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ARTICLE

Neurobiological bases of reading disorder part II: The importance of developmental considerations in typical and atypical reading

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Abstract

Decoding-based reading disorder (RD; aka developmental dyslexia) is one of the most common neurodevelopmental disorders, affecting approximately 5–10% of school-aged children across languages. Even though neuroimaging studies suggest an impairment of the left reading network in RD, the onset of this deficit and its developmental course, which may include constancy and change, are largely unknown. There is now growing evidence that the recruitment of brain networks underlying perceptual, cognitive, and linguistic processes relevant to reading acquisition varies with age. These age-dependent changes may in turn impact the neurocognitive characteristics of RD observed at specific developmental stages. Here, we synthesize findings from functional and structural magnetic resonance imaging studies to increase our understanding of the developmental time course of the neural bases underlying (a)typical reading. We first provide an overview of the brain bases of typical and atypical (impaired) reading. Next, we describe how the understanding of RD can be deepened through scientific attention to age effects, for example, by integrating findings from cross-sectional studies of RD at various ages. Finally, we accent findings from extant longitudinal studies that directly examined developmental reading trajectories beginning in the preliterate stage at both group and individual levels. Although science is at the very early

stage of understanding developmental aspects of neural deficits in RD, evidence to date characterizes RD by atypical brain maturation. We contend that exploring the developmental trajectories of RD will contribute to a greater understanding of how neural systems support reading acquisition. Further, we propose and cite evidence that the etiology of RD can be better investigated by distinguishing primary deficits from secondary impairments unfolding along development. These exciting and modern investigatory efforts can also indirectly contribute to a centered practice of early and accurate identification and optimal intervention to support the development of foundational pre-literacy skills and fluent reading. In sum, integrating a developmental understanding into the science and practice of reading acquisition and intervention is both possible and necessary.

1 | INTRODUCTION

Reading, a complex process that typically becomes automatic midway through primary school, is a challenging yet expected scholastic undertaking in childhood. The process of reading acquisition, however, is more laborious for approximately 5–10% of school-aged children because of decoding-based reading disorder (RD; aka developmental dyslexia), which is characterized by unexpected difficulties in single word reading and spelling despite adequate instruction, normal intelligence, proper motivation, and intact sensory processing (Peterson & Pennington, 2012). Reading impairment may adversely impact life domains such as academic achievement, social relationships, emotional development, and unfortunately, in most cases, these negative outcomes persist and compound into adulthood (Ferrer et al., 2015).

RD is a neurodevelopmental disorder with a partially genetic origin and is increasingly believed to be a multicomponential disorder (Moura et al., 2017; Pennington et al., 2012; Tamboer, Vorst, & Oort, 2014). Advancements in and increased access to multiple neuroimaging technologies, combined with improved analytic methods, have substantially increased our understanding of the neural correlates of typical and impaired reading, by showing consistent patterns at the meta-analytic level (Maisog, Einbinder, Flowers, Turkeltaub, & Eden, 2008; Martin, Schurz, Kronbichler, & Richlan, 2015; Richlan, Kronbichler, & Wimmer, 2009; Richlan, Kronbichler, & Wimmer, 2011; Richlan, Kronbichler, & Wimmer, 2013; Vandermosten, Boets, Wouters, & Ghesquiere, 2012), but with large individual differences and study-to-study

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Abbreviations: DWI, diffusion-weighted imaging; FA, fractional anisotropy; FG, fusiform gyrus; IFG, inferior frontal gyrus; ITG, inferior temporal gyrus; MRI, magnetic resonance imaging; MVPA, multi-voxel pattern analysis; RD, reading disorder; SMG, supramarginal gyrus; STG, superior temporal gyrus

variations (Jednorog et al., 2015). This inconsistency may have stemmed from multiple factors, with one major contributor being the implicit premise that anomalies in brain structure and function in RD are static rather than dynamic. The majority of such studies to date compared a group of individuals with RD with an age-matched control group, and some of these studies further collapsed individuals with a large age-range, perhaps because of difficulties in identifying a large sample of individuals of the same age (e.g., Brambati et al., 2004).

At the level of behavior, atypical growth of reading and related cognitive skills in RD has been repeatedly demonstrated (e.g., Lei et al., 2011; Lyytinen et al., 2006). Together with the finding that recruitment of linguistic and cognitive processes that support reading development varies with age as we detail below (Vaessen et al., 2010), it is reasonable to hypothesize that the neural manifestations of RD can vary as well in an age-dependent fashion. Specifically, individuals with RD may display aberrant developmental trajectories in both reading-related and more fundamental (e.g., lower-level sensory cortex) brain networks (Clark et al., 2014). Such knowledge of the neural correlates of RD over the course of development may provide further insights into the etiology and secondary manifestations of RD. On the other hand, understanding of the developmental timetables of reading-related brain circuitries has the potential to improve early and accurate diagnosis of RD and be valuable for the design and implementation of more efficient interventions optimized for each developmental stage. Given the significance of this issue, it is necessary to summarize and understand recent progress on the neurocognitive basis of typical and atypical reading development, which is the main aim of this review.

In the following sections, we first provide an overview of the neural circuitry of typical reading and its development and a summary on brain anomalies in RD. We then move to the central topic and focus on the neurodevelopmental characteristics in RD. We include studies of varying designs, from meta-analyses (e.g., Richlan et al., 2011) to cross-sectional comparisons among different ages (e.g., Finn et al., 2014; Xia, Hoeft, Zhang, & Shu, 2016), and longitudinal investigations (e.g., Clark et al., 2014; Morken, Helland, Hugdahl, & Specht, 2017; Wang et al., 2017). At the close, we discuss directions for further innovative neuroimaging investigations of RD and underscore the importance of combining longitudinal design with study of prereaders to lend critical insight into important topics such as the etiology of RD, early diagnosis, and optimized intervention.

