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Ola Ozernov-Palchik

Xi Yu

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Nadine Gaab

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Lessons to be learned: how a comprehensive neurobiological framework of atypical reading development can inform educational practice

Ola Ozernov-Palchik^{1,2}, Xi Yu^{1,3}, Yingying Wang^{1,3}, and Nadine Gaab^{1,3,4}

¹Laboratories of Cognitive Neuroscience, Division of Developmental Medicine, Department of Medicine, Children's Hospital Boston, MA 02115, United States

²Center for Reading and Language Research, Tufts University, Medford, MA 02155, United States

³Harvard Medical School, Boston, MA 02115, United States

⁴Harvard Graduate School of Education, Cambridge, MA 02138, United States

Abstract

Dyslexia is a heritable reading disorder with an estimated prevalence of 5–17%. A multiple deficit model has been proposed that illustrates dyslexia as an outcome of multiple risks and protective factors interacting at the genetic, neural, cognitive, and environmental levels. Here we review the evidence on each of these levels and discuss possible underlying mechanisms and their reciprocal interactions along a developmental timeline. Current and potential implications of neuroscientific findings for contemporary challenges in the field of dyslexia, as well as for reading development and education in general, are then discussed.

Introduction

'Children are wired for sound, but print is an optional accessory that must be painstakingly bolted on' [Pinker in [1], p. ix–x].

Developmental dyslexia is a heritable neurobiological condition that is characterized by an unexpected failure to develop accurate or fluent reading and affects approximately 5–17% of children [2]. Individuals with dyslexia have shown structural and functional brain atypicalities in the complex reading network which consists of (1) left inferior frontal regions, (2) dorsal temporo-parietal regions, and (3) ventral occipital-temporal regions [3,4]. The etiological basis of dyslexia is not well understood due to the complex interactions among multiple genetic risk variants and environmental factors, which collectively affect typical and atypical reading development.

This paper aims to disambiguate the genetic, environmental, cognitive, and neurobiological components that are involved in predisposing a child to developing dyslexia. In particular, it

Corresponding author: Gaab, Nadine (nadine.gaab@childrens.harvard.edu).

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integrates current experimental evidence on the development of the reading brain with Pennington's [5] multiple deficit model (MDM) of developmental disorders and van Bergen's extended 'intergenerational multiple deficit model' of dyslexia [iMDM, 6**]. It further adds a developmental perspective to the current models and reviews specific factors and underlying mechanisms that contribute to atypical reading as well as their developmental trajectories prenatally and postnatally. Additionally it reviews and suggests relationships and interplays between the various levels and proposes a descriptive multi-componential model for the etiology of development of dyslexia which should be seen as an extension rather than a modification of the current models. Furthermore, current as well as potential implications of this framework for educational practice and policy are discussed.

Genetics and the neurobiology of dyslexia

Heritability of dyslexia has been estimated at approximately 60% [7,8]. Interestingly, these estimates are much lower (20–33%) if only siblings but no parents are affected, and higher (76–78%) if both parents are affected [9].

Several candidate susceptibility genes for dyslexia (e.g. ROBO1, DCDC2, DYX1C1, KIAA0319) have been reported, the majority of which are involved in brain development [10,11*]. A tentative pathway from genetic effects to developmental brain changes and to perceptual/cognitive deficits in dyslexia has been proposed [10]. According to this hypothesis, variant function in any number of genes involved in cortical development may lead to subtle cortical malformations involving neural migration and axonal growth, which in turn results in atypical cortico-cortical and cortico-thalamic circuits. Alterations in these circuits may be associated with the range of sensorimotor, perceptual, and cognitive deficits reported in dyslexia [5].

Studies in rodents and humans have demonstrated support for this hypothesis [12–16] and several studies have linked genetic with neuroimaging studies. It has been shown that experimental interference of the dyslexia susceptibility genes in rodents causes atypical neuronal migration, which in turn results in localized matter malformations that affect cortical circuitry [16,17]. For example, in utero disruption of KIAA0319 expression in rats has been shown to result in poor neural representation of speech sounds in the auditory cortex and in impaired performance on phoneme discrimination tasks [18*,19,20]. The reported behavioral impairments in these animal studies are similar to those observed in individuals diagnosed with dyslexia [e.g., 21], especially those who showed KIAA0319 and DCDC2 variants [22]. Additionally, studies in adults and children have shown that polymorphisms in dyslexia susceptibility genes are associated with structural temporoparietal gray and white matter alterations during development [13,23–25]. For example, a common variation near the dyslexia susceptibility gene ROBO2 has been associated with expressive vocabulary skills and the development of the posterior region of an inter-hemispheric white matter pathway (i.e., splenium) [26**]. The reported brain alterations observed in neuroimaging studies are consistent with the postmortem studies of individuals with dyslexia which revealed neural ectopias in various regions important for auditory and language processing as well as reading [24]. This cumulative evidence provides a robust

support for an association between the dyslexia susceptibility genes and brain function and structural crucial for learning to read.

