedure and taking the slope value with the smallest sum of squares. The number of iterations was verified by replicating the procedure multiple times.

$$y = \frac{a}{1 + e^{-\frac{(x-d)}{c}}} + b$$

Function 1: a =amplitude of the function; b =lowest asymptote of y -axis; c =slope of the function; d =location of the category boundary.

To investigate a potential link between recalibration/adaptation aftereffects, pre-test slope and behavioural reading measures, linear regression analyses were performed in R 3.4.1 (R Core Team, 2013). In addition, all statistical analyses were also performed on the complete sample of controls to assess the reliability of our findings within a larger sample of typical readers of various reading levels.

Results

Pre-test

The results of the pre-test were used to investigate the categorical perception of the nine auditory tokens employed in this study. The left panel of Figure 3 shows the proportion of /aba/ responses per sound stimulus in children with dyslexia (dashed line) and the matched typically reading control children (solid line). These figures indicate similar categorical perception of speech sounds in the groups of typically reading children and children with dyslexia. This observation was confirmed by a 9 auditory token \times 2 (Group) repeated measures ANOVA. The ANOVA revealed an expected main effect of sound ($F(2,100)=135.03$, $p<0.001$, Greenhouse-Geisser corrected), indicating that the participants were more likely to perceive the auditory tokens closer to the /aba/ end of the continuum (BD1-BD3) as /aba/ and the tokens closer to the /ada/ end (BD7-BD9) as

/ada/. Furthermore, no difference in the overall proportion of /aba/ responses was observed between the children with dyslexia ($M=0.51, SD=0.06$) and typically reading children ($M=0.54, SD=0.11$); ($t(38)=-0.92, p=0.36$), indicating that the slope was equivalent in both groups. The right panel of Figure 3 shows the same slopes for children with dyslexia and all of the control participants tested ($n=56$), once again showing similar categorical perception in typically reading children and children with dyslexia. The goodness of fit estimation of the slopes reflected in partial R^2 values was 0.99 in the dyslexic, matched as well as the entire control group.

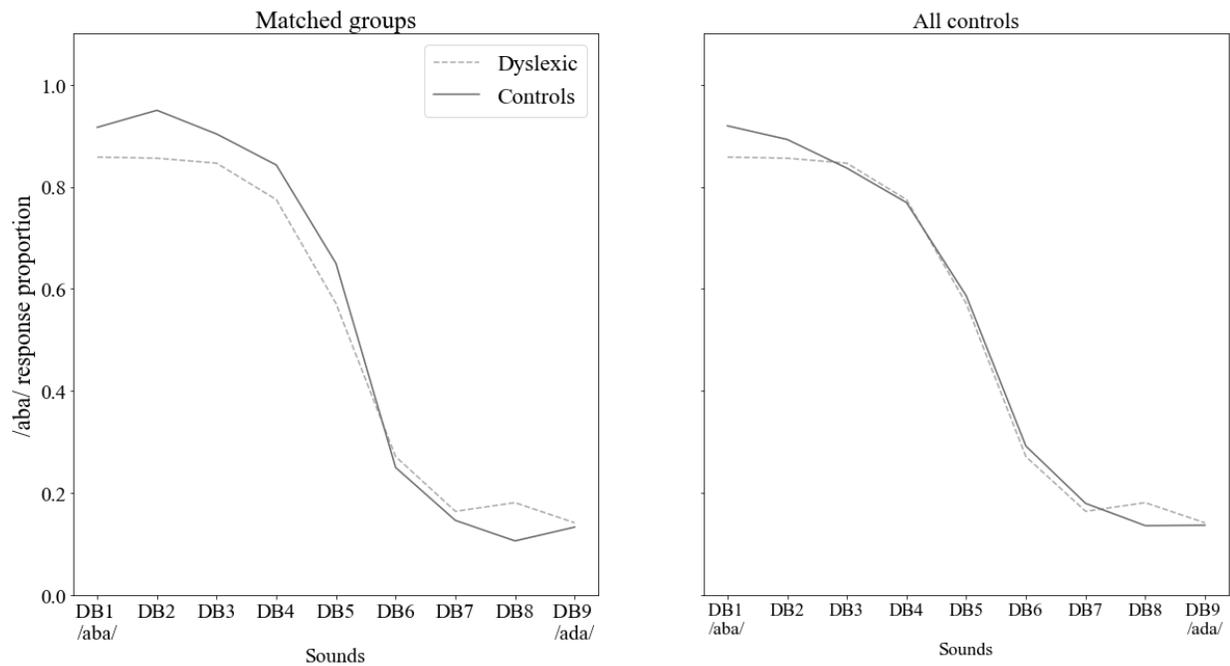


Figure 3: Pre-test results plotted as proportion of /aba/ responses for each token along the continuum. Solid lines = typical readers, dashed lines = dyslexic readers, bars = standard errors; left matched groups; right 20 dyslexic readers and 56 typical readers

Recalibration and adaptation tasks

Matched groups

During the recalibration task, participants' perception of the three post-test sounds – the most ambiguous sound ($a?a$) and its two closest neighbours ($a?a+1$ and $a?a-1$) – was influenced by the preceding exposure blocks, as seen when analysing the proportion of /aba/ versus /ada/ responses during the post-test trials. Intriguingly, both the children with dyslexia and the typically reading children showed a recalibration effect (Figure 4 top panel middle and right columns respectively).

Thus, both groups were more likely to perceive the ambiguous post-test sounds as /aba/ following ‘aba’ exposure blocks (dark grey line Figure 4 top panel). Similarly, ‘ada’ text shifted later perception towards /ada/ (light grey line Figure 4 top panel). This effect was particularly pronounced for the most ambiguous /a?a/ sound (proportion of /aba/ responses children with dyslexia 0.54 vs. 0.31, typical readers 0.57 vs. 0.31, respectively). Across both groups, the participants only seemed to show a small adaptation effect for the most ambiguous post-test sound, namely the exposure to the clear /aba/ sound in combination with ‘aba’ text shifted the perception of the post-test trials to /ada/ (light grey line Figure 4 left bottom panel). Correspondingly, being exposed to clear /ada/ in combination with ‘ada’ text led to a small shift in the perception of subsequent post-test trials towards /aba/ (dark grey line Figure 4 left bottom panel).

A 2 (Task) \times 2 (Exposure) \times 3 (post-test sounds) \times 2 (group) repeated measures ANOVA showed a significant task \times exposure \times post-test sounds interaction ($F(2,76)=3.52, p<0.05$) confirming that the participants responded differently to the post-test sounds following the two types of exposure blocks in recalibration and adaptation tasks. This was further confirmed by the significant main effects of task ($F(1,38)=31.27, p<0.001$), exposure (‘aba’ versus ‘ada’; $F(1,38)=8.65, p=0.006$), and post-test sounds ($F(1,48)=117.05, p<0.001$, Greenhouse-Geisser corrected), as well as significant task \times exposure ($F(1,38)=45.32, p<0.001$), task \times post-test sounds ($F(1,61)=3.38, p<0.05$, Greenhouse-Geisser corrected) and exposure \times post-test sounds ($F(2,76)=7.39, p<0.005$) interactions. No main effect of group was observed ($F(1,38)=1.06, p=0.31$), and none of the interactions with group were significant (all $F \leq 2.1$), corroborating the absence of significant differences in recalibration and adaptation results in children with dyslexia and typically reading children.

The results of the Recalibration task were further tested in a 2 (Exposure) \times 3 (post-test sounds) \times 2 (Group) repeated measures ANOVA. A main effect of exposure ($F(1,38)=51.43, p<0.001$), post-test sounds ($F(1,49)=84.02, p<0.001$, Greenhouse-Geisser corrected), as well as a significant exposure \times post-test sounds interaction ($F(2,76)=8.37, p=0.001$) again highlighted that the participants responded differently to the post-test sounds depending on the type of exposure block preceding them. Results yielded no main ($F(1,38)=0.054, p=0.81$) or interaction (all $F \leq 0.9$) effects for group.

Behavioural text-based recalibration results in children

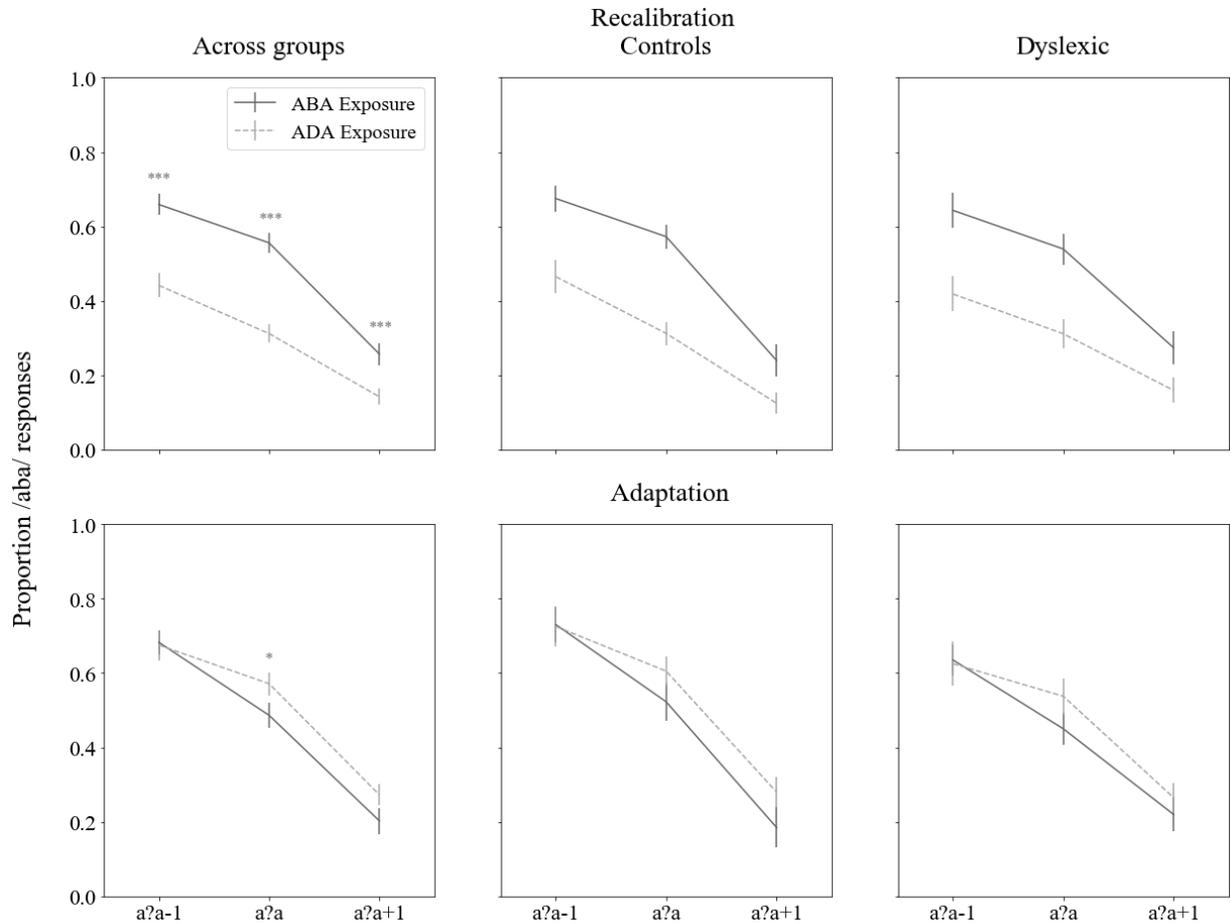


Figure 4: Results of the recalibration top and adaptation bottom tasks across groups (left), in typically reading children (middle) and in dyslexic readers (right). Vertical bars = standard error; *** $p \leq 0.001$, * $p \leq 0.05$

A 2 (Exposure) \times 3 (post-test sounds) \times 2 (Group) repeated measures ANOVA was also run on the results of the adaptation task confirming the absence of an overall adaptation effect across sounds in both groups ($F(1,38)=2.35, p=0.13$). The results revealed a main-effect of post-test sounds ($F(1,52)=80.73, p<0.001$, Greenhouse-Geisser corrected) and a non-significant trend towards an exposure \times post-test sounds interaction ($F(2,76)=2.90, p<0.06$). No other main effects or interactions were significant (all $F \leq 1.2$).

Post-hoc paired-samples t-tests were run on the proportion of /aba/ responses for each of the three post-test sounds following both exposure blocks ('aba' versus 'ada') in both tasks across groups. In the recalibration task, the analyses yielded significant differences in the proportion of /aba/ responses following an 'aba' exposure block compared to an 'ada' exposure block across all post-test sounds (/a?a/: $M=0.55, SD=0.16$ vs $M=0.31, SD=0.15$, $t(39)=6.99, p<0.001$; /a?a+1:

$M=0.26, SD=0.19$ vs $M=0.14, SD=0.14$, $t(39)=3.98, p<0.001$; and /a?a/-1: $M=0.66, SD=0.18$ vs $M=0.44, SD=0.20$, $t(39)=6.43, p<0.001$). In the adaptation task, only the proportion of /aba/ responses to the most ambiguous sound (/a?a/) was significantly different following ‘aba’ versus ‘ada’ exposure blocks ($M=0.48, SD=0.21$ vs $M=0.57, SD=0.19$, $t(39)=-2.06, p<0.05$).

To test for potential response-strategies, a paired samples t-test was run on the proportion of /aba/ responses across all three post-test sounds in the recalibration task compared to the adaptation task (van Linden & Vroomen, 2008). The results revealed a significant difference in the proportion of /aba/ responses in the recalibration task ($M=0.57, SD=0.50$) compared to the adaptation task ($M=0.14, SD=0.62; t(1,39)=6.81, p<0.001$), indicating that the children did not employ a clear response strategy thus confirming the reliability of the observed recalibration effect.

Entire control group

The same analyses were also performed on the data of the entire control group and yielded similar recalibration results. Five of the 56 participants did not complete the adaptation task, thus the statistical analyses including the task condition are based on 51 participants. A 2 (Task) \times 2 (Exposure) \times 3 (post-test sounds) repeated measures ANOVA revealed a significant main effect of task ($F(1,50)=99.53, p<0.001$), exposure (‘aba’ versus ‘ada’; $F(1,50)=15.93, p<0.001$), and post-test sounds ($F(1,69)=155.55, p<0.001$, Greenhouse-Geisser corrected), as well as significant task \times exposure ($F(1,50)=22.70, p<0.001$) and task \times post-test sounds ($F(1,67)=.82, p<0.05$, Greenhouse-Geisser corrected) interactions. The results are summarized in Figure 5, which illustrates that the participants showed a recalibration effect (dark grey line above the light grey line) but did not show an adaptation effect (no separation between the lines). A 2 (Exposure) \times 3 (post-test sounds) repeated measures ANOVA was run for each task and revealed a significant main effect of exposure ($F(1,50)=41.09, p<0.001$), post-test sounds ($F(1,70)=128.02, p<0.001$, Greenhouse-Geisser corrected), and a significant exposure \times post-test sounds interaction ($F(2,100)=4.45, p<0.05$) in the recalibration task as well as a main effect of post-test sounds ($F(1,68)=97.39, p<0.001$, Greenhouse-Geisser corrected) in the adaptation task, highlighting the presence of a recalibration effect and the absence of an adaptation effect.

Post-hoc paired samples t-tests on the proportion of /aba/ responses for each of the post-test sounds per exposure block ('aba' versus 'ada') revealed significant differences in the proportion of /aba/ responses for each of the sounds following 'aba' compared to 'ada' recalibration exposure blocks (/a?a/: M=0.52,SD=0.15 vs M=0.33,SD=0.16, $t(50)=5.80, p<0.001$; /a?a-1/: M=0.62, SD=0.17 vs M=0.46, SD=0.19, $t(50)= 5.30, p<0.001$; /a?a+1/: M=0.24,SD=0.17 vs M=0.14,SD=0.13, $t(50)=4.34, p<0.001$). None of the paired samples t-tests for the adaptation task yielded a significant result.

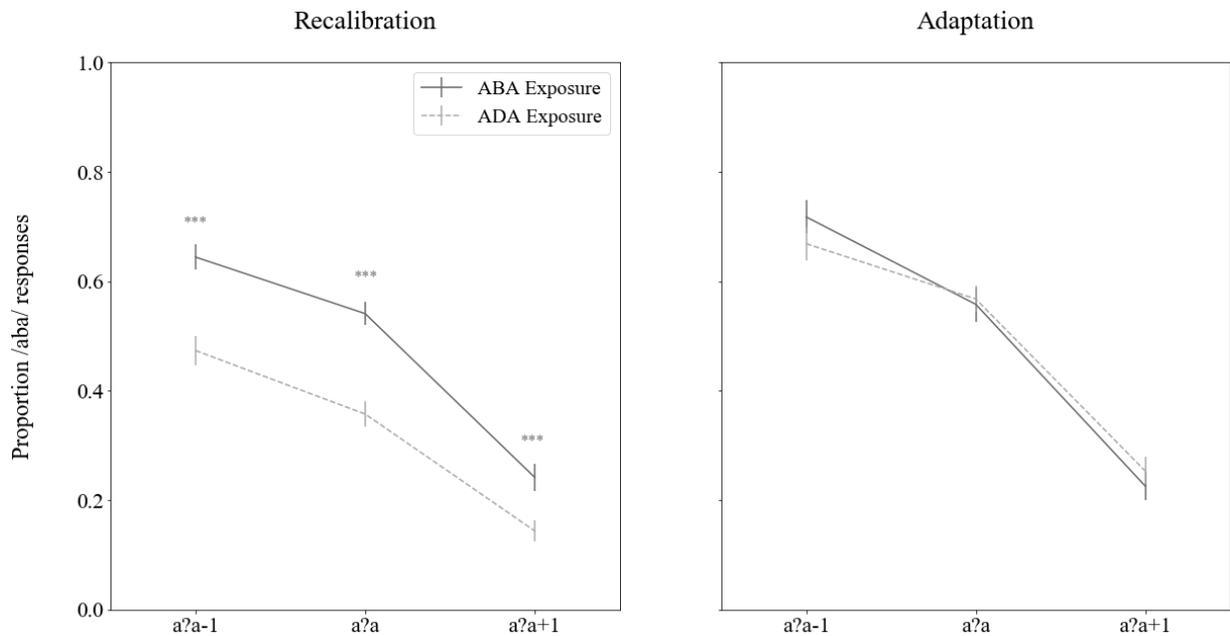


Figure 5: Results of the recalibration left and adaptation right tasks in the entire control group (N=51). Vertical bars = standard error; *** $p\leq 0.001$

Relation with standardized reading measures

Given the absence of overall group differences in recalibration, an important aspect to consider is whether the presence of this effect is related to individual differences in reading fluency, the magnitude of adaptation and/or the phoneme categorization slope. Accordingly, two separate linear regression analyses were performed in the matched groups, one to investigate potential links between the magnitude of the recalibration and adaptation effects (quantified as the proportion of /aba/ vs /ada/ responses), the individual phoneme categorization slopes and standardized reading measures. The second analysis investigated the relation between the individual phoneme categorization slopes and the magnitude of the recalibration and adaptation effects and reading

measures. Prior to running the regression analyses, the data were assessed for outliers using boxplots. In the matched groups, the analyses identified two outliers in categorization slope values, one child with dyslexia (lower quartile plus 3 times inter-quartile range) and one typically reading participant (lower quartile plus 1.5 times inter-quartile range). Similarly, 7 participants were identified as outliers in the entire control group according to the same criteria and were excluded from the subsequent regression analyses. All linear regression models initially included main effects for: group (dyslexia yes/no), recalibration and adaptation aftereffects, reading fluency and accuracy scores, and pre-test phoneme categorization slope values, as well as interactions between the main effects and dyslexia. Where applicable, these models were refined by removing interaction terms with a p-value exceeding 0.7 thus improving model fit. The reading measures were centered with respect to the overall average to facilitate interpretation.

Table 2. Results of the recalibration effect and pre-test slope regression analyses on the matched groups

<i>Predictor</i>	<i>Beta estimate</i>	<i>SE</i>	<i>t-value</i>	<i>p</i>
<i>Recalibration effect</i>				
Intercept	0.76	1.07	0.71	0.4827
Dyslexic	0.13	1.22	0.10	0.9189
Adaptation aftereffect	-0.10	0.20	-0.49	0.6264
Total Reading Fluency [T]	0.01	0.01	1.18	0.2490
Total Reading Accuracy [T]	-0.03	0.03	-1.00	0.3255
Slope	-1.25	0.69	-1.82	0.0801
Dyslexic*Adaptation aftereffect	0.66	0.27	2.43	0.0216*
Dyslexic*Total Reading Fluency	-0.04	0.02	-1.57	0.1287
Dyslexic*Total Reading Accuracy	0.04	0.03	1.33	0.1937
Dyslexic*Slope	0.80	0.83	0.97	0.3424
<i>Pre-test slope</i>				
Intercept	0.15	0.27	0.56	0.5811
Dyslexic	0.22	0.55	0.41	0.6868
Adaptation aftereffect	0.12	0.09	1.32	0.1984
Recalibration aftereffect	-0.15	0.08	-1.82	0.0792
Total Reading Fluency [T]	-0.02	0.01	-1.65	0.1093
Total Reading Accuracy [T]	0.00	0.01	0.70	0.4871
Dyslexic*Adaptation aftereffect	-0.18	0.13	-1.40	0.1724
Dyslexic*Total Reading Fluency	0.02	0.01	1.54	0.1338
Dyslexic*Total Reading Accuracy	-0.02	0.01	-1.34	0.1918

* $p \leq 0.05$

The results of the linear regression analyses of the magnitude of the recalibration effect showed a significant interaction between dyslexia and the adaptation effect (Table 2 ‘Recalibration effect’). Simple slope analyses of the interaction effect revealed a significant positive association between the strength of the recalibration and adaptation effects in children with dyslexia but not typically reading children (Figure 6). Moreover, a trend was observed in the main effect of pre-test slope on

recalibration across groups. Regression analyses of the phoneme categorization slope values did not reveal significant main or interaction effects in the matched groups. However, the main effect of recalibration did approach significance, suggesting a link between pre-test slope and the strength of the recalibration effect (Table 2 ‘Pre-test slope’). Slope values were not found to significantly differ between children with dyslexia (n=19) and typically reading children (n=19; $t(36)=-0.54$, $p=0.59$, equal variances assumed).

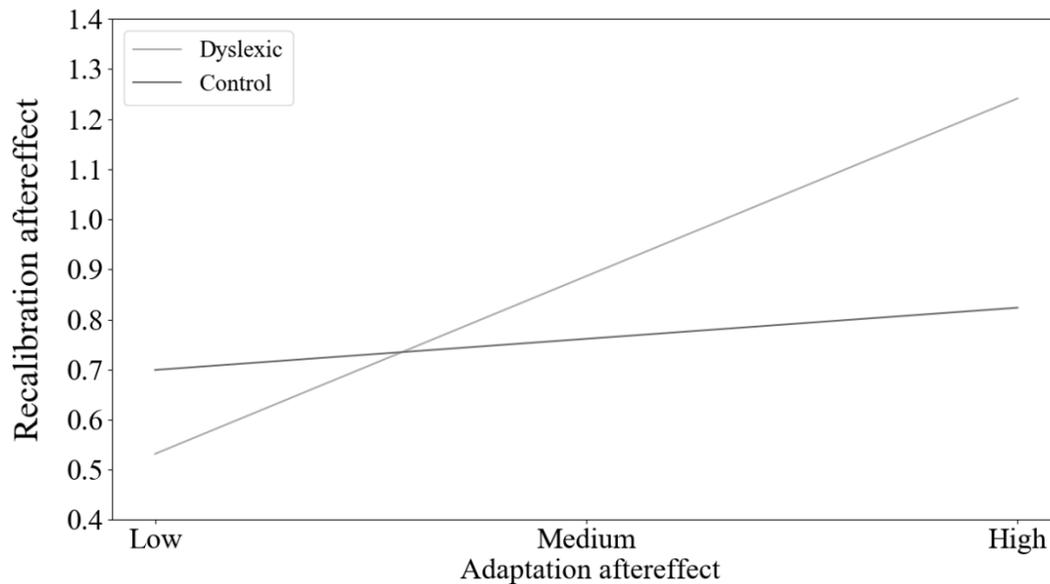


Figure 6: Simple slope analyses of the association between recalibration and adaptation. The average magnitude of the recalibration effect is plotted with respect to the relative magnitude of the adaptation aftereffect for low, average and high levels of adaptation within each group

The regression analyses of the strength of the recalibration effect and phoneme categorization were also performed in the whole control group (N=51), revealing a significant link between the strength of the recalibration effect and categorical perception of phonemes (Table 3 ‘Recalibration effect’ and ‘Pre-test slope’). Moreover, a significant association between reading accuracy and steepness of the pre-test slope was observed, with reading fluency scores also approaching significance (Table 3 ‘Pre-test slope’). These findings complement and extend those of the matched groups highlighting the influence of phoneme perception on recalibration, with the additional finding of a significant link between phoneme categorization and reading accuracy in the control group.

