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Seminar: Developmental Dyslexia

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Summary

Dyslexia is a neurodevelopmental disorder that is characterized by slow and inaccurate word recognition. Dyslexia has been found in every culture studied, and mounting evidence underscores cross-linguistic similarity in its neurobiological and neurocognitive bases. There has been considerable progress across levels of analysis in the last five years. At a neuropsychological level, the phonological theory remains the most compelling, though it is increasingly clear that phonological problems interact with other cognitive risk factors. At a neurobiological level, recent research confirms that dyslexia is characterized by dysfunction of the normal left hemisphere language network and also implicates abnormal white matter development. Studies accounting for reading experience demonstrate that many observed neural differences reflect causes rather than effects of dyslexia. At an etiologic risk level, six candidate genes have been identified, and there is evidence for gene by environment interaction. This review includes a focus on these and other recent developments.

Definition

Individuals with developmental dyslexia have difficulties with accurate and/or fluent word recognition and spelling despite adequate instruction and intelligence and intact sensory abilities[1]. The ultimate goal of reading is comprehension. However, dyslexia is defined by difficulties with decoding, while comprehension is typically relatively intact. “Poor comprehenders” show the opposite profile of adequate decoding but poor understanding for what is read (e.g.,[2]). Although some previous nosologies have confusingly lumped the two groups together (e.g., DSM-IV), the present review is concerned solely with dyslexia. Many researchers use the terms dyslexia and “reading disability” interchangeably, though as the preceding discussion makes clear, there are other forms of learning disability that impact reading. Research suggests that dyslexia represents the lower end of a normal distribution of word reading ability[3, 4]. Thus, diagnosis requires setting a somewhat arbitrary cutoff on a continuous variable.

One question has been whether the diagnostic threshold should be relative to age or IQ. The logic of IQ-discrepancy definitions is that the etiology of poor reading may differ in low versus higher-IQ individuals. In fact, there is a stronger genetic contribution to high-IQ dyslexia[5]. However, the research literature does not support the external validity of the distinction between age- and IQ-referenced definitions in terms of underlying

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neuropsychology or appropriate treatment[6-8]. Although the two definitions overlap, some individuals with clinically significant reading problems meet only IQ-discrepancy criteria (high ability, weaker-than-expected word reading) while others meet only age-discrepancy criteria (low ability, poor word reading). Thus, for clinical purposes, children who meet either an age- or an IQ-referenced definition should be identified and treated.

Epidemiology

Prevalence estimates, of course, depend on definition. A common definition sets the cutoff for reading achievement to 1.5 standard deviations (SD) below the mean for age and identifies 7% of the population; a similar IQ-achievement discrepancy definition identifies a comparable proportion[9]. There is a relatively small but significant male predominance (1.5-3:1)[10]. However, the gender difference in referred samples is even higher (3-6:1) [11]. Boys with dyslexia come to clinical attention more often than girls, apparently because they have higher rates of comorbid externalizing disorders, including Attention-Deficit/ Hyperactivity Disorder (ADHD)[12].

Comorbidities

In addition to its comorbidity with ADHD, dyslexia is also comorbid with two other disorders of language development: language impairment (LI) and speech sound disorder (SSD)[13-15]. LI is defined by problems in the development of structural language, including syntax (grammar) and semantics (vocabulary), whereas for SSD the defining problem is in the ability to accurately and intelligibly produce the sounds of one's native language. In each case, evidence indicates that the comorbidity with dyslexia is mediated by shared etiologic and neurocognitive risk factors[16, 17]. The comorbidities are clinically significant because dyslexia is not diagnosed until after a child has been exposed to formal literacy instruction, but ADHD, SSD, and LI are all likely to be apparent earlier and can thus indicate a child's risk for later reading problems. The comorbidity between reading and math disabilities in a population sample of 2nd to 4th graders was approximately 25%[18]. Thus, many students with dyslexia can be expected to struggle broadly in school and have more than a "specific" reading disability.