While more work needs to be done to identify the genes that are specifically linked to dyslexia, advances in our ‘tool sets’ for genetic analyses have vastly expanded our overall understanding of the genetics of developmental disorders such as dyslexia. For instance, research has highlighted the importance of generalist genes that are expressed throughout the brain and the nervous system, and are associated with broad cognitive functions important for learning. One such example is the COMT gene, which is involved in major metabolic functions in the brain and has been linked to general cognitive processes, such as executive function [27,28] and reading [29]. Another example is the FOXP2 gene that has been linked with disorders of speech and language, as well as dyslexia. It functions during the transcription of other genes and is thus expressed in multiple regions of the brain [30]. Discovery of the generalist genes explains the strong association in performance between reading and other domains such as language and mathematics, as well as the frequency of comorbidities between dyslexia and other disorders. This suggests that reading disability and other learning disabilities are in part governed by learning mechanisms with a general genetic basis [31,32]. Most importantly, a variety of genes have been identified that function at different time points of neurodevelopment and affect various developmental stages such as neuronal proliferation or interneuron migration, thus implicating a number of cell biological pathways critical for typical early brain development [33].

Genetically pre-determined brain structure is not fixed across development; rather, genetic makeup provides a mere blueprint for the brain architecture that serves as the basis for processing information in the environment [34]. Thus, it remains debated which brain characteristics of dyslexia predate the onset of reading instruction and which are a result of reduced reading practice (e.g. due to the daily struggle to read).

Structural and functional brain alterations in dyslexia and their emergence

Learning to read requires the coordination of an ensemble of sensory and cognitive systems, which are utilized to form the left-hemispheric neural reading circuit. A tentative model of reading development suggests that when children start to learn single word reading, superior temporal regions that are specialized for phonological processing become increasingly connected with temporo-parietal regions important for the integration of orthography with phonology [35]. Following the development of the temporo-parietal circuit for linguistic structures, the ventral occipito-temporal circuit, including lateral extra-striate, fusiform, and inferior temporal regions, becomes specialized for print and rapid word processing (i.e., sight word recognition), and a putative visual word form area (VWFA) emerges [36,37]. Then, through extensive reading practice, the ventral circuit for reading becomes increasingly automatic. The anterior inferior frontal circuit also plays an important role in reading development, although its specific contribution is not yet well defined. It is associated with various reading-related functions, including phonological processing, speech planning, lexical access, semantics [38], and comprehension [39,40], as well as with general cognitive functions, such as attention and inhibition [41]. This circuit shows increased involvement with age and reading experience [42–45].

Magnetic resonance imaging (MRI) studies in children and adults with dyslexia commonly demonstrate reduced gray matter volume indices and cortical thickness, as well as hypoactivation in left-hemispheric temporo-parietal, occipito-temporal, and inferior frontal networks (Figure 1a,b) [46,47]. Children with dyslexia display this pattern of hypoactivation even when compared to younger children with equivalent reading skills [48,49], suggesting that the observed alterations are not due to delayed maturation but are instead unique brain characteristics of dyslexia. Several papers have reported, however, that at least some brain alterations in individuals with dyslexia are likely due to impoverished reading experience [50,51]. Dyslexia has further been associated with structural differences in left-hemispheric white matter organization (Figure 1c) [52–55,56**] and reduced resting-state and task-based functional connectivity among regions important for reading has also been demonstrated [57,58].