Many studies have examined temporal (timing) properties of the neural activity in RD because of their known atypicality in processes that require fine temporal resolution such as speech sound perception (e.g., Hämäläinen, Rupp, Soltesz, Szucs, & Goswami, 2012; Hornickel & Kraus, 2013; Lehongre, Ramus, Villiermet, Schwartz, & Giraud, 2011) and print-sound integration primarily using electro- (EEG) or magneto-encephalogram (MEG) (Hahn, Foxe, & Molholm, 2014). Given space limitations, we focus specifically on spatial patterns of typical and atypical reading development by drawing from functional and structural magnetic resonance imaging (MRI) research.

## 2 | NEUROCOGNITIVE BASIS UNDERLYING FLUENT READING AND ITS ACQUISITION

The knowledge of the brain basis of typical reading and its development opens a window for understanding the neural underpinning of RD. Such studies can provide age-specific brain templates for examining whether RD deviates from typical trajectories. In this first section, we introduce the neurocognitive basis of typical reading development.

Cognitive (Taylor, Rastle, & Davis, 2013) and computational models (Seidenberg & McClelland, 1989) show that typical reading relies on the effective integration of multiple linguistic processes including orthographic, phonological, and semantic processing. In addition to domain-specific skills, domain-general abilities such as visual attention and executive functions are associated with individual differences in reading (e.g., Franceschini, Gori, Ruffino, Pedrolli, & Facoetti, 2012; Segers, Damhuis, van de Sande, & Verhoeven, 2016). One fundamental rule is that acquisition of cognitive abilities at early periods can influence later skill acquisition and impede reading development. For example, enhanced sensitivity to component features of spoken words leads to the metacognitive foundation necessary for learning to associate visual representations with phonemes, thereby impacting the development of visual word recognition (Pugh et al., 2013). Additionally, there is now evidence to suggest that the relative contributions of those cognitive skills may differ across ages. In one study, for example, while the predictive capacity of rapid naming performance for word reading fluency increased in the early grades (i.e., ages), the predictive capacity of phonological skills dropped (Vaessen et al., 2010). Further, the transparency of the writing system did not impact the findings in the three alphabetic languages used in the study (Hungarian, Dutch, and Portuguese; Vaessen et al., 2010). Along a similar line of findings, orthographic awareness is more predictive of comprehension and spelling performance at higher grade levels than at lower grade levels (Badian, 1995).

Parallel to cognitive models of nonimpaired reading, neuroimaging research has elucidated brain networks involved in typical reading (Price, 2012). These networks include primarily the left ventral system (including the occipito-temporal region—posterior fusiform gyrus [FG] and the inferior temporal gyrus [ITG]) for orthographic processing, the left dorsal system (including the temporo-parietal region—supramarginal gyrus [SMG] and posterior superior temporal gyrus [STG], as well as dorsal inferior frontal gyrus [IFG]) for phonological processing, and a more distributed system across the brain for semantic and sentence/syntactic processing (including the angular gyrus, anterior FG, temporal pole, middle temporal gyrus, and ventral IFG; Graves, Desai, Humphries, Seidenberg, & Binder, 2010; Martin et al., 2015; McNorgan, Chabal, O'Young, Lukic, & Booth, 2015; Price, 2012; Taylor et al., 2013; Vigneau et al., 2006; Vigneau et al., 2011; Figure 1a). It is worth noting that there is not a one-to-one correspondence between the activation in a single brain region and a given cognitive function. Reading always relies on the cooperation of distributed brain networks. Different from the language-specific neural systems such as those for orthographic, phonological, semantic, and sentence/syntactic processing, the functions of some brain regions (e.g., the junction of left inferior frontal and precentral sulci) are thought to be more domain-general and involved in many processes beyond language and reading (Graves et al., 2010).