Cross-Cultural Findings

Research on dyslexia historically has been strongly Anglocentric. Recently, there has been mounting attention to reading problems in other languages, with reason to expect significant cross-cultural differences. Among alphabetic languages, English is particularly difficult to learn, because the mapping between letters and sounds is less consistent than for most other languages. Thus, the historical emphasis on English may have biased our understanding of universal issues in normal and disordered reading development. [19] In population samples, consistency of orthography strongly predicts reading accuracy among school-age children.[20]. Not surprisingly, children at the lower end of the reading distribution in languages with more consistent mappings have less severe reading problems than their English-speaking counterparts, at least in terms of accuracy [21]. Difficulties with reading fluency, or speed of reading connected text, appear more comparable across languages [22]. Spelling problems may also persist in dyslexic individuals who have obtained a high level of reading accuracy in highly consistent orthographies.[23] Several recent studies have highlighted important universals in normal and disordered reading across cultures, despite linguistic differences. Cognitive predictors of early reading were similar for five European orthographies that fall along a consistency continuum (Finnish, Hungarian, Dutch, Portuguese, and French), with good agreement to previous results in English. In particular, phonological awareness (PA) was the main predictor of reading in every language, though its influence was stronger in less consistent orthographies. Other predictors, including rapid

serial naming (RSN), vocabulary knowledge, and verbal short-term memory (VSTM) made smaller contributions, with just one exception. In Finnish (the most consistent language), vocabulary had at least as large an influence on reading as did PA[24].

Recent findings of cross-cultural similarities extend to Chinese, a logographic language. In contrast to alphabetic languages, in which letters represent phonemes (individual sounds), the smallest written units in Chinese are characters representing monosyllabic morphemes (units of language that convey meaning). Phonology is not irrelevant to reading in Chinese, however. Chinese characters have phonological elements[25], and Chinese skilled readers show phonological effects on word recognition[26]. Moreover, these cross-cultural similarities extend to the perception of auditory cues important for speech perception, namely auditory rise time, as measured by a beat perception task. Individuals with dyslexia who were native speakers of English, Spanish, or Chinese[27] performed poorly on auditory rise time tasks; further, in all three languages, this task predicted both PA and reading skill. As we review later, this finding converges with recent findings of deficits in amplitude envelope tasks, in which auditory rise time is an important cue.

The neural correlates of poor reading also appear to be remarkably consistent across cultures. An influential neuroimaging study demonstrated that weak readers in English, French, and Italian all showed similar patterns of aberrant neural activation (underactivations in left temporal and occipital regions) during a reading task[28]. Of note, the reading accuracy of the Italian participants (whose orthography is most consistent) was superior to that of the English and French participants, and the Italian participants were least likely to have experienced clinically significant reading problems, though they still presented with poor fluency. A more recent study compared Chinese and English dyslexic and typical readers in an fMRI paradigm[29]. There were some language-specific differences in neural activations for typical reading. However, the effect of dyslexia was remarkably similar across languages (reduced activation in posterior and anterior left hemisphere (LH) regions), and agreed with work on the neurobiological basis of dyslexia in English. This work thus updates previous research that had suggested partly distinct neural signatures for dyslexia in Chinese versus alphabetic languages[30] but did not vary both language and disorder status within the same study. In sum, cross-cultural work suggests universality in the neurobiological and neurocognitive underpinnings of dyslexia. However, there is cross-cultural specificity in the manifestation of those underpinnings, with the same biological liability being more likely to cause significant impairment in some languages than in others.

Neuropsychology

Early theories of dyslexia postulated a basic deficit in visual processing and focused on the reversal errors commonly made by individuals with dyslexia, such as writing *b* for *d* or *was* for *saw*[31]. Vellutino[32] demonstrated that such reversal errors in dyslexia were restricted to print in one's own language, and were thus really linguistic rather than visual in nature. Since then, a great deal of research has made clear that dyslexia is a language-based disorder whose primary underlying deficit involves problems in phonological processing (processing of sounds in language). Several alternatives to the phonological theory have historically been proposed, and in recent years, there has particularly been renewed interest in a visual explanation for dyslexia. However many relevant studies include limitations similar to earlier work, such as measuring visual attention using linguistic stimuli (see [33]). Overall, the phonological account remains the most compelling, although questions certainly remain[34] .