Table 3. Results of the recalibration effect and pre-test slope regression analyses on the entire control group

<i>Predictor</i>	Beta estimate	SE	t-value	p
<i>Recalibration effect</i>				
<i>Intercept</i>	0.65	0.52	1.26	0.2138
<i>Adaptation aftereffect</i>	-0.05	0.14	-0.37	0.7147
<i>Total Reading Fluency [T]</i>	0.01	0.01	1.16	0.2527
<i>Total Reading Accuracy [T]</i>	-0.02	0.01	-1.48	0.1468
<i>Slope</i>	-0.82	0.26	-3.13	0.0033**
<i>Pre-test slope</i>				
<i>Intercept</i>	0.04	0.29	0.12	0.9017
<i>Adaptation aftereffect</i>	-0.11	0.07	-1.51	0.1388
<i>Recalibration aftereffect</i>	-0.24	0.08	-3.13	0.0033**
<i>Total Reading Fluency [T]</i>	0.01	0.00	1.81	0.0782
<i>Total Reading Accuracy [T]</i>	-0.01	0.01	-2.10	0.0425*

** $p \leq 0.005$, * $p \leq 0.05$

Discussion

In the present study, we investigated reading-induced audio-visual plasticity in 8-10 year old children with dyslexia and typically reading children by using written text to recalibrate children's perception of ambiguous speech sounds. Contrary to reported findings in adults, our results revealed that both groups of children reliably show a recalibration effect. The magnitude of the effect was significantly related to the magnitude of the adaptation effect in children with dyslexia but not typically reading children. Phoneme categorization slopes in turn revealed comparable categorization of /aba/ and /ada/ sounds in both children groups. Furthermore, extending the analyses to a sample of typically reading children of various reading levels revealed an association between phoneme categorization slope and reading accuracy. These findings emphasize the importance of studying different age groups to investigate a potential developmental trend in short-term text-induced audio-visual learning, and to uncover possible differences in mechanisms responsible for letter-speech sound coupling, phoneme perception and reading fluency in dyslexic and typical readers.

Replicating our recent findings in typically reading adults (Bonte et al., 2017; Keetels et al., 2018), our current findings show that text stimuli can successfully be used to bias the perception of ambiguous speech in 8-10 year-old children. Recalibration is proposed to rely on short-term perceptual learning mechanisms that help resolve the discrepancy between context information (e.g. lip-read speech, text) and ambiguous sound (Samuel & Kraljic, 2009; Vroomen & Baart, 2011). Unlike lip-read speech which is rooted in biology (Kuhl & Meltzoff, 1982), letter-speech

sound associations are by nature arbitrary and are learnt through explicit instruction (Fraga González, 2017; Keetels et al., 2016). Our results suggest that already during the first years of reading acquisition, at least at the behavioural level, these learned associations lead to significant perceptual shifts similar to those induced by lip-read information (van Linden & Vroomen, 2008). That is to say, simple ‘aba’ and ‘ada’ syllables lead to perceptual recalibration in 8-10 year old children in the relatively transparent Dutch orthography that is characterized by fairly consistent letter-speech sound mappings and a rather small grain size. In future studies it would be interesting to test whether similar syllables also yield significant text-based recalibration in less transparent orthographies and/or orthographies with larger grain sizes (see e.g. Brennan, Cao, Pedroarena-Leal, Mcnorgan, & Booth, 2012; Lallier & Carreiras, 2017; Paulesu et al., 2000).

The observation of significant recalibration in children with dyslexia is in line with a previous study indicating comparable context sensitivity during speech perception in 7-9 year old children with dyslexia and typically reading children at auditory, phonetic and phonological levels (Blomert et al., 2004). But how can this observation be reconciled with the absence of a significant effect in adults with dyslexia (Keetels et al., 2018)? One possible explanation for the discrepancy between findings in children and adults is that 8-10 year-old children presumably have a wider integration window for letter-speech sound coupling. EEG research investigating letter-speech sound integration in children within our age range indicates timing differences in the MMN window in response to letter-speech sound pairs. Namely, unlike in adults, in children the audio-visual MMN effect is not restricted to simultaneous presentation of letters and speech sounds (Froyen et al., 2008), but is also seen when letters are presented 200 ms prior to the speech sounds. Furthermore, the MMN response peaks at a later time point, a pattern that gradually shifts to earlier and shorter integration windows with increased reading experience (Froyen et al., 2009; Žarić et al., 2014). These changes have been proposed to reflect the automatization of letter-speech sound coupling (Froyen et al., 2008, 2009). A similar pattern, albeit with a reduced sensitivity to letter-speech sound congruency and delayed with respect to their age-matched peers, is also observed in children with dyslexia (Froyen et al., 2011; Žarić et al., 2014, 2015). A wider temporal integration window might be beneficial when resolving the conflict between the ambiguous sound and disambiguating text, and may reflect how text to speech sound audio-visual learning mechanisms are still developing during the first few years of reading instruction. Furthermore, developmental changes in the sensitivity to text may follow an ‘inverted U’ trajectory, where text is a more salient stimulus

in the first few years of reading instruction and the salience decreases with increased reading expertise (Fraga González, 2015; Maurer et al., 2008; Price & Devlin, 2011; Žarić et al., 2014). Because the children in our study fall within the age range of ‘peak’ text sensitivity, further observations of the same children in a longitudinal comparison may reveal interesting developmental trends in the text-based recalibration effect.

Another possibility that could explain the difference in results between the adults and children with dyslexia is that there might be larger inter-individual differences in adults. Thus, the adult dyslexic readers who do not show a text-based recalibration effect may suffer from a more severe form of dyslexia and/or may have switched to relying on different reading strategies circumventing one-to-one mappings of letters and speech sounds. Instead, reading is a daily occurrence for school-age children, with a presumably predominant reliance on letter-sound decoding skills especially for children with dyslexia included in our study who were at the initial phase of a dyslexia intervention with a focus on these skills.

Our results also contrast with previous findings reporting reduced sensitivity to letter-speech sound (in)congruency in children and adults with dyslexia (Blau et al., 2009, 2010, Froyen et al., 2009, 2011; Karipidis et al., 2017; Žarić et al., 2014, 2015). A possible reason for the observed differences in results may lie in the paradigms employed. While the aforementioned studies have used congruency manipulations and oddball paradigms to explore group differences between typical and dyslexic readers, we have used a more implicit measure. Recalibration typically involves the disambiguation of ambiguous speech signals based on short-term perceptual (audio-visual) learning. It is possible that, at a purely behavioural level, the task is not sensitive enough to capture subtle group differences between children with dyslexia and typically reading children. Indeed, previous studies on audio-visual integration have revealed underlying differences in brain mechanisms using neuroimaging methods despite a lack of significant differences in behavioural measures (see Nash et al., 2016; Plewko et al., 2018). In future studies it would be important to further understand the specific role of task and stimulus characteristics, as well as risk factors such as family history of dyslexia (Plewko et al., 2018; Raschle et al., 2012) in yielding these audio-visual integration deficits. Moreover a next essential step would be to combine our text-based recalibration paradigm with measurements of brain activity (e.g. Bonte et al., 2017) and investigate

whether different or comparable neural mechanisms underlie the perceptual shifts in children with dyslexia and typically reading children.

Linear regression analyses of the magnitude of the recalibration effect revealed a significant association between recalibration and adaptation in the dyslexic but not typical readers. That is, in dyslexic readers, stronger recalibration was associated with stronger adaptation effects. Furthermore, in the matched groups, the recalibration effect showed a tendency towards an association with pre-test slope across participants. This link reached statistical significance when the analyses were extended to the entire control group, suggesting a close link between the categorical perception of phonemes and short-term text-induced audio-visual learning, with sharper phoneme categorization linked to stronger recalibration effects. The findings of the matched groups were thus extended and complemented by those of the entire sample of controls. We would therefore speculate that the abovementioned pattern of results would also replicate in a larger sample of both children with dyslexia and typically reading children.

Our study did not find support for proposed differences in categorical perception of speech sounds between children with dyslexia and typically reading children. This finding is in line with previous research reporting a similar lack of group differences (Blomert & Mitterer, 2004; Snellings, van der Leij, Blok, & de Jong, 2010) or differences only in small sub-groups of dyslexic readers (Joanisse, Manis, Keating, & Seidenberg, 2000; Manis et al., 1997), but not with others that do report reduced categorical perception of phonemes in dyslexic readers (Baart et al., 2012; Boets et al., 2011). While no significant association between phoneme categorization and reading measures was observed in the matched groups, the association between phoneme categorization and recalibration did approach significance. This relationship was confirmed by the results within the whole control group, revealing a significant link between the magnitude of the recalibration effect and the individual phoneme categorization slopes. Additionally, a significant link between reading accuracy and phoneme categorization also emerged in the entire control group, corroborating previous findings indicating that speech perception and reading are mediated by children's phonological skills (Mcbride-chang, 1996) and that speech perception and phonological awareness measures are significant predictors of first grade reading accuracy in pre-schoolers (Boets et al., 2008). These findings warrant further investigation in a larger sample of dyslexic and typical readers.

Our data also revealed a small adaptation effect, with the /aba/ response proportions to the most ambiguous sound in the adaptation task reaching statistical significance across the dyslexic and typical readers. The main purpose of this task was to investigate potential response strategies and ensure the reliability of the observed recalibration effect (van Linden & Vroomen, 2008). The finding that children showed a shift in the perceptual boundary of the ambiguous post-test sounds in the direction of text in the recalibration but not adaptation task reaffirms the robustness of the recalibration effect across groups. Thus, if children had simply responded in line with the text seen during the exposure blocks for both tasks, there would be no significant difference in the proportion of /aba/ responses between recalibration and adaptation. The finding that the adaptation effect itself was only significant when both groups of children were pooled together and only for the most ambiguous sound likely reflects the previously observed developmental trend in adaptation (Sussman, 1993; Sussman & Carney, 1989; van Linden & Vroomen, 2008). Another potential explanation for the lack of adaptation effects in our study may be found in the proposed more fragile nature of the effect. While recalibration effects can already be observed after single exposure (Keetels et al., 2016), adaptation effects have been shown to develop after a longer time period, require more exposure trials to emerge, and be longer-lasting compared to recalibration effects (Vroomen et al., 2004, 2007).

Conclusion

The present study investigated text-induced changes in perception of ambiguous speech sounds in children employing text-based recalibration. Our results indicate that both 8-10 year-old dyslexic and typical readers show significant text-induced shifts in their perception of ambiguous speech. This finding is likely rooted in the flexibility of the cortical systems for letter-speech sound integration which have not yet been ‘set in stone’ at this age and are thus more flexible in terms of phonemic category perception. Furthermore, the magnitude of the recalibration effect was linked to the adaptation effect in children with dyslexia but not in typical readers. Extending these analyses to a larger sample of only typical readers revealed additional associations between recalibration and phoneme categorization as well as phoneme categorization and reading measures. Our findings highlight the importance of considering task demands and dynamic developmental changes in reading, speech perception and audio-visual learning when investigating group differences between typical and dyslexic readers. Future longitudinal research following the

same children at different stages using both behavioural and brain activity measures is thus essential to understand the neurocognitive mechanisms explaining individual differences in acquired reading levels and dyslexia.

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Author Contributions

M.B. and L.R. designed the experiment, L.R. and R.J. collected and analysed the data. M.B., L.R. and R.J. wrote the paper.

Conflict of interests

The authors declare no conflict of interests.

3

Neuroimaging findings of text-based recalibration in typically reading and dyslexic children

Based on

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Abstract

One of the proposed issues underlying reading difficulties in dyslexia is insufficiently automatized letter-speech sound associations. In the current fMRI experiment, we employ text-based recalibration to investigate letter-speech sound mappings in 8-10 year-old children with and without dyslexia. Here an ambiguous speech sound /a?a/ midway between /aba/ and /ada/ is combined with disambiguating “aba” or “ada” text causing a perceptual shift of the ambiguous /a?a/ sound towards the text (recalibration). This perceptual shift has been found to be reduced in adults but not in children with dyslexia compared to typical readers. Our fMRI results show significantly reduced activation in the left fusiform in dyslexic compared to typical readers, despite comparable behavioural performance. Furthermore, enhanced audio-visual activation within this region was linked to better reading and phonological skills. In contrast, higher activation in bilateral superior temporal cortex was associated with lower letter-speech sound identification fluency. These findings reflect individual differences during the early stages of reading development with reduced recruitment of the left fusiform in dyslexic readers together with an increased involvement of the superior temporal cortex in children with less automatized letter-speech sound associations.

Keywords: dyslexia, text-based recalibration, audio-visual integration, speech perception, reading development, fMRI

Introduction

Reading is a fundamental skill in the modern day society. Once acquired, reading is an automated process facilitating employability, communication with others and ultimately technological and societal advances. We learn to read early on in our lives by mapping speech onto strings of symbols (text) and learning their meanings and associations. While this process goes smoothly for the majority of children, 5-10% of children are diagnosed with developmental dyslexia, a reading impairment characterised by difficulties in reading fluency and spelling despite adequate schooling opportunities, motivation, intelligence and sensory abilities (Lyon et al., 2003; Peterson & Pennington, 2012).

Dyslexia is a specific learning disorder that is heritable, has a neurobiological basis and is heterogeneous in its cognitive-behavioural manifestation (Astrom, Wadsworth, & DeFries, 2007; Pennington, 2006; Schumacher, Hoffmann, Schmal, Schulte-Körne, & Nöthen, 2007; M. J. Snowling & Melby-Lervåg, 2016; Van Bergen, De Jong, Plakas, Maassen, & Van Der Leij, 2012; van Bergen et al., 2014). Despite this variability, a proposed core deficit is impaired manipulation of speech sounds - i.e. phonological skills (Goswami, 2003; Lyon et al., 2003; S. E. Shaywitz et al., 1998; Snowling, 1980, 2013). It has been suggested that children and adults with dyslexia have less intact phonological representations and/or have difficulty accessing these representations (Bonte, Poelmans, & Blomert, 2007; Noordenbos & Serniclaes, 2015; Ramus & Szenkovits, 2008). An extension of this view proposes that dyslexia involves impaired (e.g. less automatized) mapping of letters and speech sounds (Aravena, 2017; Blomert, 2011; Blomert & Willems, 2010; Kronschnabel, Brem, Maurer, & Brandeis, 2014; however see Clayton & Hulme, 2017; Nash et al., 2016), with robust letter-speech sound associations constituting a pillar of successful reading.

As a child learns to read, the left occipito-temporal cortex becomes increasingly specialised for text (Ben-Shachar et al., 2011; Brem et al., 2009; Ghislaine Dehaene-Lambertz et al., 2018; Maurer et al., 2006) and linked to speech processing areas, including the superior temporal cortex (STC; Dehaene, Cohen, Morais, & Kolinsky, 2015; Schlaggar & McCandliss, 2007). This link is illustrated by a cross-modal enhancement of STC activation by the combined presentation of letters and speech sounds (Van Atteveldt & Ansari, 2014; Van Atteveldt et al., 2004), particularly in relatively transparent orthographies such as Dutch. More specifically, functional magnetic resonance imaging (fMRI) studies have shown that presenting typical readers with matching (congruent) compared to non-matching (incongruent) letter-speech sound pairs elicits increased activation in STC (Blau et al., 2010; Karipidis et al., 2017; Van Atteveldt & Ansari, 2014). Employing this paradigm in dyslexic readers has revealed reduced letter-speech sound congruency effects in the left STC in at risk pre-readers (Plewko et al., 2018), and in children (Blau et al., 2010), adolescents (Kronschnabel et al., 2014) and adults (Blau et al., 2009; Ye, Rüsseler, Gerth, & Münte, 2017b) with dyslexia compared to their age-matched typically reading peers. Similarly, reduced activation has also been reported in higher-order visual areas in studies employing rhyme judgment tasks investigating reading-skill dependent cross modal (McNorgan & Booth, 2015) and unimodal (Hoeft et al., 2007) processing of rhyming versus non-rhyming word pairs. Together,

these studies point to aberrant neural processing of letters and speech sounds in readers with dyslexia compared to typical readers.

Congruency manipulations inherently rely on culturally learnt letter and speech sound associations. However, in children and adults with dyslexia, these links may be represented or automatized differently than in typical readers, potentially confounding the observed results. An alternative way to investigate audio-visual integration of text and speech sounds can be found in text-based recalibration. In this task, ambiguous speech is combined with disambiguating text to explore audio-visual integration of the two modalities. The task consists of two distinct parts – audio-visual exposure blocks followed by auditory-only post-test trials. During the exposure blocks, an ambiguous speech sound /a?a/ midway between /aba/ and /ada/ is combined with disambiguating “aba” or “ada” text. The visual stimuli serve as a “touchstone” for the perceptual system and aid the audio-visual integration of ambiguous speech and visual input. If the two modalities are successfully combined, the perception of the ambiguous sound will temporarily be biased towards the visual stimulus. The extent of the perceptual bias is tested in subsequent post-test trials. Here, participants are presented with the ambiguous sound in isolation (i.e. no visual input) and asked to respond if they perceive the sound as /aba/ or /ada/. Repeated exposure to the ambiguous speech sound /a?a/ in combination with e.g. disambiguating “aba” text, shifts the perception of the speech sound towards /aba/ as illustrated by a larger proportion of /aba/ responses in the post-test trials. Similarly, combining the ambiguous /a?a/ sound with “ada” text biases the later perception of the same speech sound towards /ada/ (Keetels et al., 2018, 2016). The perceptual bias represents a shift in the participant’s phoneme boundary towards the visual modality and is referred to as recalibration. Recalibration is described as a perceptual effect that relies on short-term audio-visual learning mechanisms (Samuel & Kraljic, 2009; Vroomen & Baart, 2012) and temporarily maps the ambiguous sound onto a pre-defined phoneme category (e.g. /a?a/ mapped onto /aba/). A number of visual stimuli have been shown to elicit recalibration including lip-read speech (Bertelson et al., 2003; Ullas, Formisano, Eisner, & Cutler, 2020; Vroomen & Baart, 2012), spoken word context (Norris et al., 2003; Ullas, Formisano, et al., 2020), overt speech articulation (Scott, 2016b), and most recently, text (Bonte, Correia, Keetels, Vroomen, & Formisano, 2017; Keetels et al., 2018, 2016; Romanovska, Janssen, & Bonte, 2019).

The use of text to disambiguate speech is of particular interest for dyslexia research, as this allows exploring audio-visual associations between letters and speech sounds while sidestepping task or stimulus factors involving explicit matching between specific speech sounds and text. In a study employing text-based recalibration, adults with and without dyslexia were exposed to ambiguous speech /a?a/ in combination with either a disambiguating video of a speaker articulating ‘aba’ or ‘ada’, or using “aba” or “ada” text. Intriguingly, while typical readers showed significant recalibration effects following both video and text, readers with dyslexia only showed significant recalibration when videos were used as the disambiguating visual stimuli (Keetels et al., 2018). These findings point to a specific letter-speech sound integration deficit in dyslexia rather than a general deficit in audio-visual integration. However, recent findings in 8-10 year old children employing the same paradigm, surprisingly showed comparable text-induced recalibration in typical and dyslexic readers (Romanovska et al., 2019). It has been proposed that children are particularly sensitive to text within the first few years of reading instruction (Gorka Fraga González, 2015; Froyen et al., 2008; Maurer et al., 2008; Price & Devlin, 2011; Žarić et al., 2014). Because the proposed ‘peak’ text sensitivity period falls within the age range of the children tested in the abovementioned study, the observed discrepancy in findings between children and adults with dyslexia may point to a developmental aspect of text-based recalibration. Indeed, previous research employing lip-read speech as the disambiguating visual stimulus has demonstrated a robust effect in 8- but not 5-year-olds (van Linden & Vroomen, 2008). The authors attributed this to less proficient lip-reading in the 5-year-olds and suggested that increased experience with lip reading (and by extension speech processing) likely has an effect on recalibration. In addition to possible effects of a history of reading problems, developmental differences in letter-speech sound processing may similarly underlie the reported differences in text-based recalibration between adults and children with dyslexia (Romanovska et al., 2019).

In the current fMRI study, we aimed to explore the neural mechanisms underlying audio-visual integration of ambiguous speech and text using text-based recalibration in 8-10 year-old children with and without developmental dyslexia. We were particularly interested in investigating group differences in cortical activation, given the comparable task performance behaviourally. We focused our analysis on the audio-visual exposure blocks, where previous fMRI recalibration studies in adults using lip-read (Kilian-Hütten, Vroomen, & Formisano, 2011) and text (Bonte et al., 2017) stimuli have shown the involvement of a network of brain areas related to audio-visual

processing of speech and text. The behavioural responses provided in the post-test trials were assessed to investigate the recalibration effect in both groups of children while they performed the task in the MRI scanner. In line with behavioural findings (Romanovska et al., 2019), we did not expect to see any difference in the recalibration effect between children with and without dyslexia. We did, however, expect differences in brain activation between the groups, with dyslexic readers showing less cortical activation in reading-related auditory and visual regions compared to their typically reading peers. We first explored the cortical activation pattern during the exposure blocks in a whole-brain analysis. We then furthered these analyses by focusing on regions of interest (ROIs) typically associated with audio-visual integration and reading based on children's brain activity during an adapted version of the congruency manipulation paradigms (e.g. Blau et al., 2010; Plewko et al., 2018), a passive viewing/listening task. Investigating cortical activation in these regions with a novel audio-visual integration task allowed to explore the hypothesis of letter-speech sound integration difficulties in dyslexic readers during short-term perceptual mapping of ambiguous speech to text. Finally, we performed correlation analyses to explore the links between cortical activation within the ROIs and children's reading and phonological skills.

Methods

Participants

Twenty-nine children with dyslexia (mean age 9.4 ± 0.6 years; 15 females) were recruited from a specialized institute for dyslexia healthcare, and forty-three typically reading children (mean age 8.9 ± 0.7 years; 24 females) were recruited from local elementary schools. Data of five dyslexic children were excluded from the analyses due to excessive head motion during the fMRI measurement resulting in poor data quality. The remaining 23 children with dyslexia (2 left-handed) were matched with 23 typical readers (1 left-handed) for age, gender and scores on a non-verbal subtest (block design) of the Dutch version of the Wechsler Intelligence Scale for Children-III (WISC-III-NL; Kort et al., 2005). Twenty of the children (8 dyslexic readers) had taken part in the behavioural text-based recalibration experiment (Romanovska et al., 2019) and were subsequently invited to participate in the fMRI study. The remaining twenty-six children (14 dyslexic readers) were recruited after the behavioural study was completed. Because we were interested in exploring the text-based recalibration effect in the MRI scanner and behaviourally

(offline, on a laptop computer as in the behavioural study), these twenty-six children completed the offline text-based recalibration task after the scanning session (total duration 10 minutes).

All children were native Dutch speakers with no reported hearing impairments, normal or corrected to normal vision, and no history of diagnosed comorbid developmental or neurological disorders. The dyslexia diagnosis was given by the specialised dyslexia institute based on the results of an extensive cognitive psycho-diagnostic testing procedure and all scored at or below the 10th percentile on standardized reading measures. The dyslexic readers were within the first three months of dyslexia treatment. Parents provided written informed consent for participation in the study in accordance with the declaration of Helsinki. Children received a present and a picture of them in the mock scanner as participation reward. The experiment was approved by the ethics committee of the Faculty of Psychology and Neuroscience, Maastricht University.

Literacy and cognitive skills

All participants completed computerized reading, letter-speech sound identification, and phoneme deletion tasks of the 3DM test battery (Dyslexia Differential Diagnosis; Blomert & Vaessen, 2009), as well as two sub-tests of the WISC-III-NL – verbal (similarities) and non-verbal (block design). The reading task was sub-divided into three parts – reading of high frequency, low frequency and pseudo words. Reading fluency was calculated as the total number of words read within 90 seconds (30 s per category). During the letter-speech sound identification task, the children were presented with a phoneme aurally via headphones and asked to indicate the corresponding letter(s) out of 4 possibilities on the computer screen, via button press. During the phoneme deletion task, the participants were presented with a pseudo word via headphones, followed by a phoneme from this pseudo word and asked to say out loud what the pseudo word would sound like without the phoneme (e.g. say /dauk/ without the /d/). All task instructions were simultaneously presented on the computer screen and aurally via headphones, instructing the children to perform the tasks as quickly and accurately as possible. For letter-speech sound identification and phoneme deletion, fluency scores constitute the number of correctly completed items in each task out of the maximum number of items (90 for letter-speech sound identification, 28 for phoneme deletion).

Group characteristics and comparisons between children with and without dyslexia using one-way ANOVA are shown in Table 1. As expected, the children with dyslexia scored significantly lower on the reading and phonological tasks compared to typical readers. The groups differed in the non-verbal IQ sub-test, with dyslexic children having slightly lower scores on average. Importantly however, all children were within, or indeed somewhat above the norm on this measure.

Group Age (SD) Gender ratio(m/f)	Dyslexic readers 9.4 (0.6) 10:13			Typical readers 9.1 (0.7) 10:13			Dyslexic vs. Typical readers		
	M	SD	Range	M	SD	Range	F(1,45)	p	
Reading fluency scores¹									
Word reading	77.82	20.13	40-111	121.17	27.97	74-178	36.39	0.000	
Word reading [T] ²	34.52	6.20	22-46	53.82	11.87	30-80	47.75	0.000	
Letter-speech sound identification	42	3.41	33-45	42.95	1.55	40-45	1.49	0.227	
Letter-speech sound identification [T]	44	9.73	24-59	54.43	5.31	43-64	20.38	0.000	
Phoneme deletion	13.30	6.20	5-23	17.34	4.05	8-23	8.17	0.006	
Phoneme deletion [T]	36	13.90	0-56	53.21	11.75	30-74	20.56	0.000	
IQ norm scores³									
Verbal (similarities)	11.56	2.25	8-16	15.04	1.66	12-18	35.46	0.000	
Non-verbal (block design)	10.21	2.66	7-17	11.82	1.99	7-16	5.38	0.025	
Age (months)	115.17	9.18	99-132	110	9.18	96-126	3.65	0.063	

1 Raw scores, number of correct items across three sub-groups (high-frequency, low-frequency and pseudo words) per 90s, number of correct responses out of 90 items (letter-speech sound identification) or 28 items (phoneme deletion)

2 t-Scores, age-appropriate norm scores mean 50, SD=10

3 Age-appropriate norm scores, mean = 10, SD = 3

Stimuli

The speech stimuli for the recalibration task consisted of recordings of a native male Dutch speaker pronouncing the speech sounds /aba/ and /ada/ (see Bertelson et al., 2003 for a detailed description). Both speech sounds lasted 650 ms and were used to create a nine-token continuum ranging from a clear /aba/ sound to a clear /ada/ sound by changing the second formant (F2) in eight steps of 39 Mel using PRAAT software (Boersma & Weenink, 2001). The visual stimuli consisted of the written counter-parts of the speech sounds, namely “aba” and “ada” text presented in white at the center of a black screen in ‘Times New Roman’ font (font size 50). The auditory and visual stimuli were presented using Presentation software (Version 18.1, Neurobehavioral Systems, Inc., Berkeley, CA, United States).