Dyslexia is thought to originate in genetically-driven cortical, sub-cortical, and white matter abnormalities. Accordingly, pre-reading children with a family history of dyslexia (FHD+) have exhibited atypical sulcal patterns (i.e. the arrangement, number, and size of primary cortical folds), possibly reflecting a less optimal organization of cortical function and white matter connectivity during prenatal development (Figure 1d) [59**]. Moreover, atypical neural connectivity, such as decreased white matter integrity in the arcuate fasciculus, a white matter tract connecting dorsal posterior and anterior regions, has been observed for FHD+ children as early as infancy [60**]. The notion of early atypical brain development has been further supported by several studies that showed aberrant neural responses in FHD+ infants when compared to controls. For instance, alterations in neural responses to basic speech sounds have been observed using Electroencephalography (EEG) in FHD+ newborns [61–65] and most importantly, in newborns who subsequently received a diagnosis of dyslexia [e.g., 61] or who showed atypical language and reading development in toddlerhood or elementary school [62,63,66–68]. Furthermore, at-risk preschoolers have demonstrated reduced gray matter volume and reduced cortical thickness in temporo-parietal and occipito-temporal regions [51,69] as well as hypoactivation in these regions during phonological [70] and orthographic [71,72] processing. These neural alterations in regions critical for reading-related functions can further disrupt the development and specialization of the phonological and orthographic systems as well as the connectivity of these systems with each other and other higher order components of the reading network.

Neuro-metabolic alterations in dyslexia

Magnetic Resonance Spectroscopy (MRS) is a noninvasive in vivo technique that estimates the amounts of various brain metabolites by utilizing the fact that their individual resonance frequencies are all distinct from the dominant water peak. The previously reported evidence for atypical brain development in posterior left-hemispheric regions motivates the investigation of the biochemistry and metabolic aspects underlying structural and functional alterations observed in individuals with dyslexia. To date, several studies have examined the relationship between neurometabolites and reading in individuals with and without dyslexia. Most of these studies have examined either Choline (Cho) or Glutamate (Glu) and their relationship to reading abilities/disabilities [73*,74–76]. Cho is a nutrient important for the synthesis of cell membranes and an indicator for de novo myelin and cell membrane

synthesis [77]. Developmental studies have shown an increase in the first 3 months of life with a subsequent decrease most likely due to accelerated myelination, which incorporates Cho into macromolecules associated with myelin [78]. Several studies have shown increased levels of Cho in temporo-parietal regions in adults and children with dyslexia [73*,74–76]. A relationship between poor phonological processing and increased Cho levels in adults was observed, and the Cho/Creatine (Cr) ratio accounted for a unique proportion of variance in phonological decoding, after controlling for age, cognitive ability, and timed/untimed sight-word reading [75]. A similar relationship was demonstrated in childhood, with findings of significant correlations of Cho/Cr ratios with word reading and passage comprehension [73*]. It has been suggested that elevated Cho reflects an inability to properly incorporate Cho-containing molecules into myelin [79] or the loss/disruption of normal myelin, which would increase the availability of such Cho-containing compounds, as observed in dysmyelinating disorders [80].

The neurometabolite Glu is one of the primary excitatory neurotransmitters that is utilized throughout the brain. Thus, Glu is essential for various neural functions critical for perception, cognition, and memory [81,82] peaking in concentration at approx. 4–6 months before subsequently declining until a plateau around age 2 [83]. To date, only one study has examined the relationship between reading and Glu in humans and further compared children with dyslexia to controls [73*]. The results showed that Glu/Creatine (Cr) ratio significantly correlated with phonological awareness and vocabulary at age 7 and that children with dyslexia exhibited higher Glu/Cr ratios compared to controls, which has been suggested to reflect hyperexcitability. This hyperexcitability may play an important role in the etiology and symptomology of dyslexia [73*], which has been supported by studies showing inconsistent trial-to-trial performance [84] and greater variability in neuroimaging studies [85], including brainstem responses [21], in individuals with dyslexia. Furthermore, this hypothesis is in line with animal studies observing that mutations of the dyslexia susceptibility gene DCDC2 can lead to hyperexcitability, such as spontaneous firing, reflecting atypical glutamatergic activity [86].

Perceptual and cognitive deficits and risk factors of dyslexia

The cognitive phenotype of dyslexia is heterogeneous [87]. Prior attempts to identify and describe dyslexia from a single deficit perspective were unsuccessful and instead a multi-deficit approach has been adopted by most researchers [5,88]. This approach views dyslexia as representing the interaction of multiple risks and protective factors resulting in distinct cognitive profiles along a continuum of severity of reading outcomes.

Studies examining infants and pre-reading children with a hereditary risk for dyslexia have identified atypical language development in these children, as they tend to show poor categorical speech perception, delayed onset of talking, shorter mean length of utterances, lower complexity of syllables produced, and poor receptive or expressive vocabulary [89–91]. Longitudinal studies have further demonstrated the importance of these early language skills for the development of reading. However, these symptoms have also been observed in children with a subsequent diagnosis of specific language impairment or speech sound disorders, and could be a consequence of the high occurrence of comorbidities between

dyslexia and language disorders [91–94]. Therefore, delayed language development in some children with dyslexia risk is likely indicative of a cumulative contribution of etiological factors for each disorder, rather than being a specific marker of dyslexia risk.