To acquire fluent reading, developing well-organized and connected neural systems is necessary (Blomert, 2011; Wandell, Rauschecker, & Yeatman, 2012). Taken together, cross-sectional studies (Evans, Flowers, Luetje, Napoliello, & Eden, 2016; Saygin et al., 2013; Turkeltaub, Gareau, Flowers, Zeffiro, & Eden, 2003) and longitudinal studies (Brem et al., 2010; Linkersdorfer et al., 2015; Lu et al., 2007; Maurer, Brem, Bucher, & Brandeis, 2005; Maurer et al., 2006; Myers et al., 2014; Yamada et al., 2011) indicate that the developments of brain structure and function are closely associated with typical reading acquisition. Synthesis of functional findings shows that the left temporo-parietal and occipito-temporal regions are recruited early (Brem et al., 2010), and reading development is thought to involve the initial engagement of the left and right occipito-temporal and temporo-parietal regions simultaneously, followed by disengagement of right hemisphere regions (Brem et al., 2010; Maurer et al., 2005; Turkeltaub
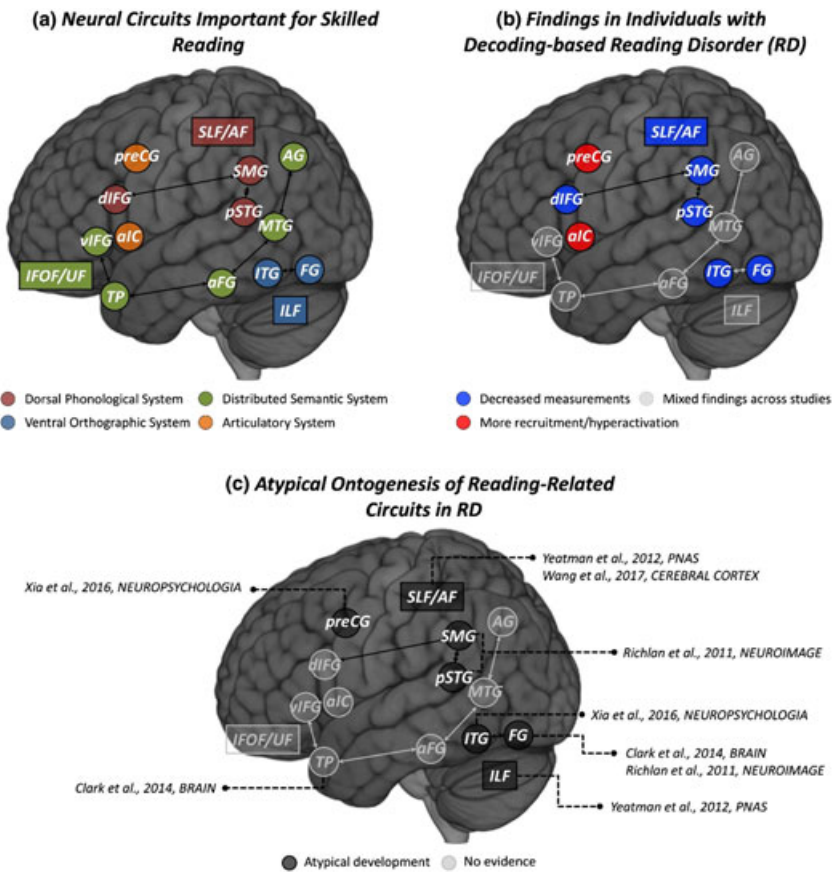
FIGURE 1 (a) Central cortical nodes and connections of four main functional systems for reading, including the dorsal phonological system, the ventral orthographic system, the distributed semantic system, and the articulatory system, are presented. Nodes: aFG, anterior fusiform gyrus; AG, angular gyrus; aIC, anterior insular cortex; dIFG, dorsal inferior frontal gyrus; ITG, inferior temporal gyrus; MTG, middle temporal gyrus, preCG, precentral gyrus; pSTG, posterior superior temporal gyrus; SMG, supramarginal gyrus; TP, temporal pole, vIFG, ventral inferior frontal gyrus; VWFA, visual word form area. Connections: AF, arcuate fasciculus; IFOF, inferior fronto occipital fasciculus; ILF, inferior longitudinal fasciculus; SLF, superior longitudinal fasciculus; UF, uncinate fasciculus. (b) Manifestations of reading disorder (RD) in the four reading-related functional systems are presented. Reduced recruitment of phonological and orthographic systems and atrophies in structural connectivity (e.g., fractional anisotropy of the left AF) related to phonological processing are reported more consistently in individuals with RD. RD children also display hyperactivation of areas in the articulatory system. Findings of anomalies in semantic processing and other white matter fibers are less consistent. (c) Dynamics of impairments in individuals with decoding-based reading disorder. Relevant studies are listed next to the regions. *Note.* (a) Two fibers have recently been proposed as a tract related to speech fluency: frontal aslant tract connects the inferior frontal cortex to presupplementary motor area; anterior segment of the arcuate fasciculus connects the inferior frontal and precentral gyri to the posterior IPL (Basilakos et al., 2014; Kronfeld-Duenias, Amir, Ezrati-Vinacour, Civier, & Ben-Shachar, 2016). However, because whether they are critical in the process for reading is currently unknown, we do not include those fibers in this review. (b) Richlan found stronger hypoactivation in LSMG in child than adult dyslexia. However, this hypoactivation is driven by more deactivation in a task compared with rest in dyslexia, which is difficult to explain. (c) In Richlan et al. (2011), pSTG showed stronger hypoactivation in adult dyslexia under a liberal threshold of $p < .005$, uncorrected. (d) The regions and connections in panel c are kept the same as a and b. Thus, not all findings are included (e.g., functional/effective connectivity; Finn et al., 2014; Morken et al., 2017)

et al., 2003; Yamada et al., 2011). In older children and adults, while the phonological left temporo-parietal region continues to be available for engagement, its recruitment generally declines as visual word recognition becomes more automatic and prominent in fluent reading, and therefore, there is less need for reliance primarily on the phonological system (Martin et al., 2015; Zhu, Nie, Chang, Gao, & Niu, 2014). The ventral occipito-temporal region associated with automatic word recognition is recruited more in older children and adults than in younger ages (Brown et al., 2005; Church, Balota, Petersen, & Schlaggar, 2011; Church, Coalson, Lugar, Petersen, & Schlaggar, 2008). A recent meta-analysis of functional MRI studies further confirmed this age-related shift (Martin et al., 2015). While typically reading children and adults activate common brain areas (e.g., occipito-temporal and inferior frontal regions) during reading, children show higher convergence in the left posterior STG and adults show higher convergence in the occipito-temporal region (Martin et al., 2015). These differences likely reflect developmental shifts in demands of reading on brain systems as described above (Pugh et al., 2001). Despite less research on the neuroanatomy (e.g., gray matter morphometry and structural connectivity) of typical reading acquisition relative to substantive evidence from multiple functional MRI studies, results are to some extent in line with the functional studies. For example, fractional anisotropy (FA)—the degree of directionality of diffusion of water molecules in the brain that is thought to reflect white matter organization—of the arcuate fasciculus at age 6 is associated with preliterate phonological skills and its volumetric maturation from age 6 to 8 predicts future reading performance (Assaf & Pasternak, 2008; Myers et al., 2014; Saygin et al., 2013). Structural maturation of regions such as the left IFG and temporo-parietal regions is also associated with the development of phonological processing and acquisition of reading skills in the short term (Linkersdorfer et al., 2015; Lu et al., 2007). To our knowledge, however, extant work has yet to examine the developmental trajectories of reading-related structural brain networks from the preliterate stage into adulthood.

Increasing evidence on the acquisition of reading network can be synthesized by the "neuronal recycling hypothesis," which proposed that "cultural inventions invade evolutionarily older brain circuits and inherit many of their structural constraints" (Dehaene & Cohen, 2007, p. 384). Reading, which evolved around 5,000 years ago, is a creation of human society. Thus, it is unlikely that humans developed a specific neural basis for reading to respond to the pressure of natural selection. In line with this hypothesis, neuroimaging studies suggest that reading does not have its own devoted network but instead recruits areas (e.g., left FG) from multiple instantiated systems (e.g., the language, visual, and attention networks; Dehaene, Cohen, Morais, & Kolinsky, 2015; Vogel et al., 2013). For example, the putative areas responding specifically to word-like stimuli are originally responsive to faces and gradually became responsive to print stimuli after receiving reading instruction (Dehaene et al., 2010). In the same study, response to the spoken language in the left planum temporale was shown to be enhanced by literacy experience, suggesting that over reading acquisition, individuals come to recruit this speech-related brain area (Dehaene et al., 2010). Furthermore, brain regions that are recruited during reading are not only dependent on experience but may also depend on the specific age (developmental stage) of the child. For example, the recruitment of a fronto-parietal network that includes the superior parietal lobule is stronger in children compared to adults during a reading task. Here, children may require extra top-down attention and control during reading (Church et al., 2008). In brief, it is plausible that the reading network is an integration of functionally specialized and evolutionarily old networks (e.g., language processing and visual processing) and more domain-general networks (e.g., frontoparietal attention or

cognitive control network) that flexibly engage with each other depending on the task at hand (Fedorenko & Thompson-Schill, 2014).