In addition to the fMRI recalibration experiment, the children performed a passive viewing/listening task with unimodal and bimodal presentation of letters and speech sounds (adapted from Blau et al., 2010). The task included four stimulus conditions: audio-visual congruent (matching letters and speech sounds), audio-visual neutral (meaningless symbols and speech sounds), auditory-only and visual-only. Speech stimuli for this task consisted of 10 Dutch consonant-vowel syllables produced by two female native Dutch speakers (/ba/, /bi/, /bu/, /da/, /fi/, /fu/, /si/, /su/, /ti/, /tu/; a subset from Correia, Jansma, & Bonte, 2015) and 3 Dutch vowels produced by two native Dutch children (one boy, one girl; /a/, /i/, /u/; a subset from Bonte, Hausfeld, Scharke, Valente, & Formisano, 2014). The stimuli were recorded in a soundproof chamber and post-processed using PRAAT software (Boersma & Weenink, 2001). All stimuli were digitized at a sampling rate of 44.1 kHz (16 bit resolution), bandpass filtered (80 – 10.5 kHz) and down sampled to 22.05 kHz. Stimulus length was equalized to 350 ms for the vowels and 340 ms for the consonant-vowel syllables using PSOLA (75 – 400 Hz for the F0 contour). Sound intensity level was equalized across stimuli and adjusted to the in-scanner headphone system (Sensimetrics, model S14, www.sens.com).

The visual stimuli for the congruent and visual-only condition were visual letters/syllables corresponding to the speech sounds, presented in white at the centre of a black screen in ‘Verdana’ font (font size 50). The visual stimuli for the neutral condition consisted of 15 meaningless symbol combinations containing two or three elements presented in a pseudo-randomized order ensuring

that no speech sound-symbol associations could be made. The symbols were presented in white on a black screen and their size was matched to the text stimuli to ensure comparable stimulus properties. In the visual-only blocks, the letters/syllables were presented in isolation, whereas in the auditory-only blocks only the speech sounds were presented while the participants fixated on a white fixation cross in the centre of a black screen. An orthogonal task was employed to assure attention and included catch trials matching the four conditions (similarly to Blau et al., 2010). The catch trials consisted of a cartoon monster (visual stimulus) and a recording of a female native Dutch speaker saying /Hello!/ (auditory stimulus) presented in isolation in the visual- and auditory-only blocks respectively. A combination of both modalities was presented in the congruent and neutral blocks.

Experimental design and Procedure

Prior to the MRI experiment, all children were trained in a mock scanner to get acquainted with the scanning environment, practice the recalibration task and help reduce head motion during data acquisition. Upon arrival, we explained the tasks that the children would be performing in the MRI scanner, namely the recalibration and passive viewing/listening task. The children then practiced in the mock scanner to get acquainted with the use of the MR compatible headphones (Sensimetrics, model S14, <https://www.sens.com>) and button boxes. During the practice, all children completed a pre-test (see 2.3.1) followed by one run of the recalibration task consisting of one “aba” and one “ada” exposure block, each followed by four post-test sounds. The children then completed motion training in order to improve subsequent (f)MRI data quality. This consisted of placing a headband containing a motion sensor on the forehead of each child while they watched a cartoon inside the mock scanner. The sensor was calibrated to tolerate 2 degrees of motion along the horizontal and vertical planes, as soon as this threshold was exceeded, the cartoon paused and shrank until the child was lying still again. This helped illustrate how still the children should aim to lie during the MRI experiment. The duration of the mock training session was approximately 20 minutes. The children then completed a 1 hour 15 minute MRI experiment and 45 minute behavioural testing after the scanning session in which they completed the reading tasks and two subsets of the WISC-III-NL. While the allotted scanning time was 1 hour and 15 minutes, the data acquisition only took 45 minutes in total. The rest of the time was used for short breaks in between tasks and taken up by placing the participants in the scanner and taking them out of the scanner.

Total testing time amounted to 2 hours and 45 minutes including two breaks – a 10 minute break after the mock scanner training and a 15 minute break after the MRI experiment.

Pre-test

During the training session, each child completed a pre-test to determine the individual most ambiguous sound for subsequent use in the recalibration task. The children were presented with all 9 sound tokens along the /aba/-/ada/ continuum a total of 98 times in a randomized order, with the 7 ambiguous sounds presented more frequently than the clear /aba/ and /ada/ sounds (see e.g. Bertelson et al., 2003; Kilian-Hütten et al., 2011; Vroomen, Van Linden, Keetels, De Gelder, & Bertelson, 2004). The participants were instructed to pay close attention to each sound and indicate whether they perceived that sound as /aba/ or as /ada/, by pressing the left or right innermost button of a button box with their left/right index finger following a response cue (Figure 1). The response cues consisted of text “aba” (left) and “ada” (right), held up by cartoon monsters created using the Monster Workshop content pack of the iClone 6 software (<https://www.reallusion.com/>). During the presentation of the speech sounds, the children viewed a black screen with a white fixation cross followed by the response cue 1 s later. Each trial was terminated after the child provided a response, triggering the presentation of the subsequent speech sound after 2 s. The total duration of the pre-test was approximately 5 minutes.

The most ambiguous speech sound was determined based on the proportion of /aba/ responses to each token along the /aba/-/ada/ continuum and was identified as the sound with an /aba/ versus /ada/ response proportion closest to 0.5 representing the phoneme boundary (Romanovska et al., 2019; Vroomen et al., 2004). This individually determined most ambiguous sound was subsequently used in the audio-visual exposure blocks and post-test trials of the recalibration task. In the post-trials, next to the most ambiguous sound, we also presented its flanking sounds /a?a/+1 and /a?a/-1 along the /aba/-/ada/ continuum.

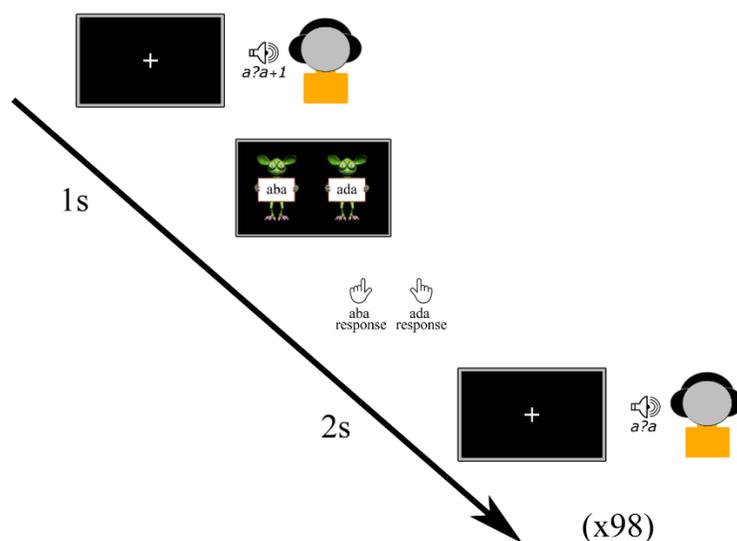


Figure 1: Pre-test

Recalibration task

The recalibration paradigm consisted of audio-visual exposure blocks and subsequent post-test trials (Figure 2). During each exposure block, the children were presented with text “aba” or “ada” in combination with the individually determined most ambiguous speech sound /a?a/ for a total of 8 times. The “aba” and “ada” exposure blocks were presented in a pseudo-randomised order, ensuring that each type of exposure block was repeated no more than twice in a row. The audio-visual stimuli were presented simultaneously (relative SOA of 0 ms), the duration of the auditory stimuli was 650 ms and visual text was presented for 1s. The inter-trial interval between subsequent audio-visual exposure trials was set to 2 s (1 TR). During the audio-visual exposure blocks, children were instructed to pay close attention to the speech sounds and text without providing a response.

Each exposure block was followed by four auditory-only post-test trials the onset of which was jittered to be an average of 10 s (4-6 TR). The jittered period between exposure blocks and post-test sounds served as the baseline in subsequent statistical comparisons and consisted of a white fixation cross in the middle of a black screen. The post-test trials were presented in a randomized order with the most ambiguous sound /a?a/ presented twice, and each of the flanking sounds /a?a/+1 and /a?a/-1 on the /aba/-/ada/ continuum presented once. Each post-test trial was followed

by a response cue containing cartoon monsters (Figure 2). The onset of the response cue was jittered 2,5 - 3 s with respect to the post-test sound and lasted 3 s. The subsequent post-test trial was presented 3 - 3,5 s following the response cue. The total ITI between post-test trials was 6 s (3 TR). Children were instructed to listen carefully to the post-test sound and respond whether they perceived it as /aba/ or as /ada/ upon the presentation of the response cue using the MR compatible button boxes. The responses were made by pressing the innermost button of the button box with the left/right index finger, as practiced in the mock scanner. Children completed a total of four runs of the recalibration task, corresponding to 24 audio-visual exposure blocks (12 with “aba” text and 12 with “ada” text) and 4*24 post-test trials. All auditory and audio-visual stimuli were presented during a 900 ms silent gap in volume acquisitions.

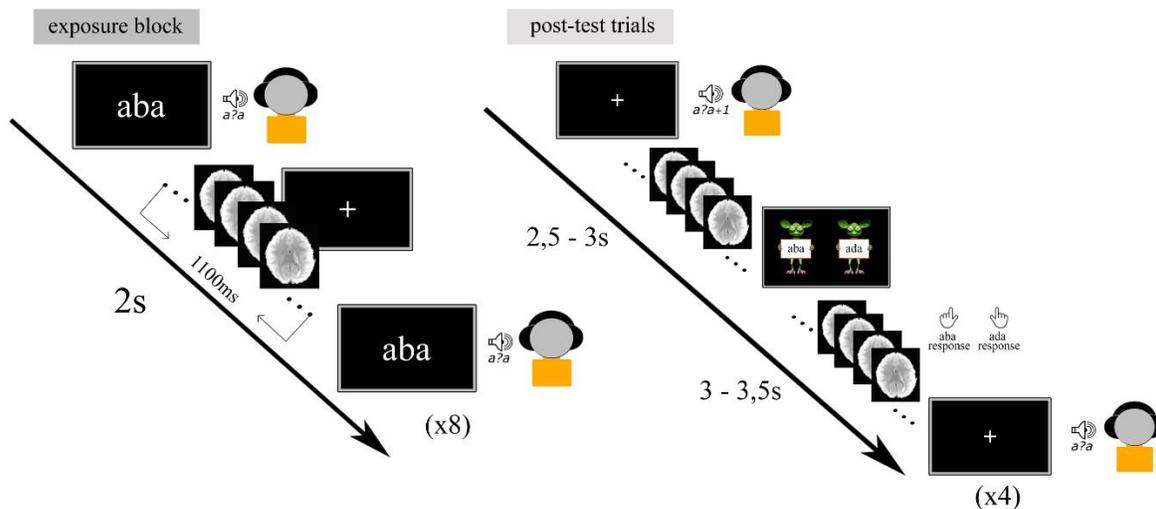


Figure 2: Text-based recalibration paradigm in the MRI environment. Left panel: timings of audio-visual stimulus presentation (8 stimuli per block) during the exposure blocks, with a 2 second inter-stimulus interval (TR), a 1100 ms acquisition period (TA), leaving 900 ms silent gaps for stimulus presentation. Right panel: timings of the subsequent post-test trials (4 stimuli per block), with jittered periods before and after the response cue presentation and the time-window in which the participants provided their response. Also here a TR of 2 seconds, and a TA of 1100 ms was used leaving 900 ms silent gaps for post-test sound presentation.

Passive viewing/listening task

At the end of the fMRI session, the children completed a single run of a passive viewing/listening task with four stimuli blocks presented in a pseudo-randomised order: bimodal speech sounds and text (congruent), bimodal speech sounds and meaningless symbols (neutral), unimodal speech

sounds, and unimodal text. Each block contained 6 stimuli presented once every 2 s (1 TR). Subsequent blocks were separated by a jittered rest period of 12 s on average (5-7 TR) which served as the baseline and consisted of a white fixation cross in the middle of a black screen. To ensure children were paying attention, an orthogonal task using pseudo-randomized cartoon monster catch trials was included (similar to Blau et al., 2010). There was a total of 6 catch trials matched for the modality of the stimuli blocks - 3 bimodal catch trials and 3 unimodal trials (2 visual). During the bimodal catch trials the children saw a cartoon monster and simultaneously heard the monster say /Hello!/, during the unimodal catch trials they only saw or heard the monster. The children were instructed to pay close attention to the stimuli because a cartoon monster was hiding somewhere between them and press the right innermost button of the button box with their right index finger as soon as they heard and/or saw the monster.

Statistical analyses behavioural data

The behavioural data were analysed using SPSS version 26.0 (IBM Corp., Armonk, NY, United States). In addition to the behavioural data collected while children were performing the recalibration task in the scanner, we also investigated each child's performance on the recalibration task outside of the scanner during the behavioural experiment (i.e. offline data). We were thus able to compare recalibration effects in and out of the MRI scanner for each child. For both, in scanner and offline data, RM ANOVA analyses were performed investigating group effects of dyslexia diagnosis on the performance of the recalibration task. The ANOVA models included the type of exposure block ("aba" vs "ada") and type of post-test sound (/a?a/,/a?a/+1,/a?a/-1) as within subject factors and dyslexia (dyslexic vs typical readers) as the between subjects factor. For the offline data, an additional between subjects factor for task order was included (before vs after fMRI) to test for potential differences in task performance between children who completed the behavioural text-based recalibration task before the scanning session compared to the children who completed the task afterwards. The Greenhouse-Geisser correction of the degrees of freedom was used for conditions violating the sphericity assumption.

To investigate the association between children's letter-speech sound processing, phonological, and reading skills, and cortical activation during the audio-visual exposure blocks we performed correlation analyses. Behavioural measures included children's non-standardized raw scores of

word reading fluency, letter-speech sound identification fluency and phoneme deletion fluency. Prior to running the analyses, all data were assessed for outliers using boxplots in SPSS. The analyses identified two dyslexic readers as outliers in the letter-speech sound fluency task (lower quartile plus 1.5 times inter-quartile range). These participants were excluded from the correlation analyses exploring the association between cortical activation and letter-speech sound fluency. All other correlations were performed on the full sample of 46 participants. Bivariate Pearson correlations were computed one at a time (i.e. for each behavioural measure separately) using the built-in ANCOVA analyses module in BrainVoyager 20.6 based on the average individual t-statistics extracted per participant from a pre-defined region of interest. The correlations were corrected for multiple comparisons by applying the False Discovery Rate (FDR) correction using MATLAB.

MRI measurements

Brain Imaging was performed with a Siemens Prisma 3T MRI scanner (Siemens Medical Systems, Erlangen, Germany) using a 64-channel head–neck coil. Five functional runs were acquired (2,5 mm x 2,5 mm x 2,5 mm resolution) with a multi-band factor of 5 echoplanar-imaging (EPI) sequence (repetition time [TR] = 2000 ms, acquisition time [TA] = 1100 ms, field of view [FOV] = 210 mm × 210 mm, echo time [TE] = 35.8 ms). Each volume consisted of 50 slices (no gap), covering the whole brain. The recalibration task was made up of four 5 minute runs and the passive viewing/listening task consisted of one 7 minute functional run. The speech stimuli were presented binaurally at a comfortable listening level via MR compatible headphones (Sensimetrics, model S14, www.sens.com), in the 900-ms silent gap between consecutive volume acquisitions. Additionally, a high-resolution structural scan (1 mm × 1 mm × 1 mm) using a T1-weighted three-dimensional MPRAGE sequence ([TR] = 2300 ms, [TE] = 2.98 ms, 192 sagittal slices) was acquired.

fMRI pre-processing

Data pre-processing and analyses were performed using BrainVoyager QX version 2.8, BrainVoyager 20.6 and 21.4 (Brain Innovation, Maastricht, The Netherlands) and custom MATLAB routines (The MathWorks, Inc., Natick, MA, United States). The functional data

underwent 3D motion correction with respect to the first volume of the first functional run (trilinear sinc interpolation), slice scan time correction and high pass temporal filtering (5 cycles per time course recalibration runs / 7 cycles passive viewing/listening paradigm). The anatomical data underwent manual inhomogeneity correction to improve white matter-grey matter boundary segmentation and was transformed into Talairach space (Talairach & Tournoux, 1988). The functional data were co-registered to the anatomical data, transformed into Talairach space, re-sampled to 3 mm iso-voxel resolution and spatially smoothed using a 6 mm FWHM Gaussian kernel. Volumes of functional runs affected by excessive head motion (≥ 3 mm translation/rotation in any direction) were removed from the run, if the number of affected volumes exceeded 20%, the run was excluded from further analyses. A one-way ANOVA of the average motion statistics for each of the 3 translation and rotation parameters did not reveal significant differences in motion between children with and without dyslexia (all $F \leq 1.85$).

For each child, individual cortical surface representations were automatically constructed based on the white matter-grey matter boundary, manually adjusted, and aligned using cortex based alignment employing a moving-target group average based on curvature information resulting in an anatomically-aligned group-average 3D cortical representation (Frost & Goebel, 2012). Each participant's functional data were projected onto their cortical surface creating surface-based time courses. All functional data were subsequently analysed per hemisphere at the surface level using the group-aligned average cortical surfaces.

Region of Interest (ROI) definition

The regions of interest were defined based on cortical activation during the congruent vs baseline condition in the passive viewing/listening task. Three participants did not complete this task (2 dyslexic readers) and data of six participants were excluded due to excessive head motion (3 dyslexic readers). The individual maps of the remaining 37 participants were each thresholded at $p < 0.05$ (uncorr.; fixed cluster threshold of 25 mm²), anatomically aligned and used to create group-based probabilistic maps (Frost & Goebel, 2012). The resulting group maps were thresholded at 60%, thus including regions of 60% subject overlap at a fixed group cluster threshold of 20 mm² for each separate group (dyslexic and typical readers). We chose to perform these analyses for each group separately to delineate regions of interest that may or may not be

specific to dyslexic or typical readers. The resulting group maps showed comparable regions of consistent activation in both groups, albeit with lower inter-subject consistency across dyslexic readers. Because of the involvement of comparable regions, we decided to create ROIs based on the combined probabilistic maps across groups. The choice for 60% overlap was based on setting a minimum criterion that included consistent activity in auditory and visual brain regions in more than half of the individual children. In practice, this threshold was especially driven by the relatively large inter-individual variability in the exact location of children's activity in the ventral visual cortex. This variability is in line with the proposition that the recruitment of the ventral visual areas is still variable around age 9, since children have not yet made a switch to fully automatized text processing at this age (Ehri, 2005; Pugh et al., 2001). In fact, at the 60% overlap threshold the ventral visual region only occurred in the map of the typical readers, which may relate to the fact that typical readers on average were closer to approaching automatized reading. Combining the ROI maps of both groups yielded four ROIs typically associated with audio-visual integration and reading including the left fusiform gyrus/occipito-temporal sulcus, bilateral superior temporal gyri (STG) and right frontal cortex (Figure 5). These regions were used in subsequent correlation analyses and group comparisons of cortical activation during the audio-visual exposure blocks in the recalibration task.

Whole brain univariate fMRI analysis

Cortical activation was assessed employing random effects (RFX) general linear model (GLM) analyses using the individual surface-based time courses of all participants. The model included one predictor for each type of exposure and post-test blocks (“aba”, “ada”; 4 predictors) as well as z-transformed motion predictors as variables of no interest to improve the signal to noise ratio. The number of runs included in the RFX analyses varied by participant due to excessive head motion (6 participants, 5 dyslexic readers) or technical difficulties during data acquisition (1 typical reader). The total number of recalibration task runs was 175 (86 runs dyslexic readers, 89 runs typical readers). Subsequent functional contrast maps (*t*-statistics) were calculated based on predictors for both exposure blocks taken together (“aba” and “ada”) compared to the fixation cross baseline. These maps were corrected for multiple comparisons using an FDR threshold of $q < 0.05$ and contrasted in whole brain group comparisons of dyslexic versus typical readers.

ROI analysis

In addition to group comparisons at the whole-brain level, we explored cortical activation during the audio-visual exposure blocks in four ROIs: bilateral STG, left fusiform and right frontal cortex in children with and without dyslexia. This was achieved by running ROI ANOVA analyses in BrainVoyager 20.6 comparing the t-statistic values within each ROI between children with and without dyslexia. We additionally conducted ANCOVA analyses in each ROI to check for potential confounding effects of individual differences in age and in scores on verbal and non-verbal sub-tests of the WISC-III-NL, as these showed significant differences between the groups (WISC sub-tests) or approached statistical significance (age). In order to explore potential links between reading skills and cortical activation within the ROIs, we also performed correlations of the individual t-statistics and reading skills.

Results

Behavioural results offline experiment

Visual inspection of the offline data revealed a clear recalibration effect across all participants as well as within the matched groups of typical and dyslexic readers (Figure 3 top panel). The children were more likely to perceive the ambiguous post-test sounds as /aba/ following an “aba” exposure block (dark grey line Figure 3 top panel) and as /ada/ following an “ada” exposure block (light grey dashed line Figure 3 top panel). The effect was especially pronounced for the most ambiguous speech sound /a?a/: proportion of /aba/ versus /ada/ responses 0.51 vs 0.33 across participants, 0.45 vs 0.32 in dyslexic readers, 0.57 vs 0.35 in typical readers.

The recalibration effect across groups was confirmed by a 2 (exposure) \times 3 (post-test sounds) RM ANOVA with between subject factors dyslexia and task order. Two participants (1 dyslexic reader) did not complete the offline behavioural experiment, thus this analysis included data of 44 out of the 46 participants. Results showed significant main effects of exposure [$F(1,40) = 27.88, p < 0.001$] and post-test sound [$F(1,64) = 146.73, p < 0.001$, Greenhouse-Geisser corrected], as well as a significant exposure \times post-test sound interaction [$F(2,80) = 5.99, p = 0.004$], showing that children’s /aba/ response proportions differed depending on the type of exposure block (“aba” versus “ada”) and post-test sound (/a?a/, /a?a/+1 versus /a?a/-1). Post hoc comparisons of /aba/

response proportions following the two types of exposure blocks across all participants confirmed a significant difference for each of the post-test sounds following “aba” vs “ada” exposure, reflecting a significant recalibration effect across children [$/a?a/$: $M = 0.51$, $SD = 0.17$, $M = 0.33$, $SD = 0.15$, $t(43) = -5.33$, $p < 0.001$; $/a?a/+1$: $M = 0.20$, $SD = 0.18$, $M = 0.12$, $SD = 0.12$, $t(43) = -2.68$, $p = 0.01$; $/a?a/-1$: $M = 0.64$, $SD = 0.18$, $M = 0.48$, $SD = 0.21$, $t(43) = -4.51$, $p < 0.001$].

The analyses also revealed a main effect of dyslexia [$F(1,40) = 4.64$, $p < 0.05$], which could either reflect a group difference in the magnitude of the recalibration effect or in their overall $/aba/$ versus $/ada/$ response proportions. To test the first possibility, we conducted a one-way ANOVA analysis comparing the magnitude of the recalibration effect between readers with and without dyslexia. Results showed no significant difference in recalibration effects between groups [$F(1,43) = 0.927$, $p = 0.341$]. The main effect of dyslexia thus likely points to a difference in overall response proportions. Indeed, the average $/aba/$ versus $/ada/$ response proportions were somewhat lower in dyslexic ($M = 0.33$) compared to typical readers ($M = 0.48$), indicating that dyslexic readers were more likely to report perceiving the ambiguous post-test sounds as $/ada/$ than typical readers.

As for possible effects of performing the behavioural task prior to or after the MRI scan, the RM ANOVA showed no main effect of task order ($F = 2.77$), and no significant interactions with dyslexia or dyslexia and task order ($F \leq 3.29$), indicating that neither dyslexia diagnosis, nor task order or their interaction had a significant effect on the recalibration results. The results did include a significant task order \times post-test sound interaction [$F(2,64) = 6.87$, $p = 0.002$] suggesting that the $/aba/$ versus $/ada/$ response proportions to the different post-test sounds were differentially influenced by whether the participants performed the task before or after the MRI (see slopes for the “aba” and “ada” exposure blocks in supplementary Figure S1). Given the lack of main- or other interaction effects with task order, these findings do not indicate differences in recalibration effects.

Behavioural results in the scanner

The behavioural results of the same participants in the MRI scanner showed a marked decrease in the magnitude of the recalibration effect (Figure 3 bottom panel). The proportions of $/aba/$ to $/ada/$ responses to the most ambiguous sound $/a?a/$ were 0.39 vs 0.35 across participants, 0.41 vs 0.38

in dyslexic readers and 0.38 vs 0.31 in typical readers. A 2 (exposure) × 3 (post-test sounds) RM ANOVA across all subjects showed only a significant main effect of post-test sound [$F(1,65) = 65.83, p < 0.001$, Greenhouse-Geisser corrected], none of the other main or interaction effects were statistically significant ($F \leq 2.3$). These results indicate that, while all participants responded differently to each post-test sound (downward slopes in Figure 3 bottom panel), the recalibration effect was not significant in either the dyslexic or typical readers.