Differences between preschoolers with and without familial risk for dyslexia have been identified on tasks measuring phonological awareness, verbal working memory, rapid automatized naming (RAN), and letter knowledge [95–97]. Phonological awareness is the meta-understanding of the sound units of oral language [98]. Verbal working memory is the memory system that is involved in the storage and active processing of current information [99]. Both have shown a significant association with a genetic (familial) risk for dyslexia as well as with the actual reading outcomes [100*,101]. A stepwise pattern of performance on these measures is commonly observed, with at-risk children with typical literacy outcomes performing worse than no-risk readers, but better than at-risk children with a subsequent dyslexia diagnosis [90,102–104]. RAN represents the ability to rapidly retrieve the name of visually presented familiar items in a serial array [105,106] and has been shown to be a robust predictor of actual reading outcomes (particularly reading fluency), especially in poor readers [102,107]. Letter knowledge measured in kindergarten is the most robust, but ephemeral (i.e. it loses its predictive accuracy beyond kindergarten), predictor of reading ability [108,109]. However, since it is strongly influenced by environmental factors, such as home literacy and preschool enrollment, letter knowledge may predominately reflect lack of experience rather than a cognitive deficit in dyslexia [110].

Atypicalities in lower-level auditory or visual magnocellular processing in individuals with dyslexia have also been reported [111–116]. Several studies have demonstrated atypical auditory processing of slowly varying acoustic signal and rapid auditory processing in pre-reading children at risk for dyslexia [62,116–119]. Individuals with dyslexia demonstrated poor ability to process short sounds and stimuli with brief transitions [120,121]. Because brief frequency transitions are important for discriminating linguistic units, it has been suggested that the phonological deficit in dyslexia stems from this lower-level sensory impairment [113]. More recently, studies reported impaired discrimination of rise time cues (a rate of amplitude change) in speech in individuals with dyslexia. These cues are important for detection of speech rhythm and prosody [122,123]. Additionally, individuals with dyslexia have been shown to perform poorly on musical rhythm discrimination and reproduction tasks [124]. Difficulty with perceiving stress cues and rhythm in speech could undermine the ability to develop adequate representations of phonemes, thereby impairing the development of phonological awareness skills [114,125]. Studies examining visual and magnocellular processing in pre-reading children have failed to reach consensus, and increasing evidence points to this deficit being a result of limited reading practice rather than an underlying deficit in the magnocellular visual pathway [126–128].

Finally, some studies provided modality-general explanations of dyslexia such as poor perceptual learning [129] and poor temporal synchronization [130]. Deficits in attention and executive function have also been demonstrated [131–133]. Since reading development and performance requires cross-modal integration, these cross-modal mechanisms play a significant role in the development of phonological and orthographic abilities and in fluent reading [130].

Environmental influences and risk factors of dyslexia

Environment has a strong influence on brain and cognitive [134–136,137**,138–140]. Prenatal factors such as maternal stress, smoking, and alcohol consumption, can affect cortical development and neural migration [141]. Children's postnatal early environment is largely shaped by cultural and parental characteristics and the environment has a significant influence on the trajectory of brain development in childhood and through adolescence [134–136,137**,138–140]. The development of brain regions that support language, reading, and executive functions are particularly affected by socioeconomic factors [135,137**]. Poor environmental conditions can exert unfavorable influence on children who are genetically predisposed for dyslexia increasing the likelihood of later reading failure [101,142]. Parents with lower educational background and socioeconomic status (SES) tend to have fewer books at home, and spend less shared reading time with their children [143]. This home literacy environment affects the development of early reading skills [110,144,145], particularly in families with low SES [146,147].

Besides individual households, negative neighborhood features such as high concentration of poverty and high family density, have imposed adverse effects on children's vocabulary and letter knowledge, both directly [148,149*] and indirectly via parental interaction [150,151]. At the onset of schooling, ineffective instructional practices, negative social perception, limited instructional resources, and other adverse academic factors may further exacerbate poor reading development in children [152,153]. Moreover, lack of parental awareness may result in negative parent–child interactions and poor psychological outcomes for the child [154]. Lack of awareness can also prevent parents and teachers from seeking effective resources for intervention and result in delayed identification of dyslexia risk [155].

Overall, environmental factors were shown to explain up to 30% of individual differences in reading [156–158]. Environmental components interact with each other in conjunction with genetic factors to form a reciprocal process creating long-lasting effects extending over generations [142]. Individuals with dyslexia are less likely to complete high school [159**], pursue higher education [160], and are at an increased risk of entering the justice system [161]. Children of these individuals would subsequently be both at a higher genetic and environmental risk.