2.1 | Summary

The brain basis of typical reading is multicomponential, consisting of the dorsal temporo-parietal cortex, the ventral occipito-temporal cortex, the frontal, and other distributed areas, which largely correspond to the phonological, orthographic, and semantic components of reading. Moreover, the brain mechanisms underlying reading are dynamic in nature, showing both stability and change over development.

3 | BRAIN BASIS OF READING DISABILITY

While an overview of the neural mechanisms underlying typical reading development is presented above, in this section, we summarize findings on neural deficits in individuals with RD. We first describe abnormalities in regional brain measurements, followed by impairments in structural and functional connectivity. Then, we turn to hyperactivation and increased regional measures that are often interpreted as compensatory mechanisms. Finally, we discuss the inconsistencies among results and introduce the importance of examining age effects in future RD studies.

3.1 | Regional anomalies in brain function and structure

In line with the consensus that phonological impairment is the most demonstrated behavioral hallmark of RD (Melby-Lervåg, Lyster, & Hulme, 2012; Morris et al., 1998), the most consistent findings in MRI research of RD have been the reduced activation and corresponding structural abnormalities in the left temporo-parietal region that is primarily important for phonological processing and the occipito-temporal region that is recruited for orthographic processing (Linkersdorfer, Lonnemann, Lindberg, Hasselhorn, & Fiebach, 2012; Richlan et al., 2009; Richlan et al., 2011; Richlan et al., 2013; Vandermosten, Boets, Wouters, et al., 2012; Figure 1b). The left temporo-parietal region is a functionally diverse area and a repeatedly reported node in RD research (Achal, Hoeft, & Bray, 2016); the ventral subdivision of the temporo-parietal region (e.g., posterior STG) is involved in phonological storage and retrieval (Chang et al., 2010; Pasley et al., 2012), while the region dorsal to it (e.g., SMG) is important for grapheme–phoneme conversion (Booth et al., 2004), and the most dorsal region may play an important role in attention (Ravizza, Delgado, Chein, Becker, & Fiez, 2004). Moreover, the function and structure of the left temporo-parietal region have been shown to be anomalous in children with RD when this group is compared to both age-matched and reading-matched controls. The results indicate that these neural manifestations are persistently anomalous (trait marker) rather than simply a maturational delay of somehow related to reading performance alone (state marker) (Hoeft et al., 2006; Hoeft et al., 2007; Xia et al., 2016).

The left occipito-temporal region primarily includes the FG and the ITG. While the posterior portion of left FG is more sensitive to low-level visual features, the anterior portion have been associated with information at the lexical level (Vinckier et al., 2007). Such hierarchical organization of the left FG is altered in RD (van der Mark et al., 2009). Adjacent to the left FG, the left ITG plays an important role in integrating multimodal information, and its

impairment has also been reported in RD in terms of both structure and function (Paulesu et al., 2001; Silani et al., 2005).

3.2 | Functional and structural connectivity anomalies in RD

Reduction in functional synchronization among reading-related brain areas (e.g., left temporo-parietal, occipital-temporal, and inferior frontal cortices) has also been observed in individuals with RD. Such disconnections exist not only during reading-related tasks (Aboud, Bailey, Petrill, & Cutting, 2016; Finn et al., 2014; Paulesu et al., 1996) but also at rest (Koyama et al., 2013; Schurz et al., 2014; Zhou, Xia, Bi, & Shu, 2015), regardless of whether receiving intervention or not (Davis et al., 2010; Koyama et al., 2013).

Consistent with findings from functional imaging studies, diffusion-weighted imaging (DWI) studies reveal that the FA of white matter fibers are associated with individual differences in reading and reading-related skills. For example, word reading and phonological processing are associated with the left superior longitudinal and arcuate fasciculi that connect dorsal frontal to temporo-parietal regions (Deutsch et al., 2005; Klingberg et al., 2000; Saygin et al., 2013; Vandermosten, Boets, Poelmans, et al., 2012; Vandermosten, Boets, Wouters, et al., 2012). Further, lexical processing such as orthographic recognition and semantic access is associated with the left inferior longitudinal fasciculus that runs between the occipital and anterior inferior temporal areas (Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012) and the inferior fronto-occipital fasciculus (Vandermosten, Boets, Poelmans, et al., 2012) that connects the occipital lobe and the frontal pars triangularis (semantic regions). This evidence together with anomalous findings in other pathways (Dougherty et al., 2007; Fan, Anderson, Davis, & Cutting, 2014a; Fan, Davis, Anderson, & Cutting, 2014b; Keller & Just, 2009), is consistent with the landmark theory that RD is a disconnection syndrome (Geschwind, 1965).

The combination of analyses on the regional functional activation patterns and connections between regions can further address important theoretical issues in RD research. For example, even though phonological processing deficit is the most consistently reported impairment in RD, it is still an open question whether phonological representation, or alternatively, access to these representations, is the central deficit (Ramus & Szenkovits, 2008). One recent study disentangled these two aspects by combining functional MRI multivoxel pattern analysis (MVPA), resting-state functional connectivity, and DWI tractography techniques (Boets et al., 2013). The authors found that the differences between the adult RD and control groups existed in both functional and structural connectivity rather than neural representations of phonemes. They concluded that it is the access to the phonological representation rather than the representation itself that is abnormal in RD (Boets et al., 2013). Such results represent a significant step forward in addressing the nature of the phonological deficit in RD (Ramus, 2014). Due to limitations including sensitivity of the MVPA method and sample characteristics (e.g., examining only one age group), replication of the results is warranted.