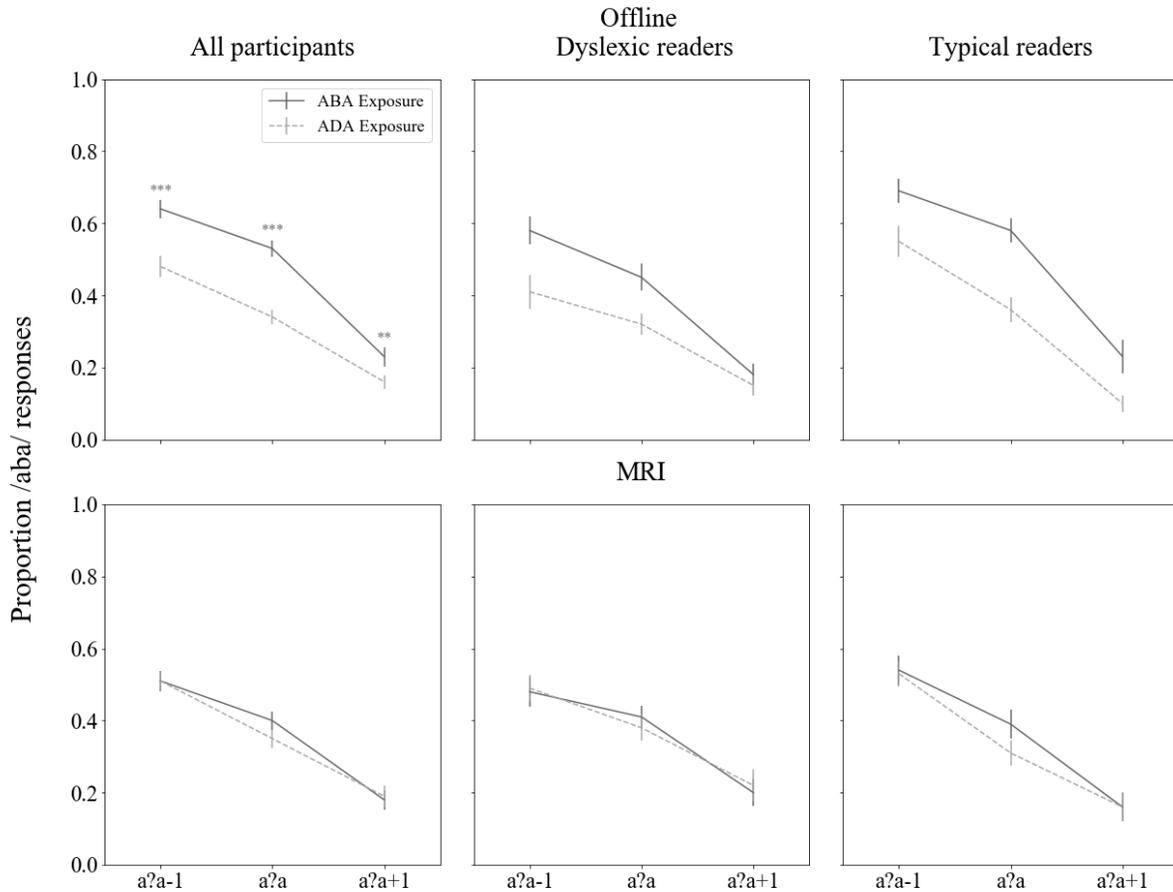


Figure 3: Behavioural text-based recalibration results; Top panel: outside the MRI scanner; bottom panel: in the MRI scanner; The graphs show /aba/ response proportions for the /a?a/-1, /a?a/ and /a?a/+1 post-test sounds following an “aba” versus “ada” exposure block. Vertical bars = standard error; ** $p \leq 0.01$ *** $p \leq 0.001$.

fMRI activity during audio-visual exposure

During the exposure blocks, paired text and ambiguous speech sound stimuli evoked significant blood-oxygen-level-dependent (BOLD) responses in a broad bilateral network of brain areas typically associated with reading and audio-visual integration (Bonte et al., 2017; Dehaene et al.,

2015; Shaywitz & Shaywitz, 2008; Van Atteveldt et al., 2004). These regions included the occipital cortex, (left) fusiform, bilateral superior temporal gyrus (STG), frontal and parietal areas (Figure 4a). The Talairach coordinates of these activation clusters are reported in Table 2. The activation pattern was largely comparable between dyslexic and typical readers (Figure 4b and c). Whole-brain comparisons of group differences between children with and without dyslexia, did not yield statistically significant results at the $FDR < 0.05$ level. We did, however observe significantly higher activation in the typical readers in a left hemisphere fusiform region at a more lenient voxel-level threshold of $p < 0.01$, corrected for multiple comparisons using a cluster threshold $p < 0.05$ that overlapped with the fusiform ROI.

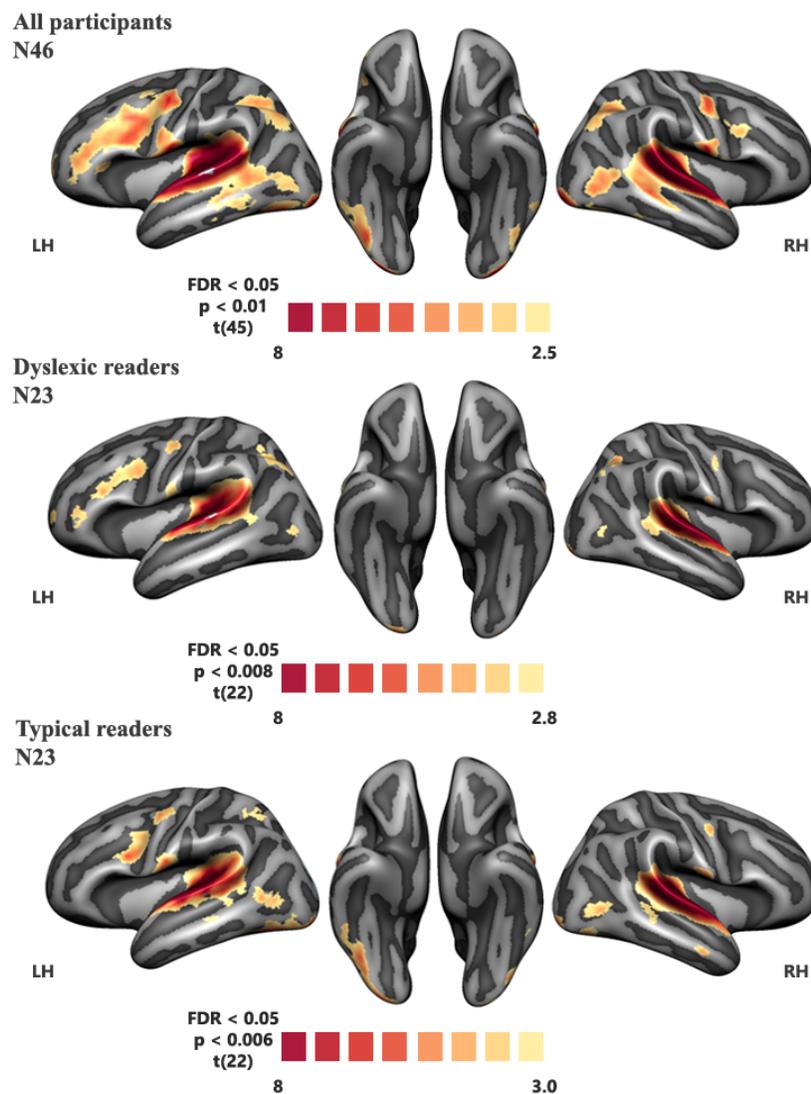


Figure 4: Cortical activation during the exposure blocks versus baseline in (a) all participants; (b) dyslexic readers; (c) typical readers

Table 2: Talairach coordinates of cortical activation clusters during the audio-visual exposure blocks compared to baseline across groups.

Area	Hemisphere	Cluster size (n vertices)	Talairach coordinates (center of gravity)		
			x	y	z
Frontal	Left	1205	-49	16	37
STG/STS	Left	3580	-66	-34	14
Parietal	Left	1373	-45	-70	49
Lateral sensorimotor	Left	478	-67	-9	24
vOTC	Left	383	-51	-70	-13
V1	Left	142	-35	-103	-9
Frontal	Right	89	51	11	39
STG/STS	Right	2992	68	-26	14
Posterior MTG	Right	261	54	-74	7
Parietal	Right	769	46	-74	51
Lateral sensorimotor	Right	333	67	-8	24
vOTC	Right	86	47	-74	-13
V1	Right	181	35	-102	-6

STG = Superior Temporal Gyrus; STS = Superior Temporal Sulcus; vOTC = ventral Occipito-Temporal Cortex; V1 = primary visual cortex.

ROI-based group comparisons and correlations

To investigate group differences in brain regions typically associated with audio-visual processing of text and speech sounds, we performed additional ANOVA analyses within the bilateral STG, left fusiform and right frontal ROIs based on independently acquired data of the congruent condition in the passive listening/viewing task. The ROI comparisons yielded a significant activation difference in the left fusiform ROI [$F(1,45) = 13.60, p < 0.01$] with reduced activation in the dyslexic compared to typical readers. Cortical activation in the other ROIs did not differ between groups (Figure 5). Additional ANCOVA analyses in all ROIs and for all three potential confounding variables (verbal and non-verbal WISC-III-NL sub-tests and age) yielded the same results, confirming that these variables did not significantly contribute to the observed (lack of) group differences.

To investigate whether our results were modulated by task performance – i.e. whether or not children show a recalibration effect – we performed the same group comparisons between dyslexic and typical readers in sub-groups of children who did show a text-based recalibration effect in the MRI (responders; 22 in total, 11 per group) and those children who did not (non-responders 24 in total, 12 per group). The analyses in responders replicated those observed in the full sample (see

supplementary Figure S2), showing that readers with dyslexia activate the left fusiform region less compared to typical readers even when they successfully recalibrated ambiguous speech perception towards the text stimuli. The analyses in non-responders did not show a group difference in the left fusiform region but did replicate the rest of our findings (see supplementary Figure S3).

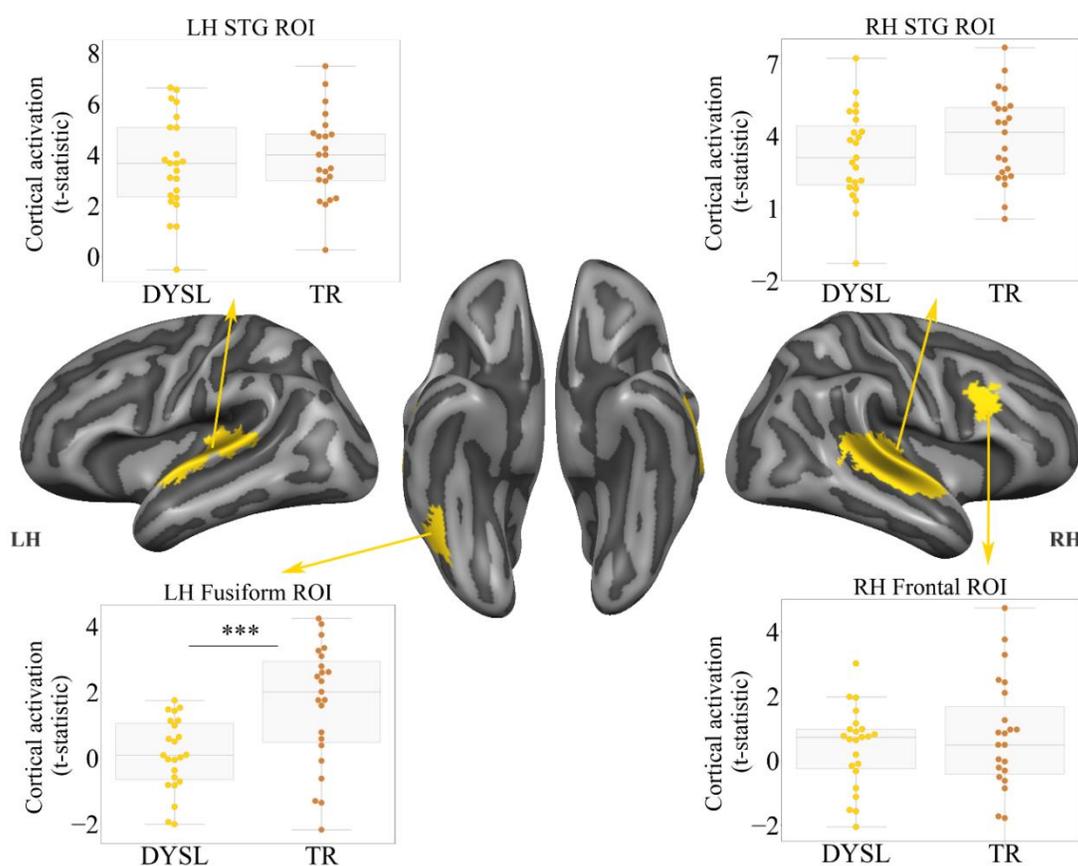


Figure 5: Group differences in cortical activation during the audio-visual exposure blocks within the regions of interest between dyslexic (DYSL; gold) and typical readers (TR; brown). Cortical activation is represented as individual t-statistics per participant (gold and brown dots) and group box-plots (grey) for each group. *** = $p < 0.001$

We subsequently performed correlation analyses between activation within each of the four ROIs and children's raw, non-standardised scores of letter-speech sound processing, reading and phonological skills. This yielded bilateral negative correlations between STG activation and letter-speech sound identification fluency (Figure 6 top panel; left STG $r(42) = -.344$, $p < 0.05$, $q = 0.02$; right STG $r(42) = -.300$, $p < 0.05$, $q = 0.02$) as well as positive correlations between reading fluency ($r(44) = .376$, $p < 0.01$, $q = 0.01$) and phoneme deletion scores ($r(44) = .307$, $p < 0.05$, $q = 0.02$) and activation within the left fusiform ROI (Figure 6 bottom panel).

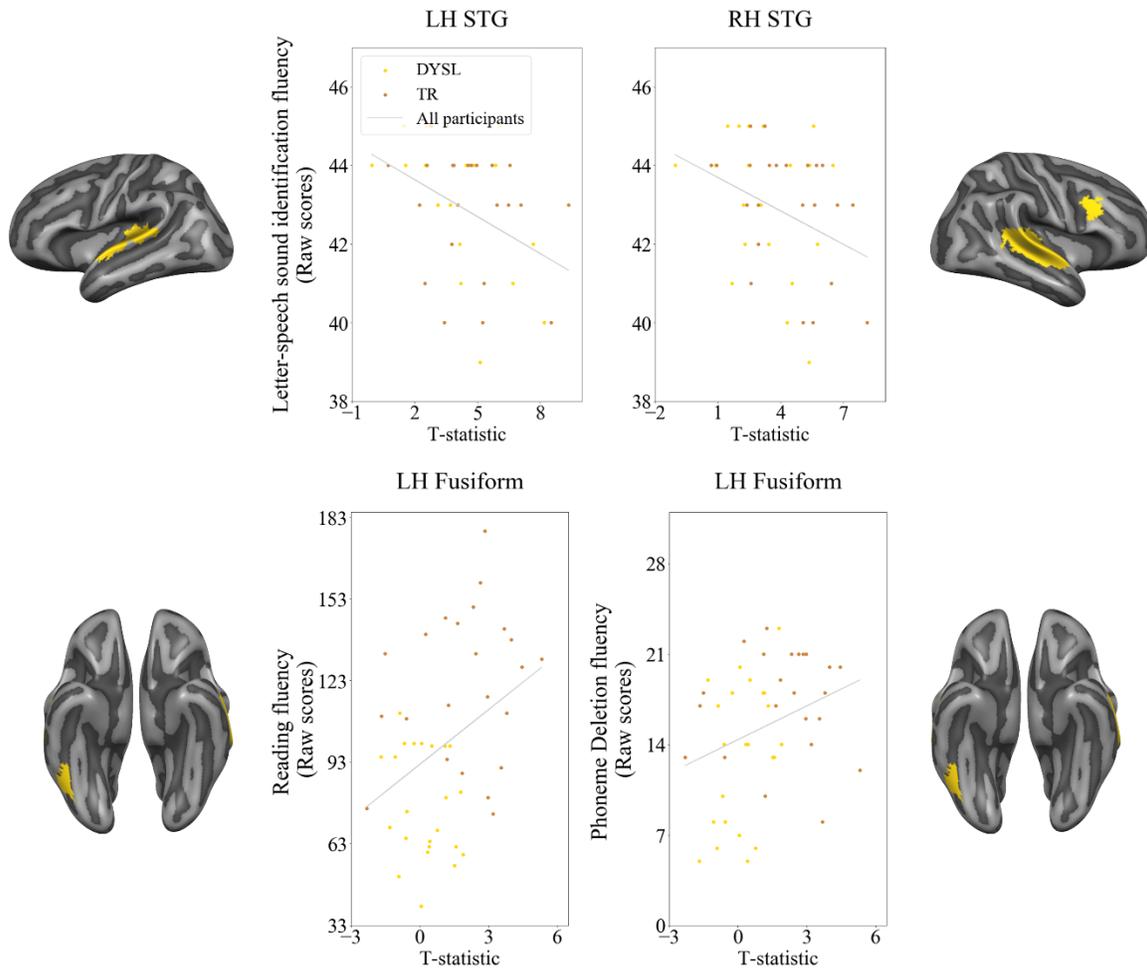


Figure 6: Results of the correlation analyses between cortical activation during the audio-visual exposure blocks within the regions of interest and children’s non-standardized reading scores; Top panel: bilateral STG; bottom panel: left fusiform region; DYSL = dyslexic readers; TR = typical readers.

Discussion

The present MRI study investigated text-based recalibration in 46 8-10 year-old children, half of whom had received an official diagnosis of dyslexia. Our fMRI findings showed activation within comparable brain areas in both groups during audio-visual exposure to letters and ambiguous speech sounds and comparable behavioural effects of text-based recalibration. A more detailed comparison did show significantly reduced activation within a left fusiform ROI for dyslexic compared to typical readers, which was correlated with children’s reading and phonological skills. Additionally, increased cortical activation in bilateral STG during exposure to text and ambiguous speech was linked to less fluent letter-speech sound identification, likely pointing to altered

processing of the audio-visual stimuli in children with less automatized letter-speech sound associations.

Our behavioural results outside of the scanner corroborate the previously reported behavioural findings showing significant recalibration effects regardless of dyslexia diagnosis (Romanovska et al., 2019). We did, however, observe slight differences in response proportions between the groups, with dyslexic readers being more likely to perceive the ambiguous post-test sounds as /ada/ compared to typical readers. Across both groups, the magnitude of the effect was reduced in the MRI scanner. This is likely due to contextual factors including scanner noise, sound quality in the MR-compatible headphones and unusual body position (performing the task lying down). Previous research has shown that the MRI environment reduces attentional focus on the task (van Maanen, Forstmann, Keuken, Wagenmakers, & Heathcote, 2016) and 8-10 year old children who are still developing their attentional skills (Amso & Scerif, 2015; Betts, McKay, Maruff, & Anderson, 2006; Klenberg, Korkman, & Lahti-Nuutila, 2001; Klimkeit, Mattingley, Sheppard, Farrow, & Bradshaw, 2004; Lin, Hsiao, & J., 1999) may be more prone to such effects. Although somewhat reduced compared to offline behavioural experiments, in adults behavioural recalibration effects tend to be preserved in the MRI setting (Bonte et al., 2017; Kilian-Hutten, Valente, Vroomen, & Formisano, 2011; Ullas, Hausfeld, Cutler, Eisner, & Formisano, 2020). Thus, a developmental trajectory of both the text-based recalibration effect and more general cognitive and attentional mechanisms may underlie the differences in text-based recalibration performance in the MRI environment between children and adults. Future research in larger groups of adults and/or older children who more consistently show a significant text-based recalibration effect in the MRI should aim to elucidate the associations between the magnitude of the recalibration effect and cortical activation. An inspection of individual behavioural performance in the scanner revealed that about half of the children in each group did show a recalibration effect. Intriguingly, unlike previous behavioural results in adults with dyslexia (Keetels et al., 2018), there was no relation between children's (non)responsiveness to recalibration and reading skills.

In terms of cortical activation, a broad bilateral network of brain areas typically associated with reading and audio-visual integration was seen, including bilateral STG, frontal and parietal brain areas. These regions overlap with those reported in a previous fMRI study employing text-based recalibration in adults (Bonte et al., 2017), as well as in studies investigating cortical responses to

letters and speech sounds in children and adults (Blau et al., 2010, 2009; Chyl et al., 2017; Kronschnabel et al., 2014; McNorgan et al., 2014; McNorgan & Booth, 2015; Plewko et al., 2018). Moreover, our results suggest that dyslexic and typical readers recruit a comparable network of cortical areas during audio-visual exposure to text and ambiguous speech sounds. The observed similarities in the brain areas activated in our study and the recalibration study in adults indicates that this network is already in place in 8-10 year-old children.

Despite this similarity at the whole brain level, our subsequent ROI analyses showed a significant reduction in brain activation in dyslexic compared to typically reading children in a region that is involved in the visual processing of text – the left fusiform (Ghislaine Dehaene-Lambertz et al., 2018; Dehaene & Cohen, 2011; Dehaene & Dehaene-Lambertz, 2016; Dehaene et al., 2010; Monzalvo & Dehaene-Lambertz, 2013). The observed group difference remained significant in an additional analysis in a subgroup of children (N=22, 11 dyslexic readers) who did show a text-based recalibration effect in the MRI scanner. This finding is in line with previous studies reporting under-activation of the left ventral occipito-temporal cortex in readers with dyslexia (Dehaene & Cohen, 2011; Hoeft et al., 2007; Paulesu, 2001; Richlan et al., 2009; Wimmer et al., 2010), as well as at-risk pre-readers (Centanni et al., 2019; I. Karipidis et al., 2017; Plewko et al., 2018). Activation within this ROI was furthermore positively associated with reading fluency and phoneme deletion, indicating that better reading and phonological skills were linked to increased left fusiform activation during audio-visual exposure to letters and ambiguous speech sounds. This finding corroborates and extends previous research reporting an association between reading fluency and accuracy and cortical activation in this region in response to text (Ben-Shachar et al., 2011; Blau et al., 2010).

The positive association between activation in the left fusiform ROI with phoneme deletion and reading scores likely reflects the ongoing refinement of letter-speech sound coupling in children within our age range. Areas in the left fusiform gyrus have been found to play a role in text-speech coupling (Graves, Desai, Humphries, Seidenberg, & Binder, 2010), categorical perception of phonemes (Conant et al., 2014), and to be modulated by auditory stimuli (McNorgan & Booth, 2015). This may be even more so in children, as previous developmental studies report more overlap in activation for visual and auditory tasks in unimodal brain areas in children compared to adults (Booth et al., 2001) as well as a transformation of bilateral higher order visual areas from

multimodal to unimodal processing over the course of (reading) development (Church, Coalson, Lugar, Petersen, & Schlaggar, 2008). Thus, we may conclude that the observed group difference in cortical activation between dyslexic and typical readers in this ROI was driven by children's reading and phonological skills and adds to the body of research showing altered processing of letters, and their mapping to speech sounds, in the left fusiform in children with dyslexia.

The comparable behavioural performance on the text-based recalibration task in children with and without dyslexia despite differences in brain activation remains to be explained. A possible interpretation could be that children with dyslexia rely more on a dorsal, more explicit reading cortical system involved in mapping letters and speech sounds and have not yet made the switch to the more automatized ventral cortical system involving the left fusiform (Pugh et al., 2001; Sandak et al., 2004). Indeed, a longitudinal study in children with and without dyslexia reported a later refinement of the ventral occipito-temporal cortex in the dyslexic readers (Morken et al., 2017). Moreover, cross-sectional studies investigating connectivity between the ventral and dorsal reading systems report aberrant connectivity in dyslexic compared to typical readers (Finn et al., 2014; Schurz et al., 2015; van der Mark et al., 2011). Although this hypothesis will need to be investigated in future studies, the dyslexic children may have achieved similar task performance through a subtle difference in the involvement of ventral versus dorsal cortical networks compared to their typically reading peers. This pattern of different neural recruitment despite similar behavioral performance is further supported by the presence of reduced left fusiform activation in dyslexic versus typical readers when restricting the analysis to those children who did show text-based recalibration in the scanner.

A potential explanation for the observed group differences in left fusiform activation despite comparable task performance could be that functional and structural connectivity between the vOTC and dorsal brain regions involved in speech processing develop differently in children with reading difficulties, likely as a result of a variety of risk- and protective factors (Ozernov-Palchik & Gaab, 2016; Perry et al., 2019; Zuk et al., 2020). It has been proposed that structural connectivity patterns between the text-sensitive visual word form area (VWFA) in the vOTC and the dorsal reading (speech processing) system are established prior to formal reading instruction in pre-reading children around the age of 5 (Saygin et al., 2016). A study in children of the same age at familial risk for developing dyslexia has furthermore shown that at-risk children who go on to

develop reading difficulties, show less activation in this region compared to both at-risk children who become typical readers and children without a familial risk (Centanni et al., 2019). Furthermore, developmental changes in functional connectivity patterns between VWFA and the dorsal reading system have been shown to parallel gains in reading fluency (Wise-Younger et al., 2017). Thus, if the connectivity patterns are already established at the pre-reader stage and those children who go on to struggle with reading show less activation in the left vOTC early on, aberrant connectivity patterns between the ventral and dorsal reading systems may have contributed to and/or underlie differences in functional activity during letter-speech sound processing as observed in the current study.