Protective factors and compensatory mechanisms

Dyslexia is a persistent condition that affects individuals throughout their lifetime. Many adults with a childhood diagnosis of dyslexia never develop fluent or proficient reading skills. Others become functional readers, but still suffer from residual difficulties in spelling, phonemic awareness, and fluency [162–164]. The latter group is often referred to as compensated dyslexic readers or resilient readers. The mechanisms through which these individuals achieve reading competency are not well investigated or understood [165]. Nevertheless, several cognitive and environmental protective factors have emerged in the literature including high intelligence, rich vocabulary, strong reliance on semantic context, large visual memory, strong reasoning skills, and the ability to maintain attention [166,167,168**,169].

Brain studies of compensated individuals have demonstrated that these individuals recruit additional regions not evident in typical controls or individuals with persistent dyslexia. For example, increased activation in the right inferior frontal gyrus (Figure 1b) has been reported across several studies during phonological processing in compensated individuals with dyslexia [164,170–172] and in response to intervention [173*].

A proposed integrative model

As discussed, dyslexia is an outcome of multiple risks and protective factors interacting at the genetic, neural, cognitive, and environmental levels. Therefore, a multidimensional etiological model is necessary for understanding dyslexia. Pennington [5] has proposed the multiple deficit model (MDM) of learning disabilities in which multiple etiological factors interact probabilistically to increase the liability for a disorder in a continuous and quantitative manner. Specifically, genetic and environmental factors interactively affect neural systems that in turn affect multiple cognitive processes, which together result in a risk profile for a single developmental disorder or multiple disorders. The MDM model provides a general framework for explaining comorbidity among developmental disorders, but it does not specify the components of each of the multifactorial levels of influence or their developmental trajectories. Van Bergen and colleagues [6] have extended the MDM into an intergenerational MDM (iMDM) by adding the intergenerational transmission of risk and of protective factors for learning disabilities. The extended model iMDM specifies the cognitive and familial environmental risk factors for dyslexia. It predicts a continuum of liability distribution for dyslexia and emphasizes the importance of parental cognitive abilities for evaluating risk in children.

The current paper further expands on MDM and iMDM by adopting a developmental approach and by specifying factors and mechanisms that contribute to the development of dyslexia. Figure 2 summarizes the components for each of the levels outlined by Pennington and van Bergen and further integrates them in a developmental framework that specifies the importance and sequel of these specific factors and mechanisms at each time point on the developmental axis as well as their developmental trajectories. Experimental evidence from neuroimaging, genetic, and behavioral studies has been incorporated to illustrate the independent significance of each of the components for dyslexia but also their reciprocal relationship. We hypothesize that this interplay between the various levels on the developmental axis determines the location(s) of the brain alterations, the severity of the alterations and the connectivity strength between brain structures that support reading. These factors can further adversely influence neural responses and the development of cognitive functions. These interplays most likely vary tremendously depending on the developmental time point and are strongly influenced by a child's environment. This is supported by studies that suggest that with the concomitant exposure to poor home literacy or instructional quality, the likelihood of FHD+ children to develop dyslexia further increases [142]. Although in the current paper psychological factors (e.g., motivation, self-efficacy) in dyslexia were not reviewed, they are nevertheless important and can serve as additional exacerbating or protective influences on reading development [174].

Implications for educational practice and policy

It is important to exercise caution when attempting to translate findings from neuroscience to practices in education and policy. Misinterpretation and over-simplification of data can cause persistent neuromyths [175] that can in turn be used to justify inadequate practices [176]. Nevertheless, since the potential gains are invaluable, the task of attempting to translate emerging findings in the prolific field of dyslexia research to real-world practices is worth undertaking. Here, we highlight several contemporary challenges in education and discuss the potential role of neuroscience in addressing these.

Can neuroscience inform a definition of dyslexia?

The high behavioral heterogeneity of dyslexia prompted some to suggest to eliminate the term dyslexia all together [2]. Neuroimaging studies are beginning to inform several of the most contentious questions historically faced by the field: for instance, the field has debated whether a multi-deficit view of dyslexia should be accepted. Several studies so far have demonstrated that literacy skills such as PA and RAN are associated with distinct neuroanatomical regions [177–179] and that children with different profiles of deficit on these skills have unique patterns of activation during a reading-related task [180]. This supports the multi-deficit approach to dyslexia by suggesting that distinct brain mechanisms are associated with the various dyslexia profiles.