3.3 | Hyperactivation, volume increase, and increased connectivity in RD

Together with underactivation and disconnectivity, hyperactivation, particularly in the left fronto-striatal network, has also been reported in RD relatively consistently (Maisog et al., 2008; Richlan et al., 2009; Richlan et al., 2011). Because brain regions in the left fronto-striatal network (inferior frontal regions and caudate) are involved in articulation (Paulesu, Frith, & Frackowiak, 1993; Riecker, Kassubek, Gröschel, Grodd, & Ackermann, 2006), a possibility is that

individuals with RD can compensate for their phonological-related impairments via an articulatory strategy. The link was directly supported by a recent meta-analysis that showed spatial overlap in the fronto-striatal network relevant for hyperactivation in RD and that involved in articulation (Hancock, Richlan, & Hoeft, 2017). Consistent with the idea that hyperactivation in the fronto-striatal network in RD is relevant to compensation, activation in this network of regions in RD (e.g., bilateral IFG, right insula, and left subcortical regions including putamen, caudate, and thalamus) have shown to be present after reading intervention in a meta-analysis (Barquero, Davis, & Cutting, 2014). It is worth noting that the articulation strategy may not be the only interpretation. For example, besides intervention-related increased activation in right IFG, postintervention functional connectivity between the left and the right IFG has also been found to be stronger in those who responded to intervention versus those who did not (Farris et al., 2011), consistent with the normative compensatory scaffolding process proposed in aging that allows individuals to perform cognitively demanding tasks. Moreover, while the functional role within the context of RD is not yet known, increased right IFG activation and increased right hemisphere white matter FA have been proven positively predictive of reading outcome in RD (but not in typical readers) and suggest a specific role of frontal and right hemisphere regions in compensation in RD (Hoeft et al., 2011). Combining evidence to date, the increased neural measures in the frontal, fronto-striatal, and right hemisphere networks could thus reflect compensatory strategies that individuals with RD develop over time. An alternative interpretation that is yet to gain substantial neurobiological support is that because the fronto-striatal network is involved in procedural/implicit learning, this type of learning plays an important role in typical language development and reading acquisition (Krishnan, Watkins, & Bishop, 2016; Lum, Ullman, & Conti-Ramsden, 2013) and RD involves deficits in procedural learning skills; hyperactivation of these regions may be a sign of anomaly in implicit learning (Lum et al., 2013; Stoodley, Harrison, & Stein, 2006). Future empirical research is warranted to directly address these alternative interpretations.

3.4 | The challenge: Brain anomalies beyond phonological and orthographic processing and developmental stage-dependent differences

Many cognitive and perceptual processing problems other than phonological deficits and associated atypical neural pathways have also been proposed as risk factors contributing to RD, in line with the multiple deficit model where the etiology of RD is multifactorial in nature and the liability for developing RD is continuous (Pennington, 2006). Though it is still necessary to identify the mechanisms in which similar RD characteristics are expressed through different combinations of multiple deficits, for example, individuals with RD may also have reduced activation in the parietal lobe during visual attention tasks (Peyrin et al., 2012; Peyrin, Demonet, N'Guyen-Morel, Le Bas, & Valdois, 2011). Further, the fronto-parietal deficit associated with domain-general processing has been identified in a recent meta-analysis (Paulesu, Danelli, & Berlingeri, 2014). This evidence supports the idea that impairments in visual processing such as visual attention span, attention shifting, and letter position processing may be critical for some individuals with RD (Jednorog, Gawron, Marchewka, Heim, & Grabowska, 2014; Valdois, Bosse, & Tainturier, 2004; Vidyasagar & Pammer, 2010). In addition, subcortical regions such as the left putamen have been identified in some studies in RD as a deficit, rather than a compensatory region that is evident after intervention, possibly associated with articulatory aspects of atypical phonological processing (Booth, Wood, Lu, Houk, & Bitan, 2007; Dole, Meunier, & Hoen, 2013; Kita et al., 2013; Pugh et al., 2013). Finally, abnormalities of networks involving

the cerebellum and thalamus have also been reported in RD research (Jednorog et al., 2015; Linkersdorfer et al., 2012), which have been associated with implicit procedural learning deficits in RD such as motor-sequence learning (Lum et al., 2013; Nicolson & Fawcett, 2007), and rapid naming processes independent from phonological processing (Norton et al., 2014).

It seems unlikely to identify all the possible risk factors and their neural pathways in a single study, and not every study agrees or points to the importance of a specific deficit in RD. Moreover, even for the relatively consistent findings in the temporo-parietal and occipito-temporal regions, some studies have failed to replicate the results of this extant work. The inconsistencies among results of studies make capturing the nature of RD a challenge and suggest that attributing the neural mechanism of RD just to the left temporo-parietal and occipito-temporal regions may be too simplistic. We propose that in addition to taking a multi-componential view that researchers often use to explain these observations, integrating a developmental perspective offers promise. For example, one DWI study did not find that children with familial risk for RD to show white matter anomaly in the expected left arcuate fasciculus (Vandermosten et al., 2015), known to be important for phonological processing (Saygin et al., 2013) in school-age children and adults (Vandermosten, Boets, Wouters, et al., 2012). Instead, this group of at-risk children displayed differences in the left inferior fronto-occipital fasciculus (Vandermosten et al., 2015), known to be important for orthographic processing (Vandermosten, Boets, Poelmans, et al., 2012), similar to older children (Cui, Xia, Su, Shu, & Gong, 2016), but has not been reported in adults with RD. Together with increasing evidence that not only orthographic processing but also phonological processing play critical roles in this ventral tract (inferior fronto-occipital fasciculus) and associated occipito-temporal region especially in young children at-risk for developing RD (Raschle, Zuk, & Gaab, 2012; Specht et al., 2009; Vandermosten et al., 2015), these findings provide an example of how a tract can play different functional significances depending on developmental stages. In the following section, we present a detailed discussion on this developmental aspect.

3.5 | Summary

Numerous RD studies have reported deficits in local measures or brain regions and functional/ structural connections among them. These anomalies are associated with behavioral impairments such as phonological and orthographic processing deficits, as well as others such as visual attention processing deficit. Increased brain activity such as hyperactivation has been identified and regarded as evidence of compensatory mechanisms. Although findings are intriguing, inconsistencies still exist. With this lack of converging evidence in mind, studying the developmental aspect of RD can further elucidate whether these observations are causally related, a result of long-term consequences of poor reading, or innate versus learned protective factors in individuals with RD.