According to the phonological theory of dyslexia, the ability to attend to and manipulate linguistic sounds is critical for the establishment and later automatization of letter-sound correspondences; these in turn underlie accurate and fluent word recognition through the

process of phonological coding. An important caveat is that the relationship between phonological skills (PA in particular) and reading is bidirectional, so that over time, poor reading also causes poor PA[35, 36]. The general consensus is that the phonological deficit results from faulty development of phonological representations, which are characterized as poorly segmented, imprecise, or otherwise degraded[37-39] (but see [40] for an alternate view).

An important question regarding the phonological theory of dyslexia is how this theory relates to recent developments in speech science regarding the nature and development of speech perception. Speech scientists complain about the "tyranny of the phoneme" or "tyranny of the orthography"[41] because these idealized representations have become reified and likely mislead us about what dimensions in the speech stream are important in development and how those dimensions are flexibly integrated to recover linguistic structures, such as words. There are longstanding controversies about the units of speech perception[42] and recent evidence demonstrates that speech representations preserve much more than phonemes. This work has led to a proposal that phonemes are not the targets of speech perception, and are mainly important in the context of learning an alphabetic written language[43]. Since children who become dyslexic have trouble with spoken language long before they encounter a written alphabet[44-46], the problem in their phonological development is probably not restricted to phonemic or segmental representations and must lie in other dimensions of the speech stream. Identifying syllables in speech is important early in development and various results suggest dyslexic children have trouble recovering syllables from the speech stream. For instance, recent studies have found dyslexic children have problems using an amplitude envelope to recover spoken words[47] and integrating various cues in word perception[48]. In the amplitude envelope (AE) task, a speech signal is filtered to remove brief acoustic cues that have traditionally been viewed as necessary for speech perception, especially the speech segmental cues that distinguish phonemes. These findings converge with results discussed earlier[27, 49] regarding deficits in dyslexia across languages in auditory rise time, an important component of what is preserved in an AE speech signal.

Related evidence comes from a recent study that found impaired voice identification in dyslexia[50]. The cues for voice identification cannot be phonemic (because we distinguish different speakers saying the same sentence) and instead include allophonic variations in how individual phonemes are produced. Taken together, the auditory rise time, AE, and voice identification results highlight that the problems in speech perception and phonological development in dyslexia are not exclusively at the phonemic level. In sum, although more research is needed to fully understand the phonological problem in dyslexia and related language disorders, such as SSD and LI, focusing only on phonemes is clearly a mistake.

For many years, a single-deficit phonological theory of dyslexia reigned. More recently, there has been mounting evidence that while phonological deficits are the rule among individuals with dyslexia, a single phonological deficit is likely not necessary and sufficient to cause the disorder. There are several ways in which other deficits could relate to phonological problems: 1) the additional deficit could be independent of the phonological deficit, with multiple deficits needed to cause the full clinical phenotype[51]; 2) there could be phonological and non-phonological subtypes of dyslexia (e.g.,[52, 53]); 3) the phonological deficit may arise from a lower-level sensory or general learning problem (e.g.,[54, 55]); 4) the phonological deficit may cause the reading problem, while other deficits are correlated for other reasons (e.g.,[56]).

Consistent with a multiple deficit account, we found that many children with SSD histories went on to develop normal literacy despite persisting deficits in PA. Furthermore, PA alone

predicted literacy outcome less well than a model that also included syntax and nonverbal IQ[13]. Similarly, Bishop and colleagues classified children according to whether they had LI only, dyslexia only, LI + dyslexia, or typical development[57]. A sizeable group of children with LI did not develop dyslexia despite early phonological skills that had been as poor as those in the LI + dyslexia group. At age 9 to 10, the LI only and LI + dyslexia both continued to demonstrate impairments in PA, but only the LI + dyslexia group had RSN deficits.