How do environmental factors influence a brain's ability to read?

Environment has a powerful impact on brain development both prenatally and postnatally. In the case of dyslexia, language and literacy environments can both predispose children for reading failure and potentially protect them despite a genetic risk. Policies and interventions that encourage parents to optimize their home literacy environment, by increasing shared reading time and using rich child-directed speech, have been shown to have important positive impacts on language and reading outcomes [110,181]. Neuroscience can play several important roles in this domain. It can, for example, shed light on the underlying mechanism through which environmental factors influence reading circuitry. For instance, a relationship between home reading exposure and activation in left-hemispheric posterior regions of the reading network as well as brain areas supporting mental imagery and narrative comprehension has been recently demonstrated [182]. This in turn can inform (a) the development of specific interventions that focus on certain aspects of home language and literacy and (b) teaching practices in the classroom, especially for children with reduced language and home literacy exposure. Furthermore, imaging can potentially assist in quantifying the influence of environmental variables on the development of language and pre-reading networks in infants, at an age where standardized behavioral language measures often fail.

Is it feasible to utilize neuroscience for the early identification of dyslexia risk?

Emerging evidence suggests that neuroimaging can enhance the prediction of reading outcomes over behavioral measures [61,63,66–68,170,183,184**,185]. Furthermore, early neural alterations in dyslexia seem to predate reading onset and reflect the differential developmental trajectory of reading brain networks as the result of genetic predisposition for

dyslexia. However, to date, these alterations cannot serve as early biomarkers, and it is unclear whether we will ever have reliable biomarkers with appropriate levels of specificity and sensitivity. Nevertheless, if proven cost-efficient and if specificity and sensitivity are maximized, there may be the possibility to utilize neuroimaging to enhance the accuracy of early identification of risk most likely in a clinical setting. While several behavioral measures show promise in predicting which children will develop dyslexia even before reading onset [95,186], early identification requires a trade-off between specificity (i.e., reducing the rate of false positives) and sensitivity (i.e., reducing the rate of false negatives) of identification, which can often result in high rates of over/under-identification. An assessment battery for early identification that consists of behavioral measures as well as neuroimaging measures may be able to maximize the specificity and sensitivity with subsequent important implications for educational practice and policy.

When is the best time to intervene for atypical reading development?

It has been shown that targeted literacy interventions are most effective when administered in kindergarten and first grade [187,188]. Across six studies, after receiving intensive instruction (number of instruction hours ranged from 30 to over 300 across studies), 56–92% of the at-risk beginning readers reached the range of average reading ability [187]. A meta-analysis comparing early intervention studies offering at least 100 sessions, reported larger effect sizes for intervention studies conducted with kindergarten and first graders than with children in 2nd and 3rd grades [188]. While these results strongly favor a customized intervention as early as possible, it may be possible to utilize neuroimaging to determine the optimal window of intervention in each child based on (individualized) neuroimaging measures of brain development.

Can brain measures assist us in determining school readiness?

Ensuring that all children enter school ready to learn is an important goal of education and policy [189]. School readiness is a multi-dimensional construct with many levels of intrinsic and environmental influences, and it has been suggested that one-dimensional behavioral measures attempting to capture whether a child possesses the emotional, behavioral, and cognitive skills needed to thrive in school are imprecise [190]. Additionally, performance on specific tasks, such as reading, is an outcome of multiple systems. For example, cognitive control, a strong predictor of school readiness, is closely linked with the affective system, but can also influence performance on behavioral measures of pre-literacy [189]. While poor cognitive control or ‘affective immaturity’ may indicate the need to delay school start and retain the child in a more intimate and individualized preschool setting, poor pre-literacy skills can instead signal the urgency for the formal literacy instruction available in kindergarten. Additionally, as discussed, neuroimaging methods can potentially reveal which specific neural systems are protracted in development or follow an alternative developmental trajectory in a particular child and therefore may inform decision-making.

What factors are important for shaping a ‘resilient’ reading brain?

As described above, several studies reported potential compensatory mechanisms that influence typical reading development in at-risk children. It remains unclear what the role of these compensatory regions is during the development of typical reading, under which

circumstances they form, if they are present prior to the onset of reading, and most importantly, which environmental or instructional factors may stimulate or hinder these alternative pathways. The answer to these questions can potentially inform a variety of educational decisions and help to build customized interventions. Children who grow up under adverse circumstances often display numerous brain alterations that affects a variety of neural circuits including the language and reading circuit [137**,191]. Neuroimaging can shed light on the relationship between protective environmental factors and the development of the reading network, for example, and most importantly its timeline in order to highlight and inform preventive strategies and interventions (e.g., does enhanced home literacy in infancy ‘remediate’ early atypical reading circuitry in children from low socioeconomic backgrounds?).