4 | DEVELOPMENTAL TRAJECTORIES OF THE BRAIN ARE ALTERED IN RD

The human brain is plastic throughout the life course, yet developmental changes are especially rapid and robust during the first two decades of life. These changes are governed by individual variations in complex interactions between their genetic endowment and environmental input (Giedd & Rapoport, 2010; Richmond, Johnson, Seal, Allen, & Whittle, 2016), which differ between typical and atypical (RD) readers (Bishop, 2015). Thus, it is conceivable that there

may be differences between RDs and typical readers throughout their developmental trajectories that vary dynamically before they learn to read, as they learn to read, and after they become readers. In other words, a better understanding of the neurobiological mechanism of RD should consider developmental aspects, such as how RD characteristics change with individual differences in brain maturation, reading experience such as print exposure, and skill (reading) acquisition, which are in principle dissociable factors (Goswami, Power, Lallier, & Facoetti, 2014). Such knowledge can help answer the long-lasting question of whether RD reflects the tail end of the normal distribution and manifests a similar developmental trajectory in the typical reading networks but with a developmental lag; or alternatively, RD-related regions show deviation from the typical developmental trajectory both in terms of shifts in spatial location and developmental time-course. It should be noted that because of the complexity and distributed nature of reading-related brain networks, it is more likely that various regions (nodes) and connections (edges) within the networks will show nonuniform patterns. That is, some parts of the networks will show developmental lag, some others may show anomalous patterns that are not consistent with a lag, and yet others may show typical developmental trajectories.

To investigate the ontogenesis of RD cognitive phenotypes and their neural substrates, following a sufficient number of high- (with a family history and therefore genetic vulnerability) and low-risk children from the earliest stage possible (e.g., fetal) before they learn to read and receive an RD diagnosis, until they reach adulthood, is optimal. However, longitudinal studies can be cost and time prohibitive. Therefore, the number of such studies is presently very few (Clark et al., 2014; Morken et al., 2017; Wang et al., 2017). Further, the proportion of individuals who develop RD is relatively low (approximately one third to one half develop RD in high-risk families, but those in the general population is approximately 5–10% as we write above; those with family history are likely to develop RD 4–8 times more than the general population; Ozernov-Palchik & Gaab, 2016; Pennington & Lefly, 2001; Willcutt et al., 2010). With these factors in mind, cross-sectional studies provide us with valuable information about atypical neurodevelopmental trajectories in RD (e.g., Finn et al., 2014; Xia et al., 2016). These studies can then be used to establish hypotheses for longitudinal investigations. In this section, we discuss and summarize the results of studies that utilized four different research strategies: (a) meta-analyses that compared different age groups; (b) cross-sectional studies of RD at various developmental stages; (c) research in prereaders; and (d) the optimal but scarce longitudinal studies.

4.1 | Meta-analyses differentiate neural anomalies between RD in children versus adults

In typical readers, adults show more consistent activation in the left occipito-temporal cortex important for orthographic processing than do children (Martin et al., 2015). In another small meta-analysis in children and adults with RD and their age-matched controls, Richlan et al. (2011) hypothesized that deficits in RD may first manifest as negatively impacting establishment of phonological representations and/or access (typically associated with left temporo-parietal region such as posterior STG) that later leads to impairment in grapheme–phoneme mapping (typically in left temporo-parietal region such as SMG) and eventually orthographic recognition (typically in the associated left occipito-temporal region). In support of this hypothesis, the authors found relatively consistent underactivation in the left occipito-temporal regions in RD adults. On the contrary and as expected, they found less consistent patterns in children with RD in the left occipito-temporal region (Figure 1c). Taken together, these two meta-analyses

of typical and RD readers suggest that the left occipito-temporal region is increasingly being recruited in typical readers from childhood to adulthood, but not in those with RD (Martin et al., 2015; Richlan et al., 2011).

As to the temporo-parietal cortex, RD children compared to RD adults showed more consistent underactivation in a temporo-parietal area, the left SMG, according to the prediction (Richlan et al., 2011). As opposed to simply a lack of activation however, this underactivation was due to the deactivation in RD during a reading related-task compared to the baseline condition (Hoeft et al., 2006; Hoeft et al., 2007; Richlan et al., 2011). Contrary to the hypothesis was the finding that RD adults compared to children showed a more consistent underactivation of the left posterior STG within the temporo-parietal region, similar to the left occipito-temporal region. Although these patterns, that is, significant decrease in abnormality in the left SMG and increase in abnormality in the posterior STG over development, were unexpected and the underlying mechanisms require future research, they reflect developmental stage-dependent abnormalities in RD. Additionally, hyperactivation in the fronto-striatal network increased over development, which has been interpreted as increased compensation with time (Richlan et al., 2011).

4.2 | Age-by-disorder interactions in cross-sectional research

Turning from meta-analysis, a second approach to examine anomalies of developmental trajectories in RD is to simultaneously compare RD with controls at different developmental stages (e.g., Finn et al., 2014; Xia et al., 2016). For example, a task-based functional connectivity study examined a group of children and adults with RD independently relative to their age-matched controls (Finn et al., 2014). There was evidence of lack of typical left lateralization in RD compared to controls in both age groups, yet this difference was qualitatively less severe in adults with RD (no direct comparisons were made). Although this study was not longitudinal, the findings may suggest that the left temporo-parietal region in RD and global measures of functional connectivity in general show maturational delay that later catches up. On the other hand, there are RD anomalies that are more pronounced in older RD individuals. In the same study by Finn and colleagues, the degree (the number of connections in graph theoretical analysis) of the visual word form area, part of the left occipito-temporal region that is an important node for orthographic processing, was significantly reduced in RD adults but not in RD children (Finn et al., 2014). This finding suggests that compared to children with RD, the abnormality in the occipito-temporal network may be more pronounced in affected adults. These results are consistent with the findings from the meta-analysis of the aforementioned occipito-temporal region in the left hemisphere (Richlan et al., 2011) and may suggest that abnormalities in this area and its connectivity are more likely a consequence of lacking reading experience due to RD rather than the cause of this disorder. Alternatively, it could be that this anomaly is causally related but intensifies in its manifestation over the life span due to when the risk genes and other biological factors come into play.