Unlike previous studies (Blau et al., 2010, 2009; Monzalvo et al., 2012), we did not find significantly reduced superior temporal cortical activity in dyslexic versus typically reading children, and this activity also did not scale with individual differences in reading and/or phonological skills (Bonte, Ley, Scharke, & Formisano, 2016; Brennan, Cao, Pedroarena-Leal, Mcnorgan, & Booth, 2013; Conant et al., 2014). This discrepancy could relate to the type of task employed (i.e. recalibration task instead of letter-speech sound congruency manipulation), use of ambiguous speech stimuli, characteristics of our dyslexia sample (children at the beginning of remediation focused on letter-speech sound automatization), or family history of dyslexia (Hakvoort, van der Leij, Maurits, Maassen, & van Zuijen, 2014; Vandermosten et al., 2020). Interestingly, our findings showed the opposite pattern where less fluent letter-speech sound identification was related to increased bilateral STC activation. This implies stronger involvement of the bilateral STC during the processing of letters and (ambiguous) speech sounds in children who are slower in the audio-visual mapping of these type of stimuli. This stronger involvement of the bilateral STC could be a result of the principle of inverse effectiveness (Wallace, Wilkinson, & Stein, 1996). This principle postulates that multi-sensory integration is the highest when stimuli from the two modalities are weak. The inverse effectiveness principle has been observed in the STS as an increased response to degraded audio-visual lip-read words (Stevenson & James, 2009) and in degraded audio-visual sentence comprehension behaviourally (van de Rijt, Roye, Mylanus, van Opstal, & van Wanrooij, 2019). While the visual stimuli in our study are clear, the auditory stimuli are ambiguous and may thus be considered “weaker” in terms of sensory input. The visual text could therefore be used to facilitate the auditory stimulus processing, increasing neural interaction and improving the stimulus identity prediction (Van Atteveldt, Murray, Thut, &

Schroeder, 2014). However, this facilitation might not be as profound in children with less fluent (i.e. automatic) letter-speech sound mapping. Thus, we might speculate that children with lower scores on the letter-speech sound identification task may have benefited more from inputs to both, the auditory and visual modality during letter-speech sound integration, resulting in the observed increase in bilateral auditory cortical activation. Another factor that influences multi-sensory integration is cue reliability, i.e. which cue is relevant for a given task (Van Atteveldt et al., 2014). Children with more automatized letter-speech sound representations may be better equipped to weigh the clear visual stimulus (“aba”/ “ada” text) as the most reliable one, therefore facilitating audio-visual integration, possibly resulting in less cortical activation. Thus, our findings imply that (1) left-fusiform activation during audio-visual exposure to letters and (ambiguous) speech sounds scales with inter-individual differences in children’s reading and phonological skills, and (2) increased bilateral STG activation may be required for (comparable) audio-visual integration in children with less automatic letter-speech sound representations.

Conclusion

The current fMRI study investigated text-based recalibration in 8-10 year-old children with and without dyslexia. Our results revealed that children within this age-group show a significant recalibration effect regardless of dyslexia diagnosis. Nevertheless, group comparisons within key reading and audio-visual integration ROIs revealed significantly higher activation in a left fusiform ROI in typical readers compared to children with dyslexia, which correlated with children’s reading and phonological skills. These findings corroborate previous research indicating altered functionality of text-sensitive left occipito-temporal cortex in dyslexic readers. The correlation analyses also showed differences in brain activation patterns in bilateral STG with more activation seen in children with poorer performance on a letter-speech sound identification fluency task. While speculative, we believe that this negative association may be linked to differential processing of the audio-visual information in children with less automatized letter-speech sound mapping. Subsequent investigations of changes in cortical activation and behavioural performance within the same cohort longitudinally will enable exploration of inter-individual differences within and across groups as their reading skills develop.

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Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

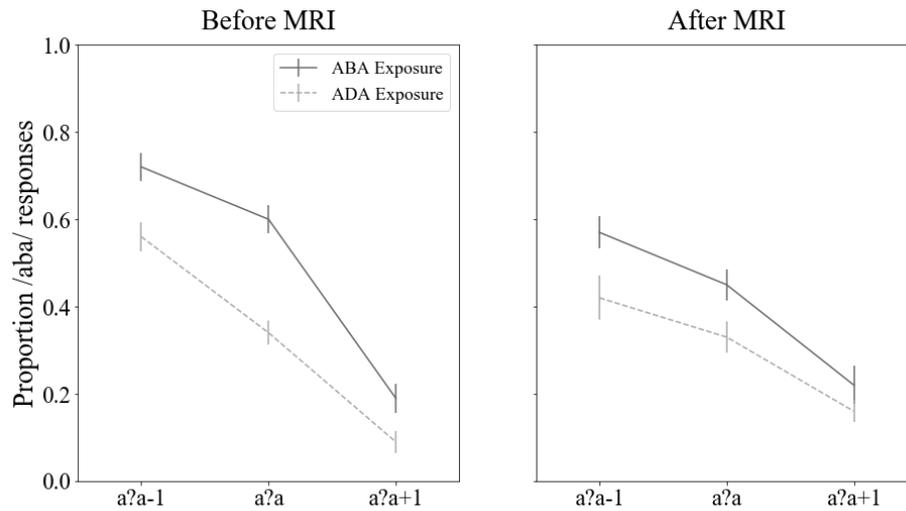
Funding

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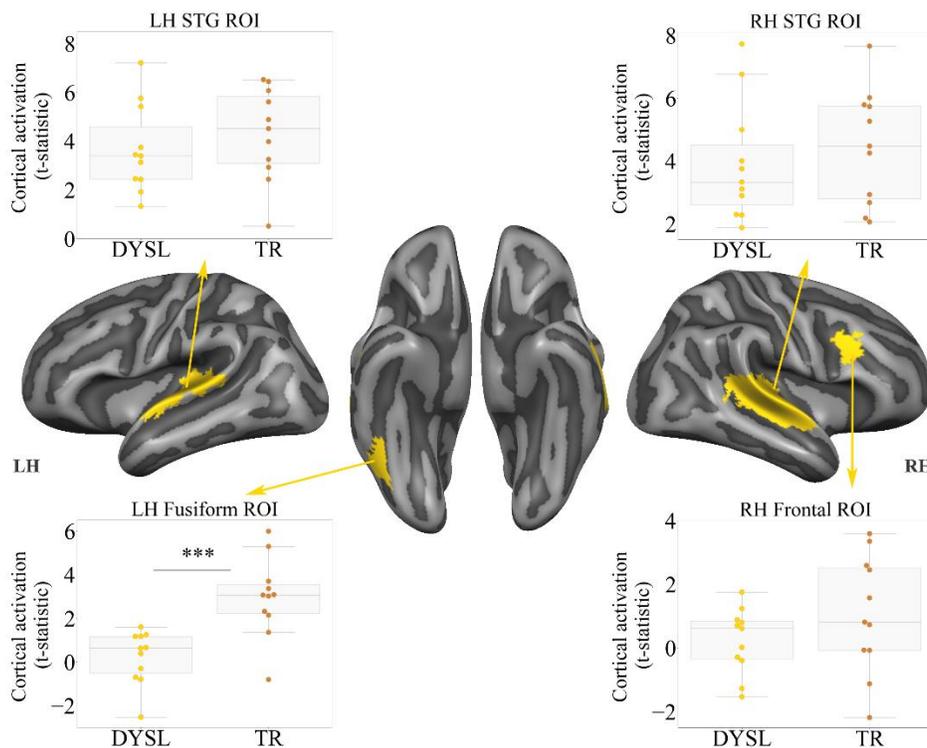
Data availability

A subset of data sets for which parents have given data sharing consent as well as all code used for task presentation and data analysis are available from corresponding author on reasonable request.

Supplementary materials

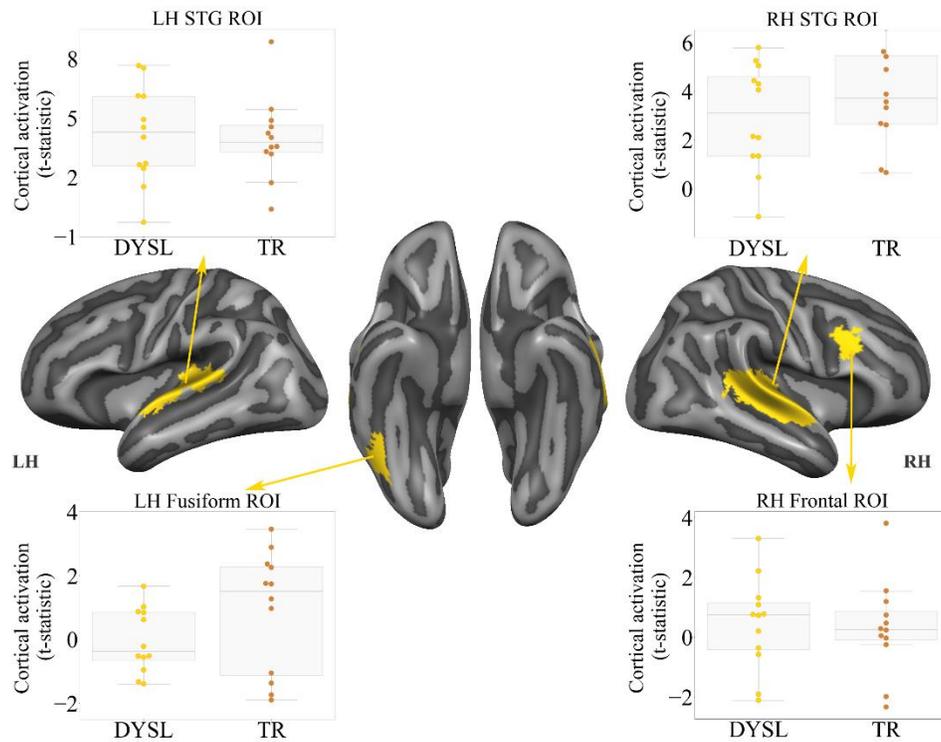


S1: /aba/ response proportions for the /a?a-1/, /a?a/ and /a?a+1/ post-test sounds following an “aba” versus “ada” exposure block in children who completed the behavioural experiment before the MRI session (left) and children who completed it afterwards (right).



S2: Group differences in cortical activation during the audio-visual exposure blocks within the regions of interest between dyslexic (DYSL; gold) and typical readers (TR; brown) who show a text-based recalibration effect in the MRI scanner. Cortical activation is represented as individual t-statistics per participant (gold and brown dots) and group box-plots (grey) for each group. *** = $p < 0.001$

Neuroimaging results text-based recalibration in children



S3: Group differences in cortical activation during the audio-visual exposure blocks within the regions of interest between dyslexic (DYSL; gold) and typical readers (TR; brown) who do not show a text-based recalibration effect in the MRI scanner. Cortical activation is represented as individual t-statistics per participant (gold and brown dots) and group box-plots (grey) for each group.

4

Longitudinal neuroimaging findings of text-based recalibration in typically reading children

Based on

Romanovska, L, Janssen, R., & Bonte, M. “Auditory cortical responses to letter-speech sound stimuli peak around age 9 in typically reading children”. *Manuscript submitted for publication.*

Abstract

While children are able to name letters fairly quickly following the onset of reading instruction, the automatization of letter-speech sound mappings continues over the first years of reading development. In the current longitudinal fMRI study, we explored developmental changes in cortical responses to letters and speech sounds across 3 yearly measurements in 8-11 year old typically reading children. We employed a text-based recalibration paradigm in which combined exposure to text and ambiguous speech sounds shifts participants' later perception of the ambiguous sounds towards the text. Our results revealed a significant developmental change in left superior temporal gyrus activity. Namely, activity in response to letter-speech sound stimuli in this region followed an inverted-u-shape developmental pattern with a peak in activation during the second measurement that was driven by 9-year-olds. This finding is reminiscent of previously reported inverted-u trajectories in children's visual cortical responses to text. The similarity in findings may hint at a more general non-linear pattern of changes in the brain's reading network associated with specific phases in the acquisition of reading skills.

Keywords: fMRI, longitudinal changes, audio-visual integration, recalibration, reading development, letter-speech sound mapping

Introduction

Reading is an evolutionary novel, culturally acquired skill that requires us to associate speech with visual symbols. The initial mappings between letters and speech sounds are typically acquired within the first months of reading instruction (Blomert, 2011; Perfetti, 2003), particularly in orthographically transparent languages with relatively consistent letter-speech sound associations such as Dutch, German, Italian or Hungarian (Borgwaldt, Hellwig, & De Groot, 2005). However, the fine-tuning and automatization of letter-speech sound integration continues while children strengthen their word decoding skills over the first years of reading development (Blomert, 2011; Ehri, 2005; Froyen et al., 2009; Žarić et al., 2014).

During this protracted developmental period brain areas involved in speech and visual letter processing become increasingly connected, both functionally and structurally (Dehaene et al.,

2015; Gullick & Booth, 2014; Schlaggar & McCandliss, 2007; Vandermosten, Boets, Wouters, et al., 2012; Yeatman et al., 2012). This drives the adaptation of the individual brain areas for the task of reading. For example, a region in the (left) higher order visual cortex, often referred to as the visual word form area (VWFA), becomes increasingly specialised for text processing (Ben-Shachar et al., 2011; Brem et al., 2009; Ghislaine Dehaene-Lambertz et al., 2018; Maurer et al., 2006). The continuous functional specialization within this brain region has been proposed to follow an inverted-u-trajectory, showing an increase in activation during early reading instruction followed by a gradual decrease in activation with reading expertise (Price & Devlin, 2011). This pattern of cortical activation in the VWFA has been reported during the first year of formal reading instruction in response to visual word presentation (Ghislaine Dehaene-Lambertz et al., 2018), as well as when comparing cortical responses to text longitudinally between kindergarten and second grade versus adult readers (Maurer et al., 2006). A similar non-linear pattern of developmental change can also be inferred from across study comparisons of neural sensitivity to (in)congruency of letter-speech sound pairs (Fraga González, Žarić, Tijms, Bonte, & van der Molen, 2017; Froyen et al., 2009; Žarić et al., 2015). Next to inverted-u-shape changes, other types of developmental trajectories, including linear changes, have also been observed for e.g. functional responses to speech sounds (Bonte, Ley, Scharke, & Formisano, 2016), white matter connectivity (Yeatman et al., 2012), and cortical grey- and white matter anatomy (Giedd et al., 1999; Gogtay et al., 2004; Hedman, van Haren, Schnack, Kahn, & Hulshoff Pol, 2012; Mills et al., 2016; Sowell et al., 2003).

The link between speech and text processing has typically been illustrated by modulations in cortical activation in response to matching (congruent) versus nonmatching (incongruent) audio-visual letter-speech sound stimuli. Functional magnetic resonance imaging (fMRI) studies employing such congruency manipulations have shown increased activation of speech sensitive areas within the superior temporal cortex (STC) in response to congruent letter-speech sound pairs compared to incongruent pairs and speech alone (Blau, Van Atteveldt, Formisano, Goebel, & Blomert, 2008; Raij, Uutela, & Hari, 2000; Van Atteveldt, Formisano, Goebel, & Blomert, 2004). Furthermore, the strength of STC responses to congruent audio-visual stimuli has been found to scale with individual differences in phonological and reading skills (McNorgan et al., 2014, 2013) and with reading problems in dyslexic readers (Blau et al., 2010, 2009; Kronschnabel et al., 2014; Ye et al., 2017b). However, congruency manipulation paradigms rely on learnt letter-speech sound mappings and involve additional cognitive and verbal working memory processes that may vary

with participants' reading (Plewko et al., 2018) and selective attention (Talsma & Woldorff, 2005) skills.

An alternative approach to investigating letter-speech sound mappings can be found in learning paradigms, such as recalibration. Recalibration studies explore short-term perceptual learning associated with mapping ambiguous speech onto a disambiguating visual stimulus (Bertelson et al., 2003; Keetels et al., 2018; Norris et al., 2003; Ullas, Formisano, et al., 2020; Vroomen & Baart, 2012). Here we employed text-based recalibration in a longitudinal fMRI design to follow changes in letter-speech sound processing in typically reading children. Our recalibration paradigm combines “aba” and “ada” text with an ambiguous /a?a/ speech sound mid-way between /aba/ and /ada/ (Bonte, Correia, Keetels, Vroomen, & Formisano, 2017; Keetels et al., 2018; Keetels, Schakel, Bonte, & Vroomen, 2016; Romanovska, Janssen, & Bonte, 2019). These clear text stimuli are combined with the ambiguous speech sound during audio-visual exposure blocks and shift the listener's subsequent perception of the ambiguous /a?a/ sound towards the text during auditory-only post-test trials. Thus, after being exposed to “aba” text combined with the /a?a/ sound, the listener is more likely to perceive the ambiguous sound as /aba/, and after combining the same ambiguous speech sound with “ada” text, it is more likely to be perceived as /ada/. This shift in perception is called recalibration and has previously been reported using lip-read speech (Bertelson et al., 2003; Ullas, Formisano, et al., 2020; Vroomen & Baart, 2012), spoken word context (Norris et al., 2003; Ullas, Formisano, et al., 2020) and overt speech articulation (Scott, 2016a). Behaviourally, reliable text-based recalibration effects have been observed in 8-10 year old children (Romanovska et al., 2019). Moreover, the strength of the recalibration effect was found to be associated with children's categorical perception of phonemes.

In this study we investigated developmental changes in cortical activation and recalibration task performance in typically reading children scanned yearly over a three year period from ages 8-9 to 10-11 years. We focused our analyses on the audio-visual exposure blocks, during which the children were simultaneously presented with the ambiguous /a?a/ sound and disambiguating text. Children's responses during the subsequent auditory-only post-test trials were used to assess the magnitude of the recalibration effect behaviourally. A previous fMRI investigation in adults has shown that during the exposure blocks, a network of brain areas associated with audio-visual integration and reading, including auditory, visual, parietal and frontal regions, is involved in

‘installing’ the perceptual bias that subsequently leads to the recalibration effect (Bonte et al., 2017). Furthermore, a similar cortical network was shown to be activated in children (Romanovska, Janssen, & Bonte, 2021). In the present study, we were particularly interested in exploring longitudinal developmental changes in these audio-visual and reading related brain areas across the measurements, and their link to task performance, and children’s phonological perception and reading skills.

Methods

Participants

A total of 43 typically reading children (mean age at time-point 1: 8.9 ± 0.7 years; 24 females) were recruited from local elementary schools in the Maastricht area in the Netherlands. Of these children, 7 completed only the first measurement, 16 completed the first 2 measurements, and the remaining 20 participants participated in all 3 measurements of the given study. Note that the relatively large number of children who dropped out after the 2nd measurement was due to an almost 4 month closure of the MRI research facilities during the first Covid-19 lock-down (March-June 2020). Of the 20 participants, one was excluded from the analyses due to poor data quality in session 3, and one participant had undergone remediation for dyslexia. The final sample consisted of 18 typically reading children who participated in all 3 longitudinal measurements (mean age at time-point 1: 8.7 ± 0.6 years; 11 females; 1 left-handed). The average time between the first two measurements was 13 months (± 1.7 months; mean age at time-point 2: 9.8 ± 0.6 years) and the average time between measurements 2 and 3 was 10.4 months (± 1.9 months; mean age time-point 3: 10.6 ± 0.59 years). The shorter time period between measurements 2 and 3 was driven by 5 participants who were scanned on average 8 months after the second measurement (range 6 – 9 months) due to planned orthodontic treatment that would have resulted in discontinuation of research participation. All children were native Dutch speakers, had no reported hearing impairments, normal or corrected-to normal vision and no history of developmental or neurological disorders. All children received a present (in session 1) or a gift card (sessions 2 and 3) for participation, along with a small, customised gift per scanning session. Parents provided written informed consent prior to each measurement in accordance with the declaration of

Helsinki. The study was approved by the ethics committee of the Faculty of Psychology and Neuroscience, Maastricht University.

Literacy and Cognitive skills

After each scanning session, the children completed computerized tasks of the 3DM test battery (Dyslexia Differential Diagnosis; Blomert & Vaessen, 2009) assessing reading and phonological skills. Additionally, at first and last measurements, the children completed two sub-tests of the Dutch version of the Wechsler Intelligence Scale for Children-III (WISC-III-NL; Kort et al., 2005) – verbal (similarities) and non-verbal (block design). The subsequent sub-tests of the 3DM were used in the present study: reading, letter-speech sound identification and phoneme deletion (elision).

The reading task was divided into three sections: reading of high-frequency, low-frequency and pseudo words. The total duration of the task was 90 s (30 s per category) and the children were instructed to read as quickly and accurately as possible. Reading fluency was calculated as the total number of words read within the time limit. During the letter-speech sound identification task, the children were presented with a speech sound aurally via headphones and asked to indicate the corresponding letter(s) out of 4 possibilities presented on the computer screen, by button press. Letter-speech sound identification fluency was calculated as the number of correctly identified items out of 90 (maximum items included in the task). The phoneme deletion task consisted of aurally presented pseudo-words, followed by an aurally presented phoneme. The children were instructed to repeat the pseudo-word without the phoneme (e.g. say /tesk/ without the /s/ sound). The fluency score for this task was calculated as the number of correctly completed items out of 28 (maximum). All task instructions were simultaneously presented aurally over headphones and visually on the computer screen. The children were instructed to perform all tasks as quickly and accurately as possible. Descriptive statistics of the sample and the reading scores across sessions are reported in Table 1.

	Session 1		Session 2		Session 3	
	Mean	Range	Mean	Range	Mean	Range
Age (years)	8.75	8 – 9.7	9.88	9.1 – 11	10.68	9.9 – 11.6
Reading fluency (raw) ⁴	113.72	74 – 178	129.29	96 – 181	137.53	99 – 201
Reading fluency (t) ⁵	52.27	30 – 80	53.17	32 – 80	53.12	30 – 80
Letter-speech sound identification fluency (raw)	42.72	39 – 45	42.29	38 – 45	42.58	39 – 45
Letter-speech sound identification fluency (t)	54.78	48 – 73	58.06	39 – 68	56.70	40 – 72
Phoneme deletion fluency (raw)	17.05	2 – 23	17.59	9 – 23	19.41	10 – 23
Phoneme deletion fluency (t)	51.72	0 – 70	58.59	37 – 80	57.29	29 – 71
WISC Verbal (Similarities) ⁶	15.22	12 – 18	-	-	15.06	10 - 19
WISC Non-verbal (block design) ⁶	12.78	9 – 19	-	-	11.88	6 - 17

Table 1: Descriptive statistics of the sample

Stimuli

The auditory stimuli employed in the recalibration task consisted of 650 ms recordings of the speech sounds /aba/ and /ada/ spoken by a male native Dutch speaker (see Bertelson et al., 2003 for a detailed description). The speech sounds were used to create a nine-token sound continuum ranging from a clear /aba/ sound to a clear /ada/ sound, with 7 ambiguous sounds in between, by changing the second formant (F2) in eight steps of 39 Mel using PRAAT software (Boersma & Weenink, 2001). The visual stimuli consisted of corresponding “aba” and “ada” text presented in white at the centre of a black screen in ‘Times New Roman’ font (font size 50). The auditory and visual stimuli were presented using Presentation software (Version 18.1, Neurobehavioral Systems, Inc., Berkeley, CA, United States).

⁴ Raw scores, number of correct items across three sub-groups (high-frequency, low-frequency and pseudo words) per 90s, number of correct responses out of 90 items (letter-speech sound identification) or 28 items (phoneme deletion)

⁵ t-Scores, age-appropriate norm scores mean 50, SD=10

⁶ Age-appropriate norm scores mean 10, SD = 3

Experimental design and procedure

All testing sessions started with a practice round in a mock scanner, followed by the actual (f)MRI scans, and ended with literacy and cognitive skill testing. During the mock scanner practice, the children were introduced to the scanner environment, including the use of in-scanner MR compatible headphones (Sensimetrics, model S14, www.sens.com) and button boxes, as well as the types of scanner sounds they would hear. At the beginning of the practice session, the children were reminded of how to perform the Recalibration task, and the scanning procedure and duration were explained. The children then completed a pre-test (see below), practiced one round of the Recalibration task and completed motion training, in order to improve later (f)MRI data quality. During motion training, an elastic headband containing a motion tracker was placed on the child's forehead. The sensor was calibrated to indicate when motion along the horizontal and/or vertical plane exceeded 2 degrees and linked to an in-house movie player software that was used to play a cartoon. As soon as head motion exceeded the 2 degree threshold, the cartoon paused and shrank until the child was lying still again. This helped illustrate how still the children should aim to lie in the real MRI scanner while doing the tasks and to get them used to the MR environment. The mock scanner session lasted approximately 15 – 20 minutes. The children subsequently took part in a 1 hour 15 minute MRI session. While the total time required for the acquisition of the functional and structural images was 45 minutes, we took the time to make sure the children were comfortable when preparing to go into the scanner and allowed for short breaks between each anatomical/structural scan to avoid fatigue. After the MRI session, the children completed the reading and phonological tasks in sessions 1, 2 and 3 (± 20 minutes) and the two subtests of WISC-NL-III in sessions 1 and 3 (± 20 minutes). The total testing time was approximately 2 hours 15 minutes. Additionally, children had 2 breaks – one after completing the mock scanner practice round, and one after the MRI scan before completing the reading and cognitive tasks.

Pre-test

During the mock scanner session, children completed a pre-test, in which they heard each of the 9 sound tokens along the /aba/-/ada/ continuum a total of 98 times in a randomized order, with the middle sounds along the continuum presented more frequently than the two clear tokens (similarly to Bertelson et al., 2003; Kilian-Hutten, Valente, Vroomen, & Formisano, 2011; Vroomen, Van

Linden, Keetels, De Gelder, & Bertelson, 2004). The children were instructed to listen carefully to each sound and to indicate if they perceived it as /aba/ or as /ada/ by pressing the left or right innermost button of the MR compatible button box with their left/right index finger following a response cue. The response cues consisted of text “aba” (left) and “ada” (right), held up by cartoon monsters created using the Monster Workshop content pack of the iClone 6 software (<https://www.reallusion.com/>). During the presentation of the speech sounds, the children viewed a black screen with a white fixation cross followed by the response cue 1 s later. Each trial was terminated after the child provided a response, triggering the presentation of the subsequent speech sound after 2 s (Figure 1). The total duration of the pre-test was approximately 5 minutes.