Which atypical reading brain learns best under which circumstances?

The multi-deficit view of dyslexia necessitates that intervention studies are individualized in order to optimize outcomes. Indeed, intervention studies have shown that treatment efficiency varies based on individual profiles of dyslexia [192,193]. Neuroimaging methods have revealed the potential to identify the unique differences across individuals with disorders, such as dyslexia, and relate those differences to future behavioral outcomes [194**]. For example, it has been shown that spatio-temporal brain activation profile in temporo-parietal regions, as measured with magnetoencephalography (MEG), prior to reading intervention in children with dyslexia predicted which children will actually benefit from the given intervention [195]. This suggests that children with neurobiological profiles that are more typical are more likely to respond well to intervention [173] and further highlights the role of compensatory neural mechanisms. In the future, neuroimaging may be utilized to determine which brain will benefit best from which intervention.

Conclusion

The current state of understanding the etiological basis of dyslexia requires cautious optimism. There is emerging understanding of each of the genetic, cognitive, neural, and environmental levels as well as the interaction among these levels. The appreciation of the complexity of dyslexia can offer multiple insights for further investigation and translation. Embracing a multifactorial model of dyslexia encourages greater interdisciplinary and a multiple-componential approach to studying and treating dyslexia.

Most importantly, using so called ‘brain-based’ tools in education for prediction and intervention is still out of reach (and may even be proven to be unfeasible). The limited number of studies, small sample sizes, and differences in criteria for defining dyslexia across neuroimaging studies hinder the generalizability of findings and their application to clinical population. Additionally, while neural measures enhance the overall prediction accuracy of behavioral measures, their additional contribution to date has been moderate and a cost-efficiency model weighing important factors such as benefits and high costs of neuroimaging has not been computed yet.

Due to the complexity described above, the application of neuroscience in education has been described ‘a bridge too far’ [196]. Indeed, historically, attempts to translate research

findings to ‘real-world’ practices have been ridden with dubious brain-based recipes for practice and premature misinterpretations of data [176,197*]. Furthermore, there has been some resistance from practitioners to the one-sidedness with which scientific knowledge has been handed down from research labs into schools. Yet, cross-disciplinary research, described above for dyslexia, has become increasingly popular and prolific. As a result, much advancement important for education and policy has been made. With this paper we hope to contribute to an increasing body of knowledge on how neuroscience research can be integrated with applied work in early identification, prevention and intervention of dyslexia, thereby maximizing intellectual and psychological outcomes for those at-risk for dyslexia.

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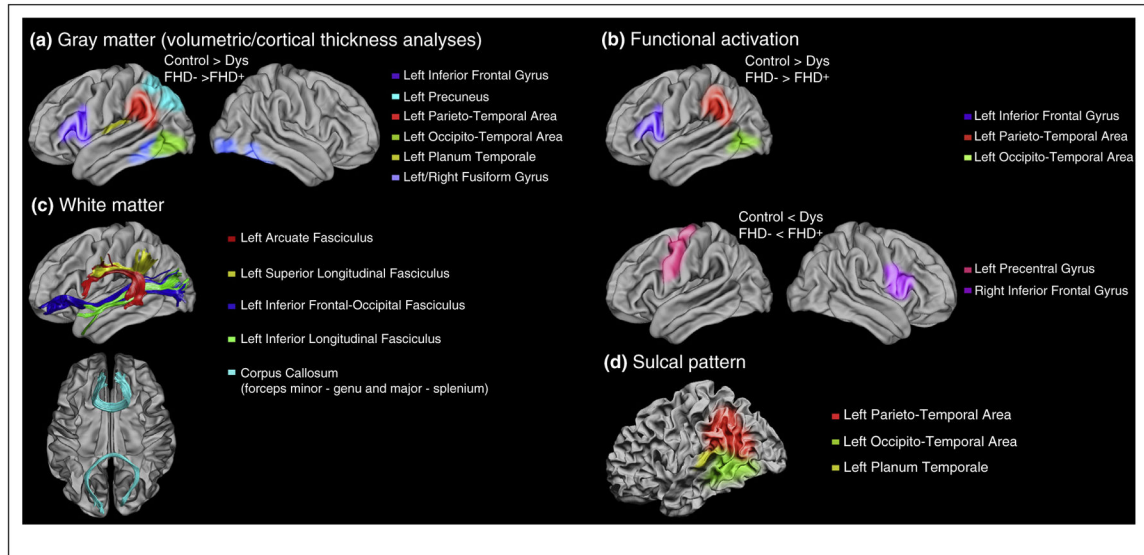


Figure 1. Structural and functional brain alterations in children with a family history of dyslexia as compared to children without familial risk. Note alterations in the inferior frontal gyrus are only observed when children develop dyslexia.