In another study, Xia et al. (2016) recruited two groups of RD children, one with a mean age 11.0 years and the other 14.1 years, as well as age-matched controls. Significant age-by-disorder interactions were found in grey matter volume of the left occipito-temporal cortex, precentral gyrus (decreasing in typical readers and increasing in RD with age), and white matter volume of genu of corpus callosum (increasing in typical readers and decreasing in RD with age), showing regionally specific differences in age-related anomalies. Because of the inherent difficulty in matching all aspects of reading and cognition in younger and older children as well as in adults

with RD as well as in typical readers, it could be that some of these differences reflect a drift in symptom severity and the inclusion criteria. Assuming that the groups are matched in demographics and cognitive and reading ability, these findings could also be taken as changes in neural profile over development. Specifically, these findings demonstrate the possible existence of abnormal developmental trajectories in regions associated with orthographic and phonological processing at the neuroanatomical level. It remains to be seen however, whether each of these deviations in developmental patterns are associated with differences in brain maturation, amount of reading-related experience including print exposure and interventions, or reading abilities and whether they are causally related or due to a secondary change.

4.3 | Exploring neural deficits in preliterate children at risk for RD

One major question in RD research is whether the neural anomalies observed in RD are the consequence of RD that manifest after formal reading instruction or precede the development of RD (Vandermosten, Hoeft, & Norton, 2016). Studies using event-related potentials found evidence that early deficits in speech sound processing, an important process that affects the establishment of typical phonological representation, are closely associated with later language and literacy development (Guttorm, Leppänen, Hämäläinen, Eklund, & Lyytinen, 2010; Guttorm, Leppänen, Richardson, & Lyytinen, 2001; Hämäläinen, Lohvansuu, Ervast, & Leppänen, 2015; Molfese, 2000; Molfese & Molfese, 1985; Molfese et al., 2002; Zuijen, Plakas, Maassen, Maurits, & Leij, 2013), highlighting the importance of early neural impairments (Leppänen et al., 2012). More recently, both structural and functional MRI have also been used to examine preliterate children at-risk for developing RD (e.g., with a family history of RD or show impairment in precursors of reading such as phonological processing) ranging from infants to preschoolers and kindergarteners (Black et al., 2012; Clark et al., 2014; Hosseini et al., 2013; Im, Raschle, Smith, Grant, & Gaab, 2015; Langer et al., 2017; Raschle et al., 2012; Raschle et al., 2015; Raschle, Chang, & Gaab, 2011; Raschle, Stering, Meissner, & Gaab, 2014; Saygin et al., 2013; Specht et al., 2009; Vandermosten et al., 2015; Williams, Juranek, Cirino, & Fletcher, 2017). Most of these studies confirmed impaired brain function and structure in at-risk preliterate children even before they received formal reading instruction or had robust language exposure (see Vandermosten et al., 2016 for a recent review). However, while some findings are similar to what is observed in children who meet the diagnostic criteria for RD, some are different. For example, Vandermosten and colleagues found that children with familial risk showed reduced FA in the left ventral inferior fronto-occipital fasciculus instead of the dorsal arcuate fasciculus that is typically observed in RD research (Vandermosten et al., 2015). Additionally, comparing children with and without RD at the preliterate period is not enough because a child is at-risk does not mean he/she will develop RD in future; in fact, only one third to one half of the at-risk children are found to develop RD (Leppänen et al., 2010; Ozernov-Palchik & Gaab, 2016; Zuijen et al., 2013). Thus, it is essential for neuroimaging studies to follow at-risk children to determine whether these children develop RD (see section below summarizing the work of Clark et al., 2014; Morken et al., 2017; Wang et al., 2017). An increasing number of researchers are beginning to utilize this research design of examining at-risk populations. For instance, Myers and colleagues conducted a longitudinal study in a cohort of beginning readers with or without familial risk for RD. While most at-risk children did not develop RD, the authors found that changes in the left dorsal fronto-parieto-temporal and the ventral occipito-temporal white matter regions from preliteracy to postliteracy were predictive of children's reading fluency in third grade (Myers et al., 2014). Importantly, the authors found that white matter change in the left

temporo-parietal region was uniquely predictive of reading outcome above and beyond environmental measures, familial risk, and pre-reading behavioral measures, suggesting a unique contribution of the development of this neural pathway to reading.

4.4 | Longitudinal studies demonstrate atypical trajectories in RD

Longitudinal design is the optimal approach to elucidate developmental trajectories because researchers can examine not only interindividual differences but also intraindividual variations directly (Clark et al., 2014; Morken et al., 2017; Wang et al., 2017). In a neuroanatomical study, at-risk preliterate children who later developed RD showed a reduction of cortical thickness mainly in the primary sensory areas (perceptual regions) compared to typical controls (Clark et al., 2014). Only after the children received formal reading instruction for several years, that is, became literate and in some cases developed RD, did the difference emerge in the known reading regions such as the left fusiform gyrus in males but not females. The authors interpreted these findings as support for the low level sensory deficit hypothesis of RD (Goswami, 2015), in which deficits in the sensory cortex affect typical maturation of higher-level areas that receive greater input from lower level regions during development.