RSN has long been hypothesized to contribute risk for reading failure independent from PA[58], and recent cross-cultural work confirms that children with PA and RSN deficits have particularly poor literacy outcome[59, 60]. Debate remains regarding how distinct RSN is from other aspects of phonological processing[61]. While RSN tasks certainly tap lexical phonology, they also correlate highly with nonverbal measures of processing speed, which in turn predict reading fluency.[62, 63] As mentioned above, there has recently been renewed interest in the role of visual attention in dyslexia[52, 54, 64-68]. Although some of this research has included serious flaws, some well-controlled studies do establish a link between visual deficits and dyslexia that cannot be fully accounted for by other factors.[54, 69, 70] One specific proposal that has yet to be tested empirically is that problems with visual attention could underlie RSN deficits and associated problems with reading fluency[54]. This proposal is attractive because the phonological theory readily explains the reading accuracy problem in dyslexia but is more challenged to account for difficulties with reading fluency, which have been shown to be more persistent developmentally, more universal across languages, and harder to remediate[71].

The studies discussed above supporting a multiple deficit view generally used correlational designs. Thus, it is possible that some deficits do not relate directly to word reading, but instead explain comorbidities or brain dysfunction. The clearest data on this question come from longitudinal studies of children at family risk for dyslexia. Across countries and languages, multiple cognitive-linguistic constructs, including semantics, syntax, PA, VSTM, and RSN consistently predict later dyslexia. The most powerful individual predictor varies with developmental level [45, 46, 72-74]. VSTM and PA appear to act as endophenotypes, because deficits in each are found among individuals at family risk who do and do not develop dyslexia. Problems with RSN and letter knowledge are more specific to dyslexia, as non-dyslexic individuals at family risk perform more normally in these domains.[75] Thus, although results vary as to which additional deficits interact with PA problems to cause dyslexia, convergent evidence suggests 1) many children with weak PA nonetheless develop normal-range literacy skill; 2) children with PA problems and other language deficits are at high risk for dyslexia; and 3) RSN deficits in dyslexia cannot be fully accounted for by the comorbidity with ADHD or other developmental disorders.

Neural Substrates

Functional findings

Because reading is a linguistic skill, we would expect it to involve activation of brain structures used in oral language processing, as well as some additional structures associated with visual object processing and establishing visual-linguistic mappings. Aberrant activation patterns in these regions would be predicted for dyslexia, and this is essentially the pattern of results reported across a large number of functional imaging studies. The most common findings, as described in several qualitative reviews, encompass abnormalities of a distributed LH language network [76, 77]. In particular, consistent underactivations have been reported in two posterior LH regions: a temporoparietal region believed to be critical for phonological processing and phoneme-grapheme conversion, and an occipitotemporal region, including the “visual word form area” (VFWA), believed to participate in whole

word recognition. In addition, abnormal activation of the left inferior frontal gyrus (IFG) is commonly reported.

This area of research has seen a number of important advances since the last *Lancet* review [76]. First, a quantitative meta-analysis of studies using reasonably similar tasks[78] has been published, and confirmed the primary findings of qualitative reviews. Second, most early imaging studies did not equate in-scanner performance or did not control for reading experience, and thus, it was not clear whether observed activation differences were a cause or result of dyslexia. In recent years, a number of studies have attempted to control for reading experience in a variety of ways. In general, findings support the view that characteristic brain changes are associated with dyslexia from an early age.

The causal relations between imaging findings and reading experience have recently been clarified through use of reading-age (RA) control groups and family risk studies. One research group has compared individuals with dyslexia to both chronological age (CA) and RA controls on visual rhyme tasks[79, 80]. The RA control design (inclusion of younger, typically developing children matched to the dyslexic participants on reading level) is often used in behavioral research as one test of whether observed group differences contribute to dyslexia. Overall, results indicated abnormal activation in dyslexic individuals, with underactivation in left temporoparietal regions relative to both CA and RA controls. Several other areas of underactivation relative to both control groups were also reported. These differed somewhat by study, one of which included school-age children and the other of which included adolescents. This research group has also compared neural activation in dyslexic and typically-developing children on a visual sentence comprehension task, treating reading level continuously rather than categorically[81]. The main finding was that poor reading was associated with reduced activation in bilateral temporoparietal cortex; no effects were found in occipitotemporal regions.