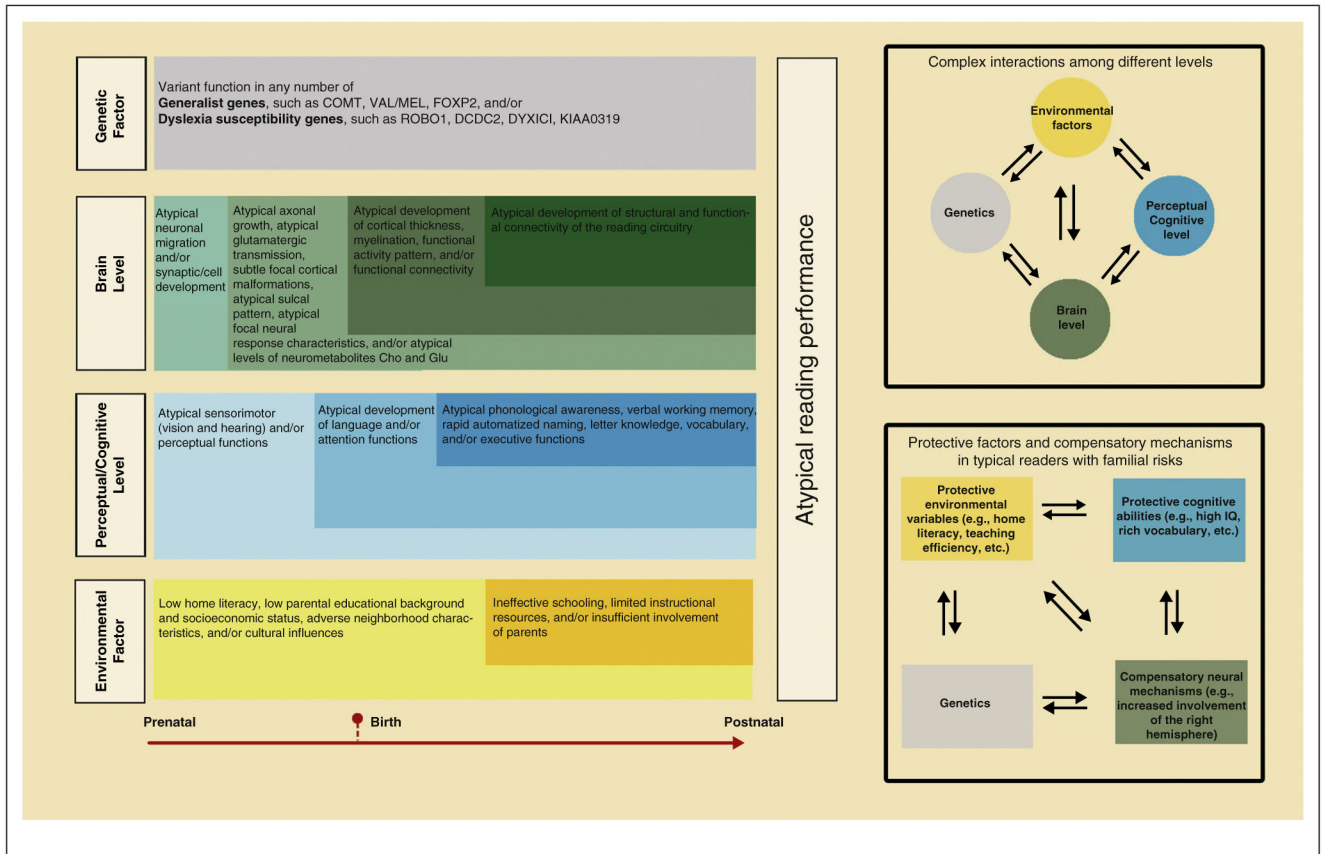


Figure 2.

Left: a summary of risk factors for dyslexia at the genetic, neural, cognitive, and environmental levels along with a developmental timeline. Top right: a diagram illustration of the reciprocal relationships among the different domains. Bottom right: a diagram illustration of the possible protective factors and compensatory mechanisms for dyslexia.