In contrast to the gray matter morphometry findings, studies focusing on structural and functional connectivity have revealed different patterns of anomalies (Morken et al., 2017; Wang et al., 2017). Wang et al. (2017) directly examined developmental trajectories of the microstructural features in twenty major white matter fibers in children who were later diagnosed with RD and compared them to those who later became fluent readers. The authors found a persistent reduction of FA in a region along the left arcuate fasciculus that connects the left STG and the IFG. Additionally, the children who ended up with RD (in this study, below one standard deviation on one of the four reading measures) displayed a slower rate of increase in connectivity. Therefore, this study demonstrates that impairments in putative reading-related structures exist before formal reading instruction and remain throughout various developmental stages. The deficit can be also influenced by factors such as environment and experience as the deviations increased with development. On the other hand, Morken et al. (2017) examined effective connectivity (i.e., functional connectivity with directional information) in preliterate children (age 6) followed through the age where children were expected to be fluent readers (age 12). Overall, they identified a surprising pattern of neural normalization that was observed by the age of 12 despite reading abilities deviating more over time. This is in contrast to the aforementioned study on structural connectivity though this study only followed children until the age of 10.2 years (Wang et al., 2017), and hence, normalization in structural connectivity may be observed if followed until an older age. Among these connectivity patterns examined, there were three patterns. First, left occipito-temporal connectivity (to left temporo-parietal [STG] and IFG regions) showed a reduction in RD compared to typically developing groups only at the preliterate stage (age 6), possibly reflecting a primary and causal deficit. This pattern is to some extent consistent with Wang et al. (2017) where at-risk children shown reduced FA in left arcuate fasciculus at the preliterate stage. Second, an emergence of significant reduction in left IFG connectivity (to precentral gyrus and inferior parietal lobule within the temporo-parietal region) in RD compared to typical readers was observed only after they had begun learning to read (age 8) and not at the preliterate stage, possibly indicating a secondary neural deficit in RD. Third, left occipito-temporal connectivity to the precentral gyrus showed stronger and not reduced connectivity only at the beginning reading stage (age 8) in RD compared to typical readers, suggesting a possibly compensatory process.

Importantly, these studies point to atypical developmental trajectories in RD that could be missed or misinterpreted if only examined deficits in RD at one time-point, especially when results from groups of children with a wide age-range are averaged (collapsed). These findings also point to the need to extend RD research to include personalized growth curves for within participant analyses of maturational change, rather than relying solely on group comparisons. While group comparison is an important approach to identify broad mechanisms and may cast shadows upon individual differences, individual difference approaches may elucidate pathways toward compensation or maximal sensitivity to intervention within certain developmental windows that likely vary across individuals.

4.5 | Summary

Emerging research shows anomalous neurodevelopmental patterns in RD that are consistent with impaired phonological and orthographic processes that are both characteristic of RD. Furthermore, individuals with RD also show different developmental trajectories of brain measures in specific regions and networks. Although these neuroimaging studies alone cannot determine causality (which was the focus of Part I of this review), they deepen our understanding of the neurobiological manifestations of RD.

5 | SUMMARY AND FUTURE DIRECTIONS

Comprehensive understanding of the neural mechanisms underlying RD is a challenging undertaking for research, yet it is necessary for accurately identifying and optimizing intervention. Extant work has laid the foundations to understand the neural mechanism of typical reading acquisition and RD: (a) typical reading relies on well-organized neural networks (e.g., the left temporo-parietal, occipito-temporal and inferior frontal areas) and efficient communications (e.g., the arcuate fasciculus and inferior longitudinal fasciculus), which are associated with specific components of reading; (b) increasing evidence in support of a multiple deficit model of RD; and (c) individuals with RD are characterized by atypical developmental trajectories of reading-related brain structure, function, and connectivity, indicating that having RD is a dynamic process rather than static.

This review primarily emphasized the developmental aspects of the neural anomalies of RD. The research to date has adopted different methodologies, each with advantages and inherent limitations. Briefly, meta-analysis can integrate results of studies with RD at different ages but is vulnerable to several factors such as reporting bias. Studies with multiple age groups can reveal the age-by-disorder interaction, but the approach is still cross-sectional in nature. Studies focused on preliteracy can serve to answer the question of whether the neural deficits existed before the start of formal reading instruction in at-risk children; however, not all at-risk children eventually meet the criteria for RD. A longitudinal design is optimal, though costly, especially within the context of MRI research, and hence, coming up with appropriate research questions that could specifically be answered using this approach is important. Much more work awaits our attention to better address the question of whether the developmental trajectories of specific neural features are neurobiologically unique aspects of RD (see also Part I of our two-part review "Neurobiological bases of reading disorder Part I: Etiological investigations"). Further, there are at least two questions that directly emerge from this review: (a) what factors influence the specific manifestations of these anomalies and (b) whether intervention can alter any of these

abnormal trajectories. Moreover, future research may have begun already (a) adopt approaches such as MVPA and network analyses to examine RD brain development as patterns and at the individual level, which can take inter-regional relationship into consideration; (b) include large-scale multi-site research on developmental trajectories using accelerated longitudinal designs to acquire a more precise time table of the onset and course of RD; and (c) examine how multiple neural risk factors interact or cumulatively contribute to this dynamic progression. We believe that these research avenues together with discoveries to date and transdisciplinary approaches will fuel pathways toward improved understanding of RD and ultimately impact how we identify and intervene to provide each child with maximal support to improve educational and related outcomes.

Finally, it is worth noting that there are other important avenues of RD research beyond the scope of this review and therefore not captured here. Briefly, these topics include but are not limited to (a) cross-linguistic comparisons of the neural mechanism of typical reading and RD (Martin, Kronbichler, & Richlan, 2016; Richlan, 2014; Rueckl et al., 2015; Zhu et al., 2014); (b) RD in multilingualism, which is becoming particularly relevant as more individuals in the world are now multilingual than monolingual, and as we discover more about cross-linguistic similarities and differences of RD (Siegel, 2004); (c) investigation of the brain basis of RD using various identification approaches and definitions of RD (a current topic with the new Diagnostic and Statistical Manual of Mental Disorders, DSM-5; American Psychological Association, 2013; Hancock, Gabrieli, & Hoeft, 2016; Simos, Rezaie, Papanicolaou, & Fletcher, 2013; Tanaka et al., 2011) as well as subtypes of RD that appear to have different neural profiles (Jednorog et al., 2014; Norton et al., 2014); (d) investigation of processes other than reading-related processes such as visuo-spatial processing that might be predicted based on atypical brain organization (Diehl et al., 2014); and (e) biomarkers and neuroprognosis where neuroimaging data are used as markers to identify and to predict the development of RD, response to intervention, and compensatory mechanisms (Cui et al., 2016; Gabrieli, Ghosh, & Whitfield-Gabrieli, 2015; Hoeft et al., 2011; Plonski et al., 2017).

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