A related approach is to investigate neural correlates of reading and reading-related tasks among young children at risk for dyslexia or who have only recently begun to experience reading failure. Compared to same-age controls, 6-year-olds at risk for dyslexia demonstrated activation abnormalities across a widely distributed set of bilateral, cortical and subcortical regions[82]. Regarding the regions most commonly reported in the literature, at-risk children demonstrated increased bilateral temporoparietal activation during an easier reading task, but reduced occipitotemporal activation on a more difficult task. Another study compared young (mean age = 8 years) dyslexic and normal readers in a reading task designed to emphasize phonological processing[83]. Children were equated on in-scanner performance (though, by definition, not on reading level). Poor readers underactivated the left inferior and middle frontal gyri, while overactivations were reported in multiple bilateral frontotemporal sites. Further, children with dyslexia demonstrated reduced left-sided specialization for the phonological task.

Other imaging technologies support the conclusion that characteristic brain differences are a cause rather than a result of dyslexia. In particular, event-related potential (ERP) studies in several languages have found that infants at family risk for dyslexia show aberrant neural response to speech sounds from as early as the first week of life,[84] and that infant ERP response predicts language learning and dyslexia risk over several years.[44, 85, 86]

Overall, results from studies attempting to control for reading experience are only partially consistent with each other and with the broader fMRI literature. However, it is clear that not all observed neural abnormalities in dyslexia result from a lack of reading experience, with convergent evidence that temporoparietal abnormalities are more likely a cause than a result of reading failure. Findings regarding the VWFA are more complicated. While

underactivation of the VWFA in adolescents with dyslexia cannot be attributed solely to reading experience, this is less clear in children. It may be that occipitotemporal regions fail to "tune" appropriately to word stimuli over time in dyslexia, consistent with a recent fMRI study of 11-year-olds[87]. This explanation attributes abnormalities of this region to an interaction between the disorder itself and exposure to print, and could be tested empirically by examining a group with low reading experience for reasons other than dyslexia.

Structural findings

The discovery that individuals with dyslexia show functional abnormalities in both posterior and anterior language networks has motivated the hypothesis that dyslexia represents a disconnection syndrome. Accordingly, a good deal of recent research has explored white matter correlates of dyslexia using diffusion tensor imaging (DTI). Indeed, the most consistent findings have included local white matter changes (as indexed by fractional anisotropy) in children and adults with dyslexia in left temporoparietal regions and in the left IFG [88-99]. Studies have consistently reported correlations between white matter integrity and reading skill.

The relations among structural and functional neuroimaging findings in dyslexia have been clarified by recent work. First, the Paulesu et al (2001) international study[28] has been followed up with gray matter (GM) and white matter (WM) structural analyses, and is the first study to examine correspondence between functional and structural findings in dyslexia in the same sample.[100] These investigators found a corresponding GM density decrease in dyslexics in the key area of functional underactivation in their previous study (left medial temporal gyrus). Consistent with other DTI studies reviewed here, they found WM decreases in the left frontal and parietal portions of the arcuate fasciculus as well as a variety of other LH sites. These structural differences replicated across the three countries and languages in the study (Italy, France, and UK).