The results of the pre-test were used to individually determine the most ambiguous speech sound along the /aba/ - /ada/ continuum for each participant, based on the proportion of /aba/ responses to each sound token. The most ambiguous sound was identified as the token with an /aba/ versus /ada/ response proportion closest to 0.5, representing the phoneme boundary (Romanovska et al., 2019; Vroomen et al., 2004). This individually determined most ambiguous sound was used in the audio-visual exposure blocks and post-test trials of the recalibration task. In addition to the most ambiguous /a?a/ sound, the post-test trials also included its two flanking sounds along the /aba/-/ada/ continuum, namely /a?a/+1 and /a?a/-1. Additionally, the resulting sigmoidal curve showing the response proportions to each sound token, served as an indicator of children’s categorical perception of the phonemes /aba/ and /ada/, with a steeper curve representing a sharper distinction between phoneme categories.

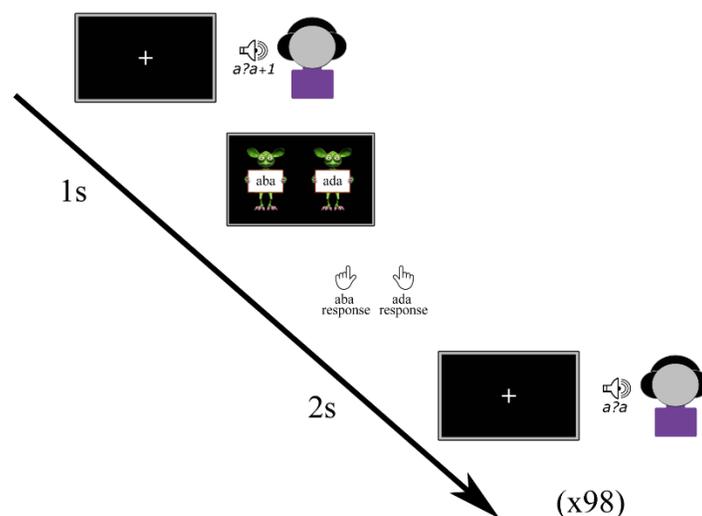


Figure 1: Pre-test

Recalibration task

The recalibration task consisted of audio-visual exposure blocks followed by auditory post-test trials (Figure 2). During each exposure block, the children were presented with either the text “aba” or “ada” in combination with the individually determined most ambiguous speech sound /a?a/ 8 times. The audio-visual stimuli were presented simultaneously (relative SOA of 0 ms), the duration of the auditory stimuli was 650 ms and visual text was presented for 1s. The inter-trial interval between subsequent audio-visual exposure trials was set to 2 s (1 TR). The /aba/ and /ada/ exposure blocks were presented in a pseudo-randomised order, making sure that the same type of exposure block was not repeated more than twice in a row. During the audio-visual exposure blocks, the children were instructed to pay close attention to the speech sounds and text without providing a response.

Each exposure block was followed by four auditory-only post-test trials, the onset of which was jittered to 10s (4-6 TR). These jittered periods served as the baseline condition, during which the children fixated on a white cross in the middle of a black screen. The post-test trials were presented in a randomized order with the most ambiguous sound /a?a/ presented twice, and each of the flanking sounds /a?a/+1 and /a?a/-1 on the /aba/-/ada/ continuum presented once. Following each post-test sound, a response cue containing cartoon monsters appeared on the screen. The duration

of the response cue was fixed to 3 s and the onset was jittered 2,5 - 3 s with respect to the post-test sound. The subsequent post-test trial was presented 3 - 3,5 s following the response cue. The total inter trial interval (ITI) between post-test trials was 6 s (3 TR). Children were instructed to listen carefully to each post-test sound and to respond whether they perceived it as /aba/ or as /ada/ upon the presentation of the response cue using the MR-compatible button boxes. The responses were made by pressing the innermost button of the button box with the left/right index finger, as practiced in the mock scanner.

Children completed a total of four runs of the recalibration task, corresponding to 24 audio-visual exposure blocks (12 with “aba” text and 12 with “ada” text) and 4*24 post-test trials. The recalibration effect was calculated as the difference in average /aba/ response proportions across the post-test sounds following the two types of exposure blocks (i.e. total /aba/ response proportion after an “aba” exposure block minus total /aba/ response proportion following an “ada” exposure block). All auditory and audio-visual stimuli were presented during a 900 ms silent gap between volume acquisitions.

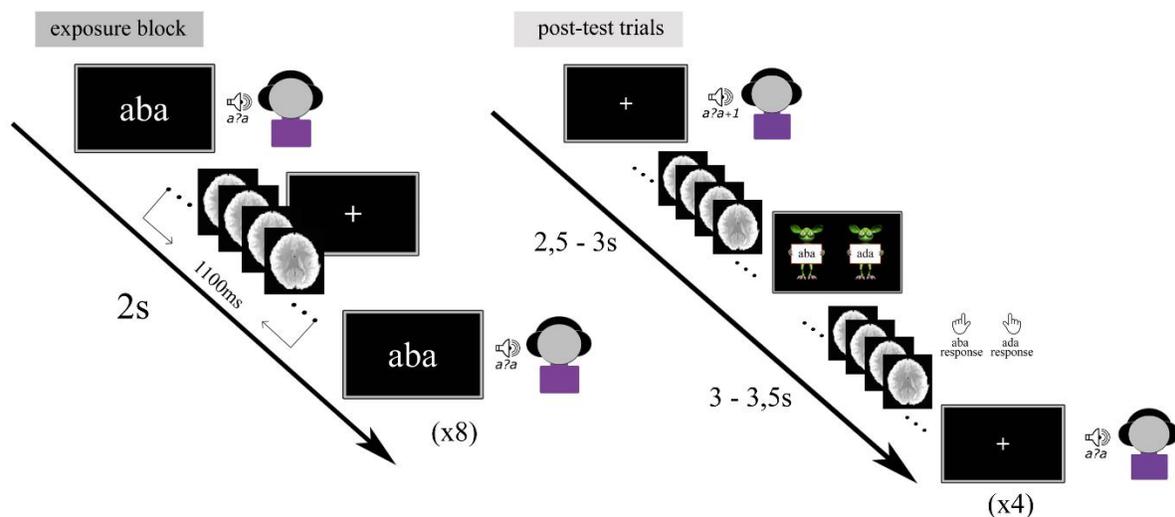


Figure 2: Text-based recalibration paradigm in the MRI environment

Statistical analyses behavioural data

Children’s performance on the pre-test and recalibration tasks was analysed using repeated measures (RM) ANOVA. The RM ANOVA analyses for the pre-test included within-subject

factors Session (1, 2, 3) and sound (1 - 9) and between-subject factor age group (younger, older). We grouped the participants according to their age at the first measurement into younger (age 8 – 8.6 years; 11 participants) and older (age 8.9 – 9.7; 7 participants) groups to explore the effect of age on recalibration and pre-test performance without confounding it with session effects. The same analyses were performed on the /aba/ response proportions of the Recalibration task. Here the ANOVA model consisted of within-subject factors: session (1, 2, 3), exposure type (“aba” vs “ada”) and post-test sounds (/a?a/-1, /a?a/, /a?a/+1) and between-subjects factor age group (younger, older). The degrees of freedom were adjusted using the Greenhouse-Geisser correction for conditions which violated the sphericity assumption. Prior to running the analyses, the data were assessed for outliers using boxplots. This amounted to 4 observations for the pre-test (two outliers – lower quartile plus 1.5 times inter-quartile range and two extreme outliers – lower quartile plus 3 times inter-quartile range) and one observation for the recalibration analyses (upper quartile plus 1.5 times inter-quartile range). For both analyses, the observations identified as outliers and extreme outliers were excluded.

The fit of the pre-test slope was estimated using the Slope Fitting tool in MATLAB 2019a (The MathWorks, Inc., Natick, MA, United States). The custom logistic function described in Romanovska et al. (2019; Function 1) was employed to obtain partial R^2 values and assess the fit of each subject-specific slope. The pre-test slope value (c in Function 1) providing the best fit to the data was obtained using the MATLAB least squares solver. To optimize the outcome, the variables in Function 1 were restricted to the following values: $0 \leq a \leq 10$, $-10 \leq b \leq 10$, $-10 \leq c \leq 10$, $-9 \leq d \leq 18$ and the best fit was determined after 30 iterations of the procedure.

$$y = \frac{a}{1 + e^{-\frac{(x-d)}{c}}} + b$$

Function 1: a = amplitude; b = lowest asymptote of y-axis; c = slope of the function; d = location of the category boundary.

(f)MRI measurements

Brain Imaging was performed with a Siemens Prisma 3T MRI scanner (Siemens Medical Systems, Erlangen, Germany) using a 64-channel head–neck coil. Five functional runs were acquired (2,5

mm x 2,5 mm x 2,5 mm resolution) with a multi-band factor of 5 echoplanar-imaging (EPI) sequence (repetition time [TR] = 2000 ms, acquisition time [TA] = 1100 ms, field of view [FOV] = 210 mm × 210 mm, echo time [TE] = 35.8 ms). Each volume consisted of 50 slices (no gap), covering the whole brain. The recalibration task consisted of four 5 minute runs, followed by a 7-minute localizer task not included in the current analyses. The speech stimuli were presented binaurally at a comfortable listening level via MR compatible headphones (Sensimetrics, model S14, www.sens.com), in the 900-ms silent gap between two consecutive volume acquisitions. Additionally, a high-resolution structural scan (1 mm × 1 mm × 1 mm) using a T1-weighted three-dimensional MPRAGE sequence ([TR] = 2300 ms, [TE] = 2.98 ms, 192 sagittal slices) was acquired.

(f)MRI pre-processing

Data pre-processing and analyses were performed using BrainVoyager QX version 2.8 and BrainVoyager versions 20.6 and 21.4 (Brain Innovation, Maastricht, The Netherlands) as well as custom MATLAB routines (The MathWorks, Inc., Natick, MA, United States). The functional data were aligned to the first volume of the first functional run and underwent 3D motion correction (trilinear sinc interpolation), slice scan time correction and high pass temporal filtering (5 cycles per time course). The anatomical data underwent manual inhomogeneity correction to improve white matter-grey matter boundary segmentation and was transformed into Talairach space (Talairach & Tournoux, 1988). To ensure all anatomical runs were well aligned across sessions, the native space anatomical data of sessions 2 and 3 was coregistered to the ACPC transformed session 1 anatomy using vmr-vmr coregistration in Brainvoyager QX. The resulting transformation file was subsequently applied to the anatomical runs of sessions 2 and 3 resulting in well aligned anatomical data. Transformation to Talairach space was performed using the transformation file of session 1.

The functional data were subsequently aligned across sessions by co-registration to the Talairach transformed anatomical data of session 1, re-sampled to 3 mm iso-voxel resolution and spatially smoothed using a 6 mm FWHM Gaussian kernel. Volumes of functional runs affected by excessive head motion (≥ 3 mm translation/rotation in any direction) were removed from the run. If the number of affected volumes exceeded 20%, the run was excluded from further analyses. This

amounted to a total of 5 runs across children in the second session and 6 runs across children in the third session. Additionally, not all children completed all four recalibration runs due to time constraints. The total number of runs not acquired across all three sessions was 12 (2 in session 1 and 5 in sessions 2 and 3). The final number of runs included in the analyses was 197: 70 session 1, 64 session 2, 63 session 3.

Individual cortical surface representations of session 1 anatomical scans were automatically constructed for each participant based on the white matter-grey matter boundary. The boundary was then manually adjusted, and aligned using cortex based alignment employing a moving-target group average based on curvature information, resulting in an anatomically-aligned group-average 3D cortical representation (Frost & Goebel, 2012). Each participant's functional data were projected onto their cortical surface to create surface-based time courses. All functional data were subsequently analysed per hemisphere at the surface level using the group-aligned average cortical surfaces.

Whole brain univariate fMRI analysis

Cortical activation across sessions was assessed using a random effects (RFX) general linear model (GLM) approach based on the individual surface-based time courses. The GLM included a predictor for each type of exposure block ("aba" and "ada"), predictors for each post-test sound (4 predictors) and z-transformed motion predictors as variables of no interest to improve the signal-to-noise ratio in the data. Based on the results of the GLM model, contrast maps (t-statistics) representing cortical activation during the exposure blocks ("aba" and "ada" blocks taken together; EXP) compared to the fixation cross baseline were created for each session and corrected for multiple comparisons with an FDR threshold of $q < 0.05$. Conjunction analyses were used to explore the differences in activation between sessions. Three conjunction contrasts were calculated – one to assess the activation differences between sessions 1 and 2: $EXP\ S1 > 0 \cap EXP\ S2 > 0 \cap EXP\ S2 > EXP\ S1$; one to assess the differences between sessions 2 and 3: $EXP\ S2 > 0 \cap EXP\ S3 > 0 \cap EXP\ S3 > S2$; and one to compare activation between sessions 1 and 3: $EXP\ S1 > 0 \cap EXP\ S3 > 0 \cap EXP\ S3 > S1$. This approach was used to limit the session comparisons to areas that showed a significant positive difference in activation compared to baseline. The resulting conjunction maps are shown at a voxel-level threshold of $p < 0.05$, corrected for multiple

comparisons using a cluster threshold $p < 0.05$. The conjunction analyses revealed a left hemisphere STG cluster that showed significant activation differences between sessions 1 and 2. The cortical activation (beta coefficients) within this cluster was assessed for significance using RM ANOVA. This comparison indicated increased activation (higher average beta coefficient value) in session 2 compared to sessions 1 and 3. The beta coefficients were further analysed using mixed regression.

Multiple regression analysis

Mixed regression analysis was performed to explore possible relations between behavioural measures and the observed changes in auditory cortical activation in the left STG (SPSS v26, IBM Corp., Armonk, NY, United States). We opted for this approach due to its reported suitability for accelerated longitudinal designs and tolerance for handling missing data (Tamnes, Bos, van de Kamp, Peters, & Crone, 2018; Vijayakumar, Mills, Alexander-Bloch, Tamnes, & Whittle, 2018). We constructed a marginal model including the beta values as the dependent variable, and within-subject variables: age (in months), reading fluency, recalibration effect, pre-test slope value, linear and quadratic time effects, as well as interactions of each time effect with the other variables. The letter-speech sound identification and phoneme deletion fluency scores were not included in the analysis as they did not show much variation across sessions (see Table 1). The two variables assessing linear and quadratic time effects allowed us to explore linear and non-linear developmental trajectories of STG activation across sessions. The quadratic time effect in particular was included to model the observed non-linear change in beta responses in the auditory cortex seen in the RM ANOVA results (see “fMRI activity during the exposure blocks”). Non-significant interactions were excluded in a step-wise manner, checking for model fit using Bayesian Information Criterion (lower value = better model fit). Prior to running the model, the data was assessed for outliers using boxplots. Six observations in total were identified as outliers/extreme outliers and excluded from the analyses. Four observations were outliers – two upper quartile plus 1.5 times inter-quartile range (one value for reading fluency, one for the recalibration effect) and two lower quartile plus 1.5 times inter quartile range (both pre-test slope values). Two additional pre-test slope values were categorized as extreme outliers, i.e. lower quartile plus 3 times inter-quartile range. Additionally, four observations had missing data – two pre-test slope values and two reading fluency measures. The final model reported below was a

Fixed-effects model estimated using Restricted Maximum Likelihood and an unstructured covariance matrix for repeated measures to optimally model the observed session effect in the left STG. Model residuals had a normal distribution and showed no heteroscedasticity. Based on the mixed regression results, we explored the cortical activation patterns within the left STG region further by dividing the participants into a younger and older age group, similarly as in the behavioural analyses.

Results

Pre-test results

The overall /aba/ response proportions to each of the 9 sound tokens indicate that all participants perceived the sound tokens closer to the /aba/ end of the continuum as /aba/ and the sounds closer to the /ada/ end of the continuum as /ada/ (see /aba/ response proportions for tokens 1-3 and 7-9, Figure 3 left panel). However, despite comparable pre-test slope shapes, the /aba/ response proportions for each of the 9 sound tokens did differ between the younger and older age groups (Figure 3). This was confirmed in a 3 (session) \times 9 (sound) \times 2 (age group) RM ANOVA analyses of the /aba/ response proportions, which revealed a main effect of sound [$F(2,23)=199.16$, $p < 0.001$, Greenhouse-Geisser corrected] and a sound by age group interaction [$F(2,23)=4.32$, $p < 0.05$, Greenhouse-Geisser corrected]. Neither the between-subjects factor age group nor the other within-subject main and interaction effects were statistically significant (all $F \leq 2.31$). To assess whether the sound by age group interaction was due to a difference in the steepness of the pre-test slopes between younger and older children, we performed an additional RM ANOVA analysis comparing the steepness of the pre-test slopes across sessions and between groups. The results did not reveal significant main- or interaction effects of session or age (all $F \leq 0.87$).

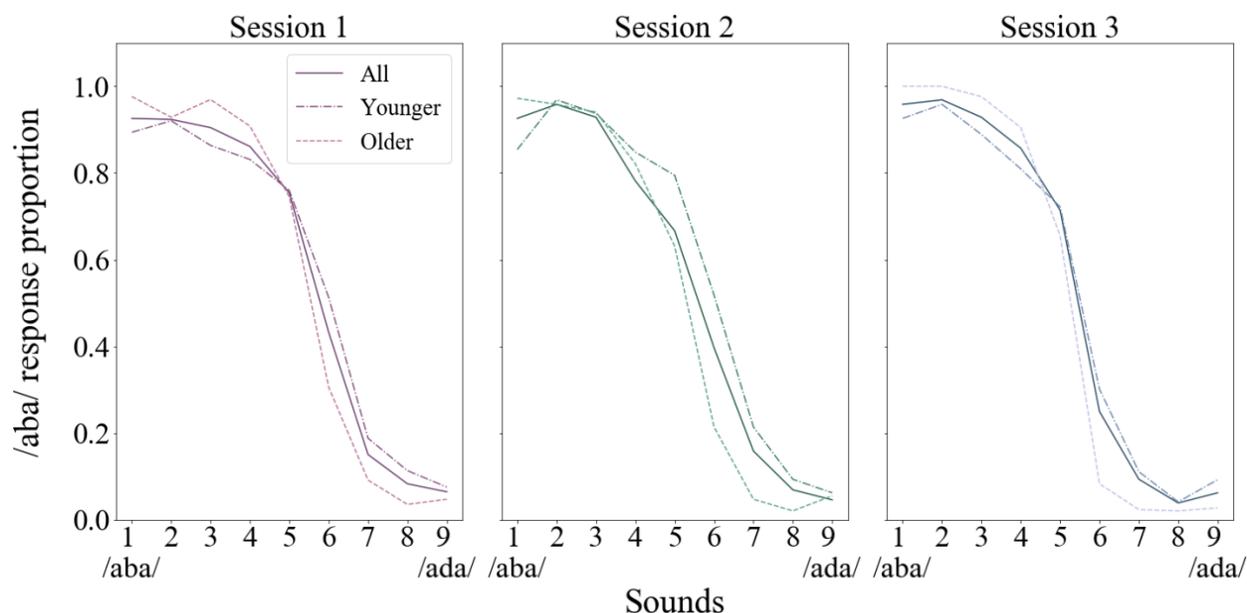


Figure 3: Pre-test results showing the proportion of /aba/ responses to each of the 9 sound tokens (1-9) on the /aba/-/ada/ continuum for all participants (solid line); younger group (dashed line) and older group (dotted line) for each of the sessions (1 -3 left to right).

Behavioural results Recalibration task

Children's responses to the post-test sounds showed a change in /aba/ response proportions across the ambiguous sound and its two flanking sounds along the /aba/-/ada/ continuum (Figure 4). As expected, there were more /aba/ responses for the sound /a?a/-1 closer to the clear /aba/ token, as well as for the ambiguous /a?a/ sound, compared to the /a?a/+1 sound that is closer to the clear /ada/ token. Accordingly, the 3 (session) \times 2 ("aba" / "ada" exposure block) \times 3 (post-test sounds) \times 2 (age group) RM ANOVA showed a main effect of post-test sound [$F(2,30)=146.96, p < 0.001$]. Additionally, a tendency for more /aba/ responses following 'aba' compared to 'ada' blocks (i.e. recalibration) seemed to increase across sessions. However, the corresponding interactions did not reach statistical significance: exposure by post-test sounds [$F(2,30)=3.12, p = 0.058$] and a three-way interaction between session, exposure block and post-test sound [$F(2,34)=2.74, p = 0.071$, Greenhouse-Geisser corrected]. Similarly, the between subjects factor age group and all other main- and interaction-effects did not reach statistical significance (all $F \leq 3.03$).

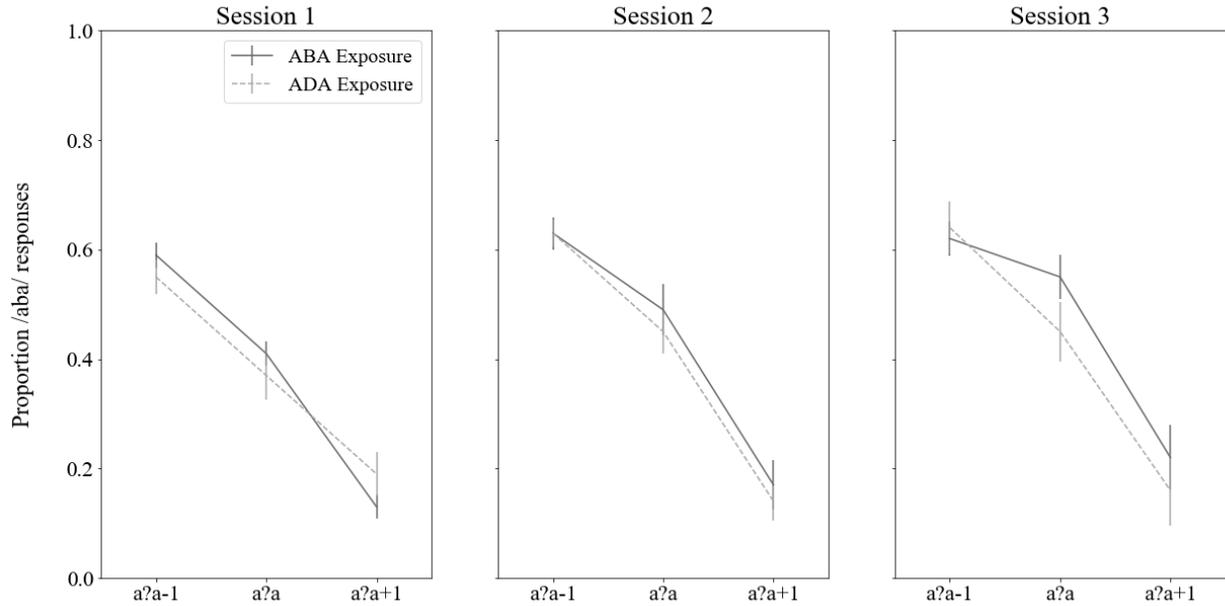


Figure 4: Behavioural text-based recalibration results showing the /aba/ response proportions (y-axis) for each of the three post-test sound tokens (x-axis) following “aba” (solid) and “ada” (dashed) exposure blocks in each MRI session

fMRI activity during the exposure blocks

The text and speech sound stimuli presented during exposure blocks of the recalibration task elicited significant activation in bilateral superior temporal gyri (STG), visual and parietal cortices, as well as in the left frontal cortex (Figure 5). Although at the given (FDR) threshold, the resulting maps appear to indicate a general broadening of this network from sessions 1 to 3, statistical comparison (conjunction contrasts) only revealed a significant session effect in a left hemisphere STG cluster (Figure 6a). To examine the pattern of activation change over time, we extracted individual beta values per session from this cluster. This revealed an inverted-u-shape response, with left STG activation peaking in session 2 (Figure 6b). We assessed the statistical significance of this session effect using RM ANOVA performed in BrainVoyager 20.6. The results confirmed higher average beta values in session 2 compared to sessions 1 and 3 [$F(2,53)=4.48, p = 0.018$].

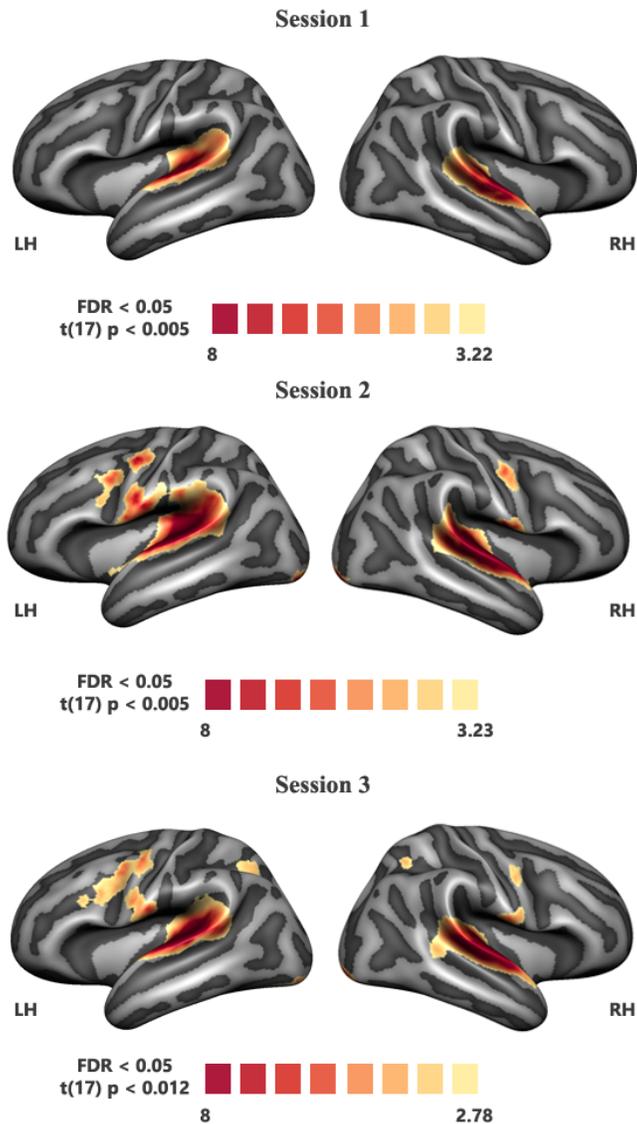


Figure 5: Cortical activation across all participants during the audio-visual exposure blocks compared to baseline in measurement 1 (top row), measurement 2 (middle row) and measurement 3 (bottom row); LH = left hemisphere; RH = right hemisphere

Mixed regression results

To explore how children's age, reading fluency and phoneme perception (pre-test slope steepness) may have influenced the change in left STG activity across sessions, we further assessed the individual beta values for each session with mixed regression. The model estimates are reported in Table 2. The analyses revealed a significant main effect of the quadratic time predictor [$F(1,11)=7.29$, $p < 0.05$], alongside a significant age by quadratic time effect interaction

[$F(1,11)=6.26, p < 0.05$]. These results confirm the observed inverted-u-shape change in the left STG cluster activation across sessions and indicate that this activation change is associated with participants' age in each session. Finally, an interaction between the pre-test slope steepness and the quadratic time effect approached statistical significance [$F(1,22)=3.74, p = 0.06$].