Consistent with the functional imaging findings, a recent family risk study[101] reported that GM decreases are present before the onset of reading instruction, and thus do not appear to be a result of reading failure. The family risk group had selective GM decreases in LH regions previously associated with dyslexia (occipitotemporal, temporoparietal, and lingual gyrus.) Furthermore, converging evidence that genetically-based brain abnormalities can cause reading problems is provided by syndromes such as periventricular nodular heterotopias (PNH),[102, 103] XXY syndrome in males,[104] and Rolandic epilepsy.[105] PNH, a cortical malformation in which nodules of heterotopic gray matter line the ventricles bilaterally, is particularly interesting because the associated neuropathology is similar to that reported in autopsy studies of dyslexia some time ago by Galaburda and colleagues.[106, 107] Those studies found increased numbers of gray matter heterotopias in individuals with reported histories of poor reading, though these findings were stronger in males[106] than females.[107]

So, an emerging and still speculative picture of the pathogenesis of dyslexia is that risk genes disrupt neuronal migration mainly in the LH, leading to GM and WM changes in parts of the language/reading network. Regarding the relation between GM and WM changes, it is certainly possible that migration errors could lead to disruption in WM tracts, but there are other possible ways that WM tracts could be disrupted.[108, 109] Altered connectivity in specific WM tracts (the left superior longitudinal fasciculus) compromise the acquisition of language and cognitive skills important for reading.

Of course, more direct evidence is needed for the links in this causal chain. Perhaps most critically, we need genetic neuroimaging studies that test the link between candidate genes for dyslexia and the structural and functional neuroimaging findings discussed here. We also

need to replicate the small study documenting GM decreases (and test for WM changes) in children at family risk for dyslexia before the onset of reading instruction.

Even though the causal arrow in dyslexia appears to point, in part, from brain to reading skill, there is no question that reading changes the brain, as documented by neuroimaging studies of dyslexia treatments[110] and of adult illiterates.[111] So, it is likely that the neuoimaging phenotype in dyslexia includes a mix of both kinds of effects and disentangling these will require more longitudinal work, starting with very young children.

Etiology

Like all other behaviorally-defined disorders, the etiology of dyslexia is multifactorial, involving multiple genes and environmental risk factors. Dyslexia is familial and moderately heritable[112] and has been linked to nine risk loci (DYX1-DYX9, www.gene.ucl.ac.uk/nomenclature/) through replicated linkage studies,[113, 114] though not every study has replicated these results.[115, 116]

The main advance in the genetics of dyslexia since the previous *Lancet* review[76] has been the identification of six candidate genes (DYX1C1 in the DYX1 locus on chromosome 15q21; DCDC2 and KIAA0319 in the DYX2 locus on chromosome 6p21; C2Orf3 and MRPL19 in the DYX3 locus on chromosome 2p16-p15; and ROBO1 in the DYX5 locus on chromosome 3p12-q12) and studies of their role in brain development (for a review, see [117]). Four of these genes (all but the two DYX3 genes) have been shown in animal models to influence neuronal migration and axon guidance and to co-regulate each other; very little is currently known about the functions of the two DYX3 candidate genes. So, it now appears that four of the candidate genes for dyslexia are part of a genetic system that controls an important aspect of prenatal brain development that has been implicated in the pathogenesis of dyslexia by various structural brain studies, as discussed above.

Two more recent studies have identified new candidate genes for dyslexia, both on chromosome 18 (MC5R, DYM, and NEDD4L)[118] and one shared with LI (CMIP),[119] but these results need to be replicated.

Despite this important progress, much remains to be done to fully understand the etiology of dyslexia. First, there has not been a genome-wide association study of dyslexia and the known loci do not account for most of the heritability of dyslexia found in twin studies. So, like other complex traits, dyslexia has a “missing heritability” problem. Second, although there has been some progress in understanding the etiology of the comorbidities of dyslexia, much remains to be done to identify loci that are shared and not shared by dyslexia and disorders comorbid with it: ADHD, LI, and SSD. Third, it is unknown whether dyslexia exhibits any of the newer genetic mechanisms found in other neurodevelopmental disorders, including copy number variations, parent of origin effects, and epigenetic effects. Fourth, much remains to be learned about the role of the environment in the etiology of dyslexia. We do know that the heritability of dyslexia declines linearly with decreasing parental education[120] (a bioecological gene by environment interaction), but we do not know which proximal environmental factors mediate this interaction. Reasonable candidates include the language and preliteracy environments that parents provide to their children, but direct tests of those hypotheses are needed. Finally, although there is robust cross-cultural research on dyslexia, dyslexia has been less studied in lower SES groups, in non-Caucasian ancestry groups, and in children with a bilingual background, such as Hispanic-American children. A universal account of normal and abnormal reading development needs to encompass those understudied groups.

Treatment

The development of evidence-based treatments for dyslexia has benefitted from our understanding of its neuropsychology, and the best interventions provide intensive, explicit instruction in PA, the alphabetic principle and phonics, word analysis, reading fluency, and reading comprehension.[121, 122] Much more is known about effective remediation of reading problems in younger than in older children. In addition, it appears to be easier to treat accuracy than fluency problems, perhaps in part because fluency is so dependent on reading experience, which varies dramatically by reading level. It may be nearly impossible for poor readers to "close the gap" in print exposure once they have accumulated several years of reading failure, but there is some evidence that fluency problems can be prevented with appropriate intervention in kindergarten and first grade, at least over the short term[123, 124]. An important conclusion is that professionals should not wait until children are formally diagnosed with dyslexia or experience repeated failures before implementing reading treatment, when remediation has been shown to be less effective than early intervention.[125]

Recent work on treatments for reading failure[126] support the following conclusions: 1) intervention is most effective when provided in a one-to-one or small group setting;[127] 2) successful interventions heavily emphasize phonics instruction; and 3) other valuable treatment elements include training in PA, supported reading of increasingly difficult connected text, writing exercises, and comprehension strategies. Many effective treatments are relatively low-cost, further highlighting the importance for public health of early identification, prevention, and treatment of dyslexia.

There are individual differences in how well individuals with dyslexia respond to treatment, with about half of successfully treated children maintaining gains for at least one to two years. The well-documented preschool predictors of later reading skill (i.e., PA, letter name and sound knowledge, and rapid serial naming) also predict treatment response, although more research is needed on this question.[128] Regarding long-term prognosis independent of treatment, language skill is a known protective factor for both children and adults with dyslexia[74, 129, 130].

There are a growing number of intervention-imaging studies investigating how remediation of dyslexia alters brain activity. This research has been reviewed in more detail elsewhere.[76, 110] Briefly, effective intervention appears to promote normalization of activity in the LH reading and language network that has shown reduced activity in dyslexia. In addition, increased right hemisphere activation has been reported following dyslexia treatment, which is sometimes interpreted as reflecting compensatory processes.

While there is a solid evidence base for treatments emphasizing direct instruction in reading and phonological training, several alternative therapies either lack sufficient evidence or have been shown to be ineffective for dyslexia and thus, should not be recommended to children and families (for a review, see[131]). Most of these therapies are based on sensory-motor theories of dyslexia and include training in rapid auditory processing (e.g., Fast ForWord®), various visual treatments (colored lenses, vision therapy), and exercise/ movement-based treatment (e.g., vestibular training).

Concluding Remarks

Of all the neurodevelopmental disorders, dyslexia has been the most studied and is the best understood. The field continues to benefit from reciprocal relations between basic and clinical neuroscience, and there has been considerable progress over the last five years in understanding dyslexia's cross-cultural manifestation, etiology, neuropsychology and neurobiology. Much of the most exciting recent work includes an interdisciplinary focus that

cuts across these levels of analysis. This research has helped to promote scientific knowledge and public health, and at the same time, underscores the complexity of the development of reading difficulties. Future research will address important questions both within and across levels of analysis. For example, we still need to learn more about the nature of the phonological deficit and how this problem interacts with other linguistic and non-linguistic risk factors, the developmental course of neural abnormalities and how these predict treatment response, and which environmental risk factors contribute to the development of poor reading and whether these are the same across demographic groups. Learning the answers to these questions will inform our knowledge of language and literacy development and will also lead to improvements in the lives of children who struggle to learn to read.

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