Variable	B estimate	Significance	95% CI	
			lower	higher
Intercept	-0.407	0.798	-3.695	2.881
Age in months	0.007	0.568	-0.019	0.034
Reading fluency	0.005	0.123	-0.001	0.011
Steepness of the pre-test slope	-0.204	0.331	-0.632	0.223
Recalibration effect	-0.034	0.891	-0.550	0.481
Linear time effect	-0.189	0.295	-0.556	0.177
Quadratic time effect	-2.075	0.019	-3.752	-0.398
Age in months * Quadratic time effect	0.016	0.029	0.002	0.029
Steepness of the pre-test slope * Quadratic time effect	-0.291	0.066	-0.605	0.021

Table 2: Model parameters of the best-fitting Fixed-effects marginal model; B estimate = beta value estimate; CI = confidence interval

To explore the age effect further, we separated the children into a younger (aged 8 during first measurement) and older (aged 9 during the first measurement) age group and plotted the average beta responses per group (Figure 6cd). The resulting graphs suggest that the younger age group drives the inverted-u-shape change. Namely, children who were on average 9 years old during session 2 showed a distinct peak in left STG that decreases by session 3. The older age group on the other hand, showed a relatively constant response within the STG cluster across sessions. We did, however observe a heterogeneity in activation changes across sessions within each age group, possibly pointing to individual differences in the exact timing of developmental changes (grey lines Figure 6cd).

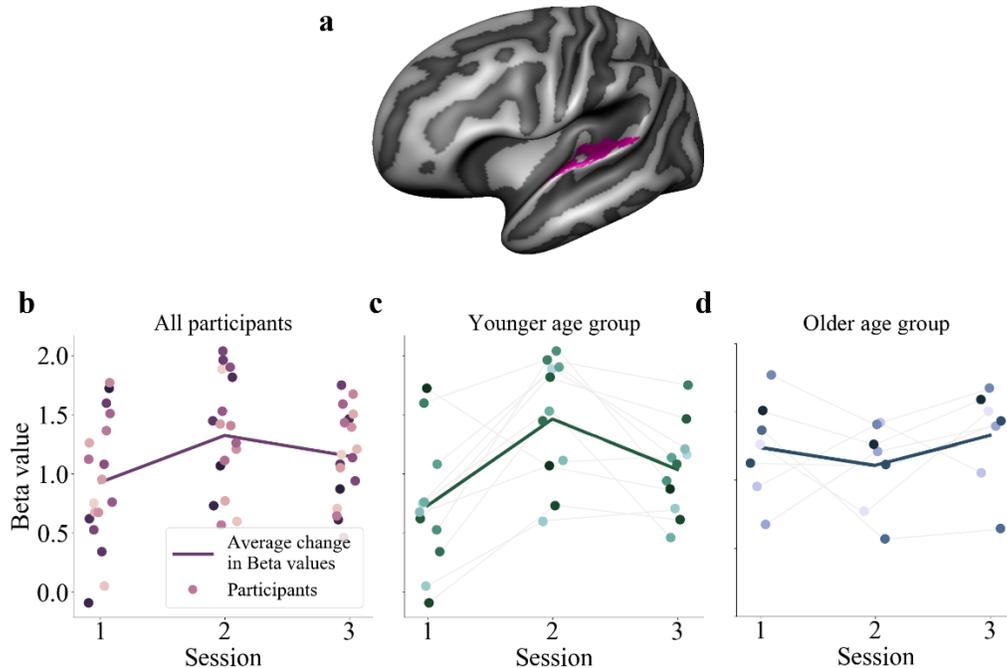


Figure 6: Top: (a) left hemisphere STG region showing a significant difference in cortical activation between sessions. Bottom: Individual beta values (y-axis) per participant (scatter dots) per session (x-axis) across participants (b), in the younger group (c) and in the older group (d). Light grey lines represent the individual trajectories of change in cortical activation across sessions

Discussion

In this longitudinal fMRI study, we investigated developmental changes in the brain's reading network using a text-based recalibration paradigm in typically reading children aged 8-9 to 10-11 years across 3 measurement time points spaced approximately 1 year apart. Our fMRI results showed a significant inverted-u-shape change in cortical activation in a left hemisphere STG region, with a peak in activation during session 2 that was driven by children aged 9 during that session.

All children successfully performed the text-based recalibration task, as reflected in the different /aba/ response proportions to the ambiguous post-test sounds following each type of exposure block. However, like in a previous study in 8-10 year-old children, these behavioural recalibration effects did not reach significance in the MRI scanner environment (Romanovska et al., 2021), while children in this age range did show significant text-based recalibration in an offline behavioural study (Romanovska et al., 2019). This discrepancy can likely be attributed to the

acoustic noise, and/or altered (visual) attentional focus in MRI environment (Kobald, Getzmann, Beste, & Wascher, 2016; van Maanen et al., 2016). Overall, the recalibration effect appeared to increase in strength across sessions, approaching significance by the last measurement. This may point to a strengthening of the text-based recalibration effect, or to general (developmental) improvements in e.g. attentional mechanisms and/or increased familiarity with the MRI environment with time. In line with a developmental effect, typically reading adults have been reported to show reliable recalibration effects both in and out of the MRI scanner (Bonte et al., 2017; Kilian-Hutten et al., 2011; Ullas, Hausfeld, Cutler, Eisner, & Formisano, 2020).

To investigate cortical activation associated with audio-visual processing of letters and speech sounds and its potential links to behavioural and reading measures, we focused our fMRI analyses on the audio-visual exposure blocks of the recalibration task. Our results showed bilateral cortical activation patterns across the sessions in brain areas previously linked to audio-visual integration and reading (Blau et al., 2010, 2009; Chyl et al., 2017; Dehaene et al., 2015; McNorgan et al., 2013; Van Atteveldt et al., 2004), as well as to text-based recalibration specifically (Bonte et al., 2017). These brain areas included bilateral superior temporal gyri, occipital and parietal areas as well as the left frontal cortex. Comparisons of brain activation between sessions revealed a left hemisphere STG cluster that was more active in session 2 compared to session 1. A closer investigation of activation within this cluster yielded an inverted-u-shape response that was statistically significant and driven by the younger age group, aged 9 during session 2. This developmental change is reminiscent of cross-sectional results reported in adults and children of different age groups in previous electroencephalography (EEG) studies employing an audio-visual oddball paradigm with letters and speech sounds. These studies have indicated audio-visual deviancy responses in two time windows – a mismatch negativity response (MMN) around 100-250 ms, associated with automatic processing of audio-visual letter-speech sound stimuli (Froyen et al., 2008; Näätänen, 2001; Žarić et al., 2014) and a sustained late negativity (LN) response associated with more “effortful” and deliberate integration mechanisms (Froyen et al., 2009; Žarić et al., 2015, 2014). Using this paradigm, 8-9 year-old typically reading children were observed to have a relatively wide audio-visual integration window and more pronounced audio-visual MMN and LN responses (Žarić et al., 2014) compared to both younger and older children (Froyen et al., 2009) as well as adults (Froyen et al., 2008). That is, the findings reveal an apparent evolution from an LN-only response in 7/8-year olds to both MMN and LN responses and a broad audio-

visual integration window in the 8/9-year olds, followed by increasing selectivity across 11-year olds and adults. This pattern of results arguably reflects a switch from more effortful to automatized audio-visual processing, with fully automatized letter-speech sound processing in adults. Our longitudinal STG findings may reflect a similarly enhanced response to letter-speech sound mappings in children around 9 years of age.

Based on previous findings, we expected that higher order visual areas would show a similar age-driven peak in activation. Studies investigating text specialization and sensitivity using both EEG and fMRI have shown inverted-u activation patterns of developmental change within ventral occipito-temporal cortex and the VWFA in particular (Gorka Fraga González et al., 2017; Maurer et al., 2006, 2011, 2008; Price & Devlin, 2011), accompanied by a similar change in grey matter volume of the left occipito-temporal sulcus (Ben-Shachar et al., 2011). The fact that we did not observe significant session-differences in vOTC activation in the current sample may be due to a lack of statistical power or, alternatively, task characteristics or age group differences. The exposure blocks of text-based recalibration combine a clear visual stimulus (text) with an ambiguous speech sound. The combination of the two modalities likely produces different auditory percepts across trials. This could result in an enhancement of activation in speech sensitive STG regions, that have been shown to encode these type of perceptual changes (Bonte et al., 2017; Bonte, Hausfeld, Scharke, Valente, & Formisano, 2014; Kilian-Hütten et al., 2011; Yi, Leonard, & Chang, 2019), especially at the age where letter-sound associations are in the process of becoming automatized.

Beyond changes specific to audio-visual integration of letters and speech sounds, reading and spoken language development may mutually lead to the refinement of cortical responses to speech during reading development. It has been proposed that learning to read in an alphabetic script in particular, alters phonological processing by magnifying the phonological representations of the smallest-possible visual unit (often a single letter) and is accompanied by a developmental increase in STG responses observed during auditory rhyme judgement tasks in alphabetic compared to logographic orthographies (Brennan et al., 2013). These reading-induced changes in speech perception may further affect categorical perception of phonemes (Harm & Seidenberg, 1999) and interact with reading skills (Conant et al., 2014). The observed peak in STG activation in session 2 may reflect such reading-related changes in cortical responsiveness to speech. Indeed, the

interaction between the inverted-u-response and pre-test phoneme categorization slope did approach significance. Developmentally, categorical perception of phonemes has been associated with left-lateralized activation of posterior STG that scales with increasingly distinct definition of phoneme categories in 7-12 year-old children (Conant et al., 2014). Furthermore, the STG shows distinct phoneme-category specific activation patterns following categorical learning and subsequent perception of novel speech sounds (Ley et al., 2012), as well as task-dependent (Bonte et al., 2014; Yi et al., 2019) and recalibration-induced (Bonte et al., 2017; Kilian-Hutten et al., 2011) changes in speech sound representation. Thus, our findings may reflect changes in cortical activation associated with reading development as well as the ongoing refinement of the brain's speech perception system.

Children may also show individual differences in the exact timing of developmental turning points related to e.g. learning phases in acquiring solid letter-speech sound mappings and cortical sensitivity to text stimuli. In line with this, we did observe individual differences in cortical activation changes across sessions within the left STG. It has been shown that children reach developmental milestones at different times (e.g. Flensburg-Madsen & Mortensen, 2018; Taanila, Murray, Jokelainen, Isohanni, & Rantakallio, 2005). Changes in cortical activation associated with these transitions may vary per brain region or involve different brain networks depending on the individual and behavioural goal. Previous research has shown a non-linear increase in text-responsiveness in the VWFA both, during the first year of reading instruction (Ghislaine Dehaene-Lambertz et al., 2018) as well as during the first two years of schooling compared to adult readers (Maurer et al., 2006). Our findings suggest that speech (and text) sensitive regions in the left STG follow a different developmental time course compared to other reading-related brain areas, including the vOTC. A more detailed investigation of different task- and region-dependent developmental trajectories and their relation to reading related skills is needed to elucidate these findings.

In terms of underlying developmental mechanisms of change, inverted-u-type trajectories are reminiscent of those associated with children's skill learning. When learning a skill, children benefit from both active strategies (e.g. explicitly mapping letters and speech sounds) as well as passive mechanisms such as statistical and associative learning (Shrager & Siegler, 1998; Siegler & Araya, 2005; Siegler, 2005). The use of active strategies during the early stages of learning

serves as input for the passive mechanisms and the dynamics of the two change over the course of skill acquisition. Namely, with increased proficiency, children begin to rely less on the explicit mechanisms and instead switch to fast, automatized processing supported by passive mechanisms such as associative learning (Crowley, Shrager, & Siegler, 1997). In line with this, skill learning in general is thought to reflect an expansion-renormalisation pattern, with an initial increase in cortical activation/volume in the key areas involved in the acquisition of a specific skill, followed by a decrease once proficiency is reached (Lövdén, Garzón, & Lindenberger, 2020; Wenger, Brozzoli, Lindenberger, & Lövdén, 2017). Because reading is a culturally acquired skill, similar mechanisms may underlie the inverted-u activation pattern in our longitudinal results, in line with the proposed prolonged time-course of letter-speech sound automatization (Blomert, 2011; Froyen et al., 2009).

In conclusion, the observed longitudinal inverted-u-trajectory in the strength of 8-11 year-old children's left STG responses to speech sounds and letters, together with previous findings in higher order visual areas, point to regionally specific functional changes in the developing reading network. Ours are the first findings showing this type of developmental trajectory in a speech (and text) sensitive auditory cortical region, and may reflect the fine-tuning of letter-speech sound mappings representing a gradual switch from more effortful to automatized processing. Future longitudinal studies with larger sample sizes are needed to verify the observed inverted-u-pattern of responses within these areas and the reading network as a whole and to establish their link to individual differences in typical as well as atypical reading development.

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5

Summary and General discussion

Summary

The aim of this dissertation was to explore letter-speech sound processing in typically reading children and children with developmental dyslexia using a longitudinal three-year fMRI design. We employed a novel text-based recalibration paradigm where we bias the perception of an ambiguous speech sound in the direction of disambiguating text (text-based recalibration). This allowed us to tap into short-term audio-visual learning mechanisms involving letter-speech sound mapping in children with varying reading proficiency. Our design further allowed tracking the developmental changes in brain activation associated with letter-speech sound processing across the three-year period.

Summary

Reading is a fundamental skill that facilitates employability, cultural, societal and scientific advances as well as communication between people. However, it is a culturally acquired skill that the human brain has learnt to accommodate through functional and structural plasticity mechanisms that link visual and speech processing areas (Rueckl et al., 2015; Van Atteveldt et al., 2004). One of the proposed pillars of successful reading development is the automatization of letter-speech sound mappings. Difficulties in creating such automatic links have been suggested to underlie reading difficulties in readers with dyslexia (Aravena, 2017; Blomert, 2011), particularly in languages with fairly consistent letter-speech sound mapping such as Dutch. In the longitudinal research study reported in this dissertation, our aim was to investigate letter-speech sound mappings employing a text-based recalibration paradigm in 8-11 year old children of varying reading proficiency, including readers with dyslexia and to link our findings to children's reading and phonological skills.

The project started with a behavioural study investigating text-based recalibration effects in 8-year-old children with and without dyslexia, described in chapter 2. We observed significant recalibration effects in children with and without dyslexia, namely the children's perception of an ambiguous /a?a/ sound mid-way between an /aba/ and /ada/ sound was biased by the simultaneous presentation of this sound with clear "aba" or "ada" text stimuli. This resulted in a perceptual shift reflected in a tendency to perceive the ambiguous speech sound in line with the text (i.e. as /aba/ following "aba" text exposure and as /ada/ following "ada" text exposure). Unlike a previous study reporting a lack of text-based recalibration in adult readers with dyslexia (Keetels et al., 2018), our

findings in children did not reveal any group differences in task performance. The effect was however, positively associated with perceptual adaptation in the dyslexic readers. During the adaptation paradigm, the children were exposed to unambiguous matching letter-speech sound pairs. This elicits the opposite perceptual effect compared to recalibration – fewer responses in line with text – i.e. more /ada/ responses following “aba” sound + text exposure and more /aba/ responses following “ada” sound + text exposure. The reason why such a positive association was only observed in children with dyslexia remains to be investigated. The analyses were further extended to a larger sample of only typically reading children and showed that children who had a well-defined /aba/ - /ada/ phoneme boundary showed stronger recalibration effects, indicating that phonological perception affects the magnitude of text-based recalibration. Moreover, a more distinct phoneme boundary was associated with better reading accuracy, pointing to a close association between phonological processing and reading outcome. Overall, the findings of comparable recalibration effects in children but not in adults with and without dyslexia could indicate a developmental trajectory in audio-visual processing of letters and speech sounds. Indeed, the children in both groups were in the early stages of reading development when brain circuits for letter-speech sound processing are still being fine-tuned. Additionally, the dyslexic readers were in the first months of remediation specifically focused on letter-speech sound mappings. Once the children with and without dyslexia start to reach a stable level of reading fluency with continued reading development, they may rely on partly different brain networks/areas for audio-visual integration and reading, possibly leading to the observed behavioural differences in adults.

In chapter 3, we investigated cortical activation in 9-year old children with and without dyslexia while they performed the text-based recalibration task in the MRI scanner during the first longitudinal measurement. Our aim was to explore the neural mechanisms associated with text-based recalibration and to investigate potential group differences in cortical activation despite the comparable behavioural task performance. In line with the behavioural findings reported in chapter 2, we did not observe any differences in recalibration task performance between the groups. The magnitude of the text-based recalibration effect was, however, reduced in the MRI and - at the group level - no longer reached significance. This could be linked to contextual effects of performing the task in the MRI environment, including the background scanner noise and sound quality in the MR-compatible headphones. Moreover, previous research has shown that the

Summary

scanner noise can reduce (visual) attentional focus in the MR environment (Kobald et al., 2016; van Maanen et al., 2016), as 9-year-old children are still developing their attentional skills (e.g. Amso & Scerif, 2015), they may be especially susceptible to such effects. Overall, children in both groups showed comparable cortical activation in brain areas associated with audio-visual integration and reading and typically reported in studies employing congruency manipulation paradigms in children (Blau et al., 2010; Plewko et al., 2018) and recalibration studies in adults (Bonte et al., 2017; Kilian-Hütten et al., 2011). Nevertheless, children with dyslexia did show less activation in a left hemisphere fusiform region compared to typical readers during the simultaneous presentation of text and ambiguous speech. Across participants, cortical activation within this region was positively correlated with reading fluency and phonological skills. These observations corroborate previous research showing a reduced response in the left fusiform in children with dyslexia, as well as an association between fusiform activation and reading proficiency. The correlation with phonological processing likely reflects maturational processes in this area from multimodal (auditory and visual) processing in children within our age range to unimodal (visual only) stimulus processing in experienced readers (Church et al., 2008). We also observed a correlation between activation within bilateral superior temporal gyri and children's letter-speech sound identification fluency in the entire sample. This indicates an increased involvement of auditory cortical regions during audio-visual processing of letters and speech sounds in children with less automatized letter-speech sound associations. Taken together, our findings illustrate the reading-dependent inter-individual variability in cortical responses to audio-visual letter-speech sound stimuli in 9-year old typical and dyslexic readers.

In chapter 4, we explored longitudinal changes in cortical activation in response to the audio-visual ambiguous speech and text stimuli over a three year period consisting of annual MRI measurements in a group of 8-11 year-old typically reading children. Behaviourally, recalibration did not reach statistical significance in any of the three measurement sessions, similarly to the results of chapter 3. However, the overall magnitude of the effect did increase from session 1 to 3 and approached significance by the last measurement, potentially reflecting a developmental trend in the text-based recalibration effect. Cortical activation elicited by the audio-visual speech and text stimuli across sessions largely overlapped with the network seen in chapter 3 and spanned brain areas associated with audio-visual integration and reading. While upon visual inspection, this network appeared to broaden from measurements one to three, comparisons of cortical

activation between sessions only revealed a significant difference in activation between sessions 1 and 2 in a left hemisphere superior temporal gyrus region. The activation within this region was found to follow an inverted-u-response, showing a peak in activation in session 2 that was linked to children's age. Specifically, the peak was observed in children who were on average 9 years old during the second measurement. We did, however, observe inter-individual variability in the functional activation trajectories across the sessions indicating potential differences in the timing of the peak and/or variability in the brain regions involved in letter-speech sound mapping. The inverted-u-trajectory of left superior temporal gyrus activation is in line with previous studies reporting a similar response pattern in higher order visual areas (Gorka Fraga González et al., 2017; Maurer et al., 2006, 2011, 2008; Price & Devlin, 2011) and can be explained in terms of more general skill learning mechanisms in children. It has been proposed that learning a new skill involves active mechanisms e.g. explicit mapping between letters and speech sounds during reading instruction as well as passive, statistical and associative learning that for example facilitates automatic processing of text in fluent readers (Siegler, 2005). Applied to reading development, the inverted-u trajectory likely reflects the switch from explicit/effortful letter-speech sound mapping to automatized, fluent reading. The reported peak in cortical responsiveness to text around age 9 has furthermore been proposed to be associated with predictive coding mechanisms in higher order visual areas, and taken to represent cortical activation due to high prediction errors that later decrease resulting in a downward slope in activation with improved reading fluency (Price & Devlin, 2011). Given the involvement of the auditory and visual cortices in letter-speech sound mapping, their similar developmental trajectories may reflect a more global developmental pattern of the reading network.

The three empirical chapters of this dissertation report findings of a novel text-based recalibration paradigm previously only researched in adult readers and represent the first behavioural and neuroimaging results using this paradigm in children. The combination of ambiguous speech and text allowed us to explore letter-speech sound processing in children with varying reading proficiencies using short-term perceptual learning rather than over-learned matching and non-matching letter-speech sound pairs that may be influenced by processing or task strategies involving implicit/explicit matching of the stimuli, or children's self-beliefs regarding e.g. their reading ability. Our behavioural results showed comparable text-based recalibration effects in all children, indicating that there were no overall differences in task performance between children

Summary

with and without dyslexia. We did however, observe differences in brain activation between the groups, with dyslexic readers showing less activation in a left hemisphere fusiform area compared to typically reading children that furthermore scaled with children's reading and phonological skills. Activation within this brain region has previously been associated with reading proficiency and automatic processing of text in experienced readers (Ben-Shachar et al., 2011; Dehaene-Lambertz et al., 2018; Pugh et al., 2001). The reported difference in activation between children with and without dyslexia could therefore point to differences in the level of automatization of letter-speech sound mappings and the use of alternate brain areas to perform the same task in dyslexic readers. A longitudinal investigation of brain activation during recalibration task performance in typical readers revealed an age-driven increase in left superior temporal gyrus activation around age 9 compared to ages 8, 10 and 11. This finding indicates a heightened cortical response to audio-visual letter-speech sound stimuli around this age. Taken together, our research highlights the dynamic inter-individual variability in cortical activation during audio-visual integration of letters and speech sounds in children aged 8-11 during the first years of reading instruction and its close association to children's reading and phonological skills.

General discussion

When learning to read, children are taught to link spoken language to visual symbols (text) representing specific speech sounds and their combinations. The initial steps in reading acquisition focus on creating these associations, whereas further practice increases familiarity with text and written forms of words that later on results in fast, automatic and rather effortless processing of text stimuli. While the initial mappings between speech and text are learnt fairly quickly (Blomert, 2011; Perfetti, 2003), the automatization of these associations continues to develop over the first years of reading acquisition (Blomert, 2011; Froyen et al., 2009). Furthermore, it has been suggested that less automatized letter-speech sound mappings underlie reading difficulties in developmental dyslexia (Aravena, 2017; Blomert, 2011). The research reported in this dissertation explored letter-speech sound processing in children of varying reading proficiency using a text-based recalibration paradigm in a longitudinal design consisting of three annual MRI measurements. This paradigm combines an ambiguous speech sound /a?ɑ/ mid-way between /aba/ and /ada/ with disambiguating visual "aba" or "ada" text. The text stimuli bias the subsequent

perception of the ambiguous speech sound towards the text, reflecting the integration of the two modalities and mapping of ambiguous speech onto text.

Our behavioural findings showed no difference between children with and without dyslexia in recalibration task performance. However, subsequent neuroimaging results did reveal group differences in a left fusiform region showing less activation during the task in dyslexic compared to typical readers. Higher activation within this regions was associated with better reading fluency and phonological skills across children. We additionally observed an association between letter-speech sound identification fluency and cortical activation in bilateral superior temporal regions, with less fluent identification associated with higher activation in both dyslexic and typical readers. The longitudinal analyses in typically reading children across all three MRI measurements further revealed that cortical activation in a left hemisphere superior temporal gyrus region in response to letter-speech sound pairs follows a non-linear inverted-u-trajectory, indicating a period of increased cortical responsiveness around age 9. These results show the dynamic changes in cortical activation during the first years of reading instruction and illustrate the close link between children's reading and phonological skills and cortical activation during letter-speech sound mapping. Our findings stress the importance of taking into account inter-individual differences in reading and phonological skills when interpreting brain activation results, particularly during the first years of reading instruction.

The advantage of text-based recalibration

Given the abovementioned role of letter-speech sound mapping and automatization in (dys)fluent reading, our aim was to explore audio-visual learning and integration in children with and without dyslexia employing an experimental paradigm that taps into the mechanisms underlying letter-speech sound mapping. Text-based recalibration is a short-term audio-visual perceptual learning paradigm (Samuel & Kraljic, 2009; Vroomen & Baart, 2012) that maps ambiguous speech onto disambiguating text. The use of text to disambiguate speech requires active integration of the auditory and visual modalities that engages left-lateralized dorsal (phonological) and ventral (visual) systems of the cortical reading network. Compared to congruency manipulation and oddball paradigms which employ well-known matching (congruent) and non-matching (incongruent) letter-speech sound pairs that are likely fairly automatized, the disambiguation of

speech using visual cues arguably requires a more active contribution of audio-visual integration mechanisms. Moreover, the processing of congruent and incongruent audio-visual letter-speech sound pairs relies on a matching/non-matching judgement that may be biased by task strategies or characteristics (Basu Mallick et al., 2015), personal beliefs regarding task performance (particularly in readers with dyslexia) or more general factors including reading skills (Plewko et al., 2018). Furthermore, given the often observed difficulties in letter-speech sound automatization in dyslexia, the associations between letters and speech sounds may be represented, processed or learned differently in readers with dyslexia. Text-based recalibration provides an interesting paradigm to study these underlying problems because the letter-speech sound pairs in this paradigm result from “real time” perceptual learning — i.e. mapping the ambiguous speech sound onto text. We specifically instructed the children that there were no incorrect responses in this task and that we were simply interested in seeing how they perceive the speech sounds during the post-test trials. This was particularly important for less fluent readers and children with dyslexia, who have often already established negative self-beliefs about their performance on reading (related) tasks and experienced setbacks during reading development. The use of audio-visual ambiguous speech and text pairs therefore allowed us to limit the confounding effects associated with well-established letter-speech sound mappings behaviourally and to explore the involvement of the dorsal and ventral reading systems in letter-speech sound mapping using fMRI.

Behavioural performance on the text-based recalibration paradigm in children

One of the proposed core deficits underlying the reading difficulties in developmental dyslexia is impaired (i.e. less automatized) mapping of letters and speech sounds (Blomert, 2011; Kronschnabel et al., 2014). Support for this hypothesis has mainly been shown by neuroimaging studies investigating letter-speech sound congruency effects in dyslexic and typical readers (Blau et al., 2010, 2009; Froyen et al., 2011; Kronschnabel et al., 2014; Moll et al., 2016; Žarić et al., 2015, 2014). Indeed, a study employing the text-based recalibration paradigm in adults with and without dyslexia also lent support to this hypothesis. Namely, unlike typical readers, adult readers with dyslexia did not show a significant text-based recalibration effect (Keetels et al., 2018), while both groups showed comparable recalibration based on lip-read speech. The comparable text-based recalibration effects in our sample of children aged 8-10 (chapter 2), therefore, came as somewhat of a surprise. However, the discrepancy in findings between children and adults with

dyslexia can be explained from a developmental perspective. The children in our sample were within the first years of reading instruction and included children with dyslexia in the first 3 months of remediation specifically focused on letter-speech sound mapping and automatization. At this time, reading has not yet become a fully automatized skill and children are still fine-tuning letter-speech sound mappings as reflected by EEG findings reporting a wider audio-visual integration window in children within the same age group (Froyen et al., 2009; Žarić et al., 2014). It can therefore be argued that children's audio-visual processing and integration mechanisms are quite malleable during early reading development and potentially rely more on processing in the dorsal reading system to successfully combine the two modalities. The dorsal system spans posterior temporal and inferior parietal and frontal regions and is involved in phonological processing and establishing the mappings between letters and speech sounds during initial reading instruction (Pugh et al., 2001). Higher engagement of the dorsal system in children within our sample is supported by our findings of an inverted-u-trajectory in the left superior temporal gyrus (STG) region longitudinally (chapter 4) and the observed increase in activation in bilateral STG in children with less fluent letter-speech sound identification regardless of dyslexia diagnosis (chapter 3). Adults, on the other hand, likely have well-established (i.e. less malleable) mechanisms underlying letter-speech sound processing and rely on a combination of the dorsal and ventral reading systems. It has furthermore, been proposed that cortical responsiveness to text peaks around age 9 (Maurer et al., 2008; Price & Devlin, 2011). Enhanced processing of text in text-based recalibration would likely result in a more pronounced perceptual bias of the ambiguous sound towards the disambiguating text stimuli. Moreover, text processing has been proposed to be less efficient/automatic in readers with dyslexia (e.g. Richlan, 2019). Thus, if the discrepancy in findings between adults and children with dyslexia is driven by differences in their reliance on the dorsal phonological system and in cortical responsiveness to text, children around age 9 may still be able to compensate less efficient text processing using alternate pathways, which may no longer be the case for adults. An additional explanation for the discrepancy in behavioural results could be the proposed developmental nature of text-based recalibration – i.e. the effect is less stable in children as reflected in the decreased magnitude of recalibration in the MRI scanner (see below and chapters 3 and 4). Moreover, the adult readers with dyslexia were all university students/graduates who had likely developed alternate (compensatory) strategies to successfully integrate text and speech sounds therefore constituting a specific sub-group of dyslexic readers.

Despite reliable recalibration effects behaviourally, we observed a reduction in the magnitude of the text-based recalibration effect in the MRI scanner reported in chapter 3, which rendered the effect no longer statistically significant. The MRI environment and scanner noise in particular have been associated with decreased (visual) attention (Kobald et al., 2016; van Maanen et al., 2016). It is an unusual environment and position (lying down) to perform a cognitive task. Furthermore, the scanner noise may not only alter attentional mechanisms, but may also affect auditory perception. While we did present all auditory stimuli in a silent gap between volume acquisitions, this is not the same listening environment as performing the task in a quiet room, as was the case in the behavioural study. It is thus likely that all these factors contributed to the observed decrease in the magnitude of recalibration. While it illustrates the relative fragility of the text-based recalibration effect, this finding too could be developmental in nature, as the magnitude of recalibration gradually increased across all three measurement sessions in typically reading children (chapter 4), approaching statistical significance by the last measurement. A previous fMRI study employing text-based recalibration in typically reading adults showed significant effects both in and out of the MRI scanner (Bonte et al., 2017), the same is true for recalibration paradigms employing lip-read and lexical stimuli in adults (Kilian-Hütten, Valente, Vroomen, & Formisano, 2011; Ullas, Hausfeld, Cutler, Eisner, & Formisano, 2020). Thus, the observation of an increase in the magnitude of the effect from ages 8-9 to 10-11 in children could reflect general maturation of e.g. attentional mechanisms and/or an overall increase in the familiarity of the MRI environment. Finally, because the sample size was smaller than anticipated due to closure of the scanning facilities during the corona virus crisis, the behavioural recalibration effect in the MRI may reach statistical significance in a larger sample, given that the statistical analyses in our current sample were approaching significance. Future research in children of a larger age range, preferably using a longitudinal approach, is needed to explore the proposed developmental effects of text-based recalibration behaviourally both in and out of the MRI scanner.

Group differences, developmental changes in cortical activation and their link to the reading network

While we did not observe behavioural differences in the text-based recalibration effect in children with and without dyslexia, functional MRI responses during the audio-visual exposure blocks did show a group difference in cortical activation within a left fusiform region (chapter 3). The left

ventral occipito-temporal cortex (vOTC), which includes this region and houses the putative visual word form area is part of the left-lateralized ventral reading system associated with automatized processing of text in fluent readers (McCandliss et al., 2003; Pugh et al., 2001; Sandak et al., 2004). It has been proposed that, over the course of reading development, the ventral system matures based on input from the dorsal reading system (Gorka Fraga González et al., 2014, 2017; Pugh et al., 2001). When a child first learns to read, they rely on the dorsal system to learn letter-speech sound mappings. With continued reading development, an eventual switch from a relatively stronger reliance on the dorsal to the ventral system is made (Pugh et al., 2001), representing a change from effortful/explicit letter-speech sound mapping to automatized processing. The differential activation patterns within the left fusiform in our sample could indicate less automatized text processing and, by extension, less reliance on the ventral reading system in the dyslexic readers. Integrating these findings with the proposed dynamics of the two reading systems, one could speculate that children with dyslexia engage the dorsal reading system to a larger extent than typical readers of the same age to successfully map letters and speech sounds, which could relate to their often observed difficulties in the automatization of these mappings (Blomert, 2011). A relatively larger reliance on the dorsal reading system in general in children within our age range may be the reason why our behavioural findings contrast those seen in adults. This explanation is supported by the observed increase in response to audio-visual stimuli in the left STG (chapter 4) around age 9 and the correlations between letter-speech sound identification fluency and bilateral STG activation across dyslexic and typically reading children of the same age (chapter 3). Combining these findings with the abovementioned increase in cortical responsiveness to text and a broader audio-visual integration window, it is likely that children around age 9 still engage the dorsal reading system for letter-speech sound mappings with the switch to ventral, more automatized processing made in older children. The engagement of the dorsal system in reading and letter-speech sound processing may be especially enhanced in less fluent typical readers and readers with dyslexia, as evidenced by the group difference in left fusiform activation between dyslexic and typical readers and the positive correlations between reading fluency and phonological skills and activation within this region across participants (chapter 3). Thus, our behavioural findings of comparable text-based recalibration may be specific to children between ages 8 and 11, with group differences emerging at a later stage in older children.

The difference in left fusiform activation between children with and without dyslexia in the given research is in line with previous findings showing less vOTC activation in dyslexic readers (Dehaene & Cohen, 2011; Hoeft et al., 2007; Paulesu, 2001; Richlan et al., 2009; Wimmer et al., 2010). It has been proposed that, compared to typical readers, readers with dyslexia show compensatory (over) activation in frontal brain areas (anterior part of the dorsal reading system) and under activation of the left posterior dorsal reading system (including auditory and parietal areas), as well as the ventral system (Shaywitz et al., 2002; Shaywitz & Shaywitz, 2008; Shaywitz et al., 1998; Werner & Noppeney, 2010). While the findings of aberrant activation within the left dorsal reading system in readers with dyslexia are often mixed, with some studies reporting additional activation in homologous right hemisphere regions (Hoeft et al., 2011; Paz-Alonso et al., 2018; Richlan et al., 2009; Richlan, Kronbichler, & Wimmer, 2011; Waldie, Wilson, Roberts, & Moreau, 2017), the reduced activation of the ventral reading system is well-established. Indeed it has previously been suggested that adult readers with dyslexia continue to rely on more phonology-based processing of text (i.e. the dorsal system Finn et al., 2014) compared to typical readers. Taken together, these results point to a greater involvement of the dorsal system (potentially bilaterally) in readers with dyslexia. The variability in observed cortical activation patterns across studies may be linked to the differences underlying connectivity between the two systems of the brain's reading network in dyslexic and typical readers and their changes over the course of reading development.

An interesting subsequent question is how the dynamic changes of the reading network relate to changes in functional activation longitudinally. In chapter 4, we observed a non-linear pattern of changes in brain activation across the three fMRI measurements in a left superior temporal gyrus (STG) region in typically reading children. The activation changes followed an inverted-u-trajectory, with a peak in session 2 compared to sessions 1 and 3 that was driven by 9-year-old children. This was the first fMRI study showing an inverted-u-shape activation pattern in response to audio-visual letter-speech sound stimuli in the auditory cortex. A similar pattern in the same age group has previously been reported in studies exploring responses to text in higher-order visual areas (vOTC; Fraga González et al., 2017; Maurer et al., 2006, 2011, 2008; Price & Devlin, 2011) and in response to audio-visual deviants in EEG research using oddball paradigms (Froyen et al., 2009; Žarić et al., 2014). A proposed explanation for the inverted-u cortical activation trajectory

in higher order visual areas is predictive coding. With no predictions of the spelling of a specific word or integration between letters and speech sounds being made prior to reading instruction and a developmental change from poor prediction accuracy marked by high prediction error and vOTC activity followed by a decrease in activation associated with improved prediction accuracy and fluent reading (Price & Devlin, 2011).

Because the mapping of letters onto speech-sounds is central in reading acquisition and development, the similar non-linear trajectories in auditory and visual brain areas could reflect a global developmental pattern of the reading network during the first stages of learning to read. An increase in functional connectivity between the left inferior parietal cortex (dorsal reading system) and left posterior occipito-temporal cortex (ventral reading system) has been reported in children from ages 5 to 7 longitudinally (Yu, Raney, et al., 2018). This strengthening of functional connections was furthermore related to increased phonological skills. Another longitudinal study exploring functional connectivity between the dorsal and ventral reading systems reported a decrease in connectivity between the left parietal cortex and fusiform between ages 11 and 14 that was associated with better reading fluency (Wise Younger et al., 2017). Taking the results of these two longitudinal studies together, a similar inverted-u-trajectory can be observed in functional connectivity between the dorsal and ventral reading systems with an initial strengthening of connections followed by a decrease in connectivity. White matter tracts connecting these systems have been proposed to undergo similar reading-related changes (Yeatman et al., 2012). The changes in functional connectivity likely reflect the specific reading stage 8 – 11 year old children have reached. Around this age, the children have already established robust letter-speech sound mappings and start to transition from letter-by-letter reading to chunking letter strings into corresponding syllables and making the initial steps to automatized sight word reading (i.e. reading words as whole units) essentially representing a switch from effortful decoding of single letters and speech sounds to automatized processing of letter strings and words (Ehri, 2005). Thus, the observed peak in text responses in the left vOTC and left STG in response to letter-speech sound pairs may indeed reflect an overall developmental trajectory of the brain's reading network, potentially representing the point at which children make the switch from more effortful to more automatic text processing.

The importance and challenges of performing longitudinal studies

The research reported in this dissertation was based on a longitudinal fMRI study spanning three yearly measurements and explored developmental changes in cortical activation to letter-speech sound stimuli in 8 – 11 year old children of varying reading proficiency. Previous longitudinal studies have shown dynamic reading skill related developmental changes in functional and structural connectivity between areas of the dorsal and ventral reading systems (Myers et al., 2014; Vanderauwera, De Vos, et al., 2018; Wise Younger et al., 2017; Yeatman et al., 2012; Yu, Raney, et al., 2018) and aberrant connectivity between these systems in readers with dyslexia (Chyl et al., 2019; Hoeft, McCandliss, Black, Gantman, Zakerani, Hulme, 2010; Morken, Helland, Hugdahl, & Specht, 2017). These findings indicate that cortical connectivity patterns are closely associated with reading development and differ depending on children's age and reading fluency. The variability in the exact timing (e.g. Morken et al., 2017) and nature of these changes between children results in ever shifting cortical activation differences between fluent and poor readers and likely contribute to the mixed research findings frequently observed in cross-sectional research. Comparisons made in cross-sectional studies inevitably contrast different groups of children of different ages and/or reading proficiency. Such comparisons are inherently confounded by inter individual differences of children and groups of children being compared. Longitudinal research gives us the opportunity to begin to disentangle these mixed findings by investigating developmental changes and inter individual differences in cortical developmental trajectories within and between groups of children. Here each child serves as their own control across measurement sessions, thus incorporating the between subject variability into the research design and by extension enhancing the reliability of findings. While this is the main strength of longitudinal research designs, they do come with some challenges. The main challenging aspect of conducting longitudinal research is the time-intensive nature of it. The majority of the PhD project was dedicated to data collection, up to the last months in which we strived to collect as many final data sets as we could after the re-opening of the fMRI scanning facilities which had been closed for a period of 4 months due to the Covid-19 pandemic. While the upside of this is a data-rich project that offers a lot of opportunities to investigate various brain and behaviour between- and within-subject comparisons, further analyses and publication of the data collected during the project will continue after the PhD project is officially finished.

Another challenge in longitudinal designs is maintaining a large-enough sample size in the face of children and their families discontinuing their participation in the research project. Longitudinal research is a commitment not only for the researchers running the studies but also for the children and families volunteering their time to participate in them. We made sure to be as flexible as we could when planning follow-up measurements taking into account e.g. planned orthodontic treatments. Additionally, we put a lot of effort into remaining in contact with the families by posting updates of our findings on the research group's website that were also sent out to parents via e-mail. We sent summer holiday and Christmas cards to all our participants every year and organised a children's symposium to inform the families of our findings and give them a chance to ask questions about reading development, dyslexia, the importance of neuroimaging and our research. This worked very well, and we did not have many participants dropping out over the three year period, unfortunately the majority of discontinuations were caused by the closing of the scanning facilities during the first lockdown in March 2020. Overall, researchers embarking on longitudinal studies need to be mindful of the time-intensiveness of this kind of research and make sure to account for potential drop outs when deciding on a sample size at the beginning of the study. Finally, staying in touch with the children and families not only to report on the findings of the research but also e.g. by sending holiday cards will help form a friendly connection between the researchers and the families, creating a nice research atmosphere and helping to keep the families engaged in the study.

Future perspectives

Our findings have illustrated the importance of considering between subject variability in reading (related) skills when interpreting brain activation differences between children of varying reading fluency. We have furthermore shown that comparable task performance in children with dyslexia may involve alternate brain regions/networks and that cortical activation in response to the same type of audio-visual letter-speech sound stimuli undergoes dynamic changes during the first years of reading instruction. An important aspect of our research was to link these differences to children's reading and phonological skills. We observed positive correlations between activity levels in the left fusiform and children's reading fluency and phonological processing, as well as negative correlations between activity levels in bilateral STG regions and letter-speech sound mapping fluency (chapter 3). We also observed individual variability in left STG responses across

the three measurements in typical readers (chapter 4), with some children showing a peak in session 2 while others showed linear activation trajectories across sessions. While the latter findings were not linked to reading measures, an association between changes in cortical activation across sessions and categorical perception of phonemes did approach statistical significance. Taken together, these findings illustrate the intricate associations between brain activity and reading (related) skills. It furthermore highlights the reading skill-dependent variability in cortical activation across participants. Keeping in mind that brain activation patterns reflect interactions between the dorsal and ventral reading systems, it is particularly important to link between-subject variability in developmental brain dynamics of the cortical reading network to reading skills and reading outcome.

Longitudinal research offers the opportunity to explore not only between- but also within-subject variability and its contribution to reading. Investigating the developmental trajectory of the reading network in children with varying reading fluency would help further our understanding of the links between brain function and reading outcome. Eventually, the field could strive to link developmental brain dynamics at various ages/stages of reading development to reading outcome. Such predictions would prove valuable in guiding support and remediation in struggling readers and readers with dyslexia. Finally, it is important to broaden our scope of research beyond the conventional reading network. There is evidence of sub-cortical and attentional /executive function network contribution to reading (Alvarez & Fiez, 2018; Bailey, Aboud, Nguyen, & Cutting, 2018; Chen et al., 2019; Fernandez et al., 2016; Finn et al., 2014). Taking into account these factors alongside other covariates such as family history of dyslexia and socio-economic factors may help paint a more complete picture of inter-individual variability in reading skills. The ambitious goal to account for a multitude of factors involved in reading outcome is not impossible to reach and can be achieved by large-scale studies across a number of research institutes. Such big data investigations could help resolve and clarify the mixed findings reported in our research field.

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Learning to read involves making associations between spoken words and symbol strings (text). It has been proposed that this coupling of spoken and written language may be particularly difficult in children with dyslexia. The research conducted in the scope of this doctoral thesis aimed to explore how the coupling between letters and speech sounds differs in children of varying reading skills, including children with dyslexia. We conducted a three year longitudinal study with annual measurements, which allowed us to follow the dynamic, individual developmental changes in the neural processing of these couplings. To study learning processes involved in coupling letters to speech sounds we used a novel text-based recalibration paradigm in which the combination of “aba” or “ada” text with an ambiguous speech sound /a?a/ mid-way between /aba/ and /ada/ temporarily biases children’s perception of the ambiguous sounds towards the text. To investigate how children’s brains processed the letters and speech sounds we looked at the behavioural task performance (i.e. whether they perceived the ambiguous sound as /aba/ or as /ada/ after text exposure) as well as brain activation during the task using magnetic resonance imaging.

Despite similar behavioural task performance, children with and without dyslexia showed different brain activation in response to letters and speech sounds. Namely, children with dyslexia showed less brain activation in an area involved in text processing compared to typically reading children, indicating that they may have additionally relied on other brain areas to successfully link letters and speech sounds. We also saw that regardless of whether or not a child had dyslexia, more activation in this brain area was associated with better reading skills. Moreover, children who were slower in combining letters and speech sounds, regardless of dyslexia diagnosis, had more activation in auditory brain areas important for successfully linking of speech and text. These findings show that reading proficiency is closely associated with brain activation, with differences between poor and fluent readers represented as increased or decreased activation depending on the brain area and its role in reading.

We also explored developmental changes in brain activation of typical readers during a three year period when the children came to our scanning facility once a year. We found that a brain area involved in speech processing and important for linking letters to speech sounds is activated more strongly when children are nine years old as compared to ages 8, 10 and 11. These findings suggest that there is a specific time window when children learn to read, during which their brains are more

sensitive to letters and speech sounds. This time window around age nine has been proposed to indicate a turning point in text processing. Namely, around this time, children start to rely less on explicit sounding out and linking of letters and speech sounds and instead begin to process text more automatically.

To summarize, the research reported in this dissertation has shown that brain activation is tightly linked to children's reading skills and, importantly, that different brain areas may be active in children with and without dyslexia to perform the same task. The observed associations between brain activation and reading skills have shown the importance of taking into account children's reading performance when researching and interpreting brain activation results, regardless of a dyslexia diagnosis. Our findings have enhanced the reading research field and will help improve our understanding of reading development, as well as provide new directions for future studies. The close links between brain activation and reading skills observed in our research are informative for dyslexia healthcare institutes as well as readers with dyslexia and their families, as it helps them better understand the neural mechanisms involved in reading and dyslexia and guide remediation and education.

The research findings reported in this dissertation have been presented in international scientific conferences and are continuously communicated to the families who took part in the research. We publish all of our most recent findings on our research group's website¹ and communicate this to the parents via e-mail. This website was created at the beginning of the project ('Project Leeswinst') and alongside updates of our findings, contains useful and practical information about the study for the participating families. In addition to scientific conferences that allowed us to interact with and gain feedback from experts with diverse scientific backgrounds, we also organised a children conference in February 2019 for the families of children participating in our longitudinal research project. The conference was organized during the afternoon and included a children-focused presentation about reading development, dyslexia and the brain, colourful poster

¹ <https://mbic-languagelab.nl/en/>



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presentations with updates on our research findings and a tour of the scanning facility for the family members who had not previously accompanied our participants. This offered the children and parents an opportunity to ask questions about the research and more general topics related to reading, brain development and brain scanning. Beyond the communication to families, the conference was also reported in a regional newspaper² disseminating our findings to the general audience and raising awareness of developmental research in Maastricht. Furthermore, representatives of the regional dyslexia institute attended the conference and asked insightful questions about our findings and their relevance for dyslexia remediation. Overall, our research project aimed to link brain activation to reading performance in children during the first years of reading instruction to better understand reading development and reading difficulties underlying dyslexia. The findings were informative for both, the scientific community as well as the children and families who took part in the research.

² https://www.limburger.nl/cnt/dmf20190220_00093446



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Curriculum vitae

Linda Romanovska was born on July 21st 1989 in Aizkraukle, Latvia. After her family moved to Luxembourg when she was 14, she attended the European School of Luxembourg I and obtained the European Baccalaureate in 2008. After doing some soul searching regarding her academic interests, she enrolled in the Bachelor in Psychology program at Luxembourg University in 2010 and obtained her Bachelor's degree in Psychology in 2014. She pursued her interest in research and psychology by enrolling in the Neuropsychology Research Master track at Maastricht University the same year and obtaining a Research Master degree in Cognitive and Clinical Neuroscience in 2016. Later that year, her scientific journey continued with a PhD position researching reading development in children with and without dyslexia ("Project Leeswinst") at Maastricht University, Faculty of Psychology and Neuroscience (Cognitive Neuroscience department) under the supervision of Prof. Milene Bonte.

Publications

Peer-reviewed journals:

Romanovska L, Janssen R, Bonte M (2021) Cortical responses to letters and ambiguous speech vary with reading skills in dyslexic and typically reading children. *NeuroImage: Clinical*. doi: <https://doi.org/10.1016/j.nicl.2021.102588>.

Romanovska L, Janssen R, Bonte M (2019) Reading-Induced Shifts in Speech Perception in Dyslexic and Typically Reading Children. *Front. Psychol*. doi: [10.3389/fpsyg.2019.00221](https://doi.org/10.3389/fpsyg.2019.00221).

Conference contributions:

Romanovska L., Janssen R., De Martino, F., Bonte M. (2019, August). *Text-induced shifts in speech perception in children with and without dyslexia: Distinct cortical activation patterns underlie similar behavioural findings*. Poster session at the 11th annual meeting of the Society for the Neurobiology of Language, Helsinki, Finland.

Romanovska L., Janssen R., De Martino, F., Bonte M. (2019, April). Audio-visual integration of letters and speech sounds in dyslexic and typically reading children. Poster session at the Capturing Developmental Brain Dynamics workshop, Leiden, The Netherlands.

Romanovska L., Janssen R., Bonte M. (2018, September). *Reading-induced shifts of cortical speech representations in dyslexic and typically reading children*. Poster session at the 6th annual Flux Congress, Berlin, Germany.

Romanovska L., Janssen R., Bonte M. (2018, June). *Reading-induced shifts of cortical speech representations in dyslexic and typically reading children*. Poster session at the Special Interest Group (SIG) 22 Neuroscience & Education of the European Association for Research on Learning and Instruction (EARLI) meeting, London, United Kingdom.

Timmers I., Romanovska L., van de Ven, V. G., Smeets, R. J. E. M., de Jong J. R., Kaas, A. L. (2016, September). *Resting state functional connectivity patterns of cognitive/emotional and sensorimotor networks differ in opposite ways in chronic pain*. Poster session at the 16th World Congress on Pain, Yokohama, Japan.

Romanovska L., Timmers I., van de Ven, V. G., de Jong, J. R., Kaas, A. L. (2016, June). *Differences in resting state functional connectivity patterns of cognitive/emotional and sensorimotor networks in chronic pain*. Poster session at the Dutch Neuroscience Meeting, Lunteren, The Netherlands.