Guest Editorial

Dyslexia

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This section of the special issue of the *Journal of Child Neurology* is devoted to dyslexia, the most common of the learning disabilities. As a result of a series of well-designed research studies, many of which were supported by the National Institute of Child Health and Human Development,[1] there has been an enormous advance in our understanding of the neurobiology, cognitive features, and natural history of dyslexia,[2] which are briefly reviewed here. The two articles in this section address the important issue of treatment.

At an anatomic level, dyslexic brains are structurally atypical. Under the microscope, one sees an increased number of ectopic neurons and other minor anomalies, scattered across the cortex but maximal in the left hemisphere.[3] Unusual patterns of hemispheric asymmetry that reflect differences in the relative size of certain brain regions, as well as anomalous gyral and sulcal patterns, are noted.[4–7] Most exciting are the functional neuroimaging studies that reveal the distinctive pattern of activation that emerges when a person with dyslexia is reading. Compared with the normal reader, there is decreased activity in the posterior left hemisphere and a lack of synchrony between the posterior and anterior areas in the left hemisphere, increased activity in the homologous areas of the right hemisphere, and a relative increase of activity in the frontal cortex.[8–14] These changes are seen in young children and so are presumably the result of an early neurobiologic process. Children with dyslexia are not different from normal readers when dealing with purely visuospatial tasks, but as the phonologic processing demands of the task increase, they do not display the systematic and correlated increase in activity in visual cortex and temporoparietal association cortex (angular gyrus and Wernicke's area) that normal readers display. Readers who are dyslexic (particularly male readers) activate the left inferior frontal gyrus to a greater extent than do readers who are not dyslexic. Women with dyslexia tend to activate right hemisphere structures to a greater extent. These functional neuroimaging findings are also supported by research using magnetoencephalography, which has found that patients with dyslexia either activate left posterior structures slowly or not at all when presented with words[15,16] and do not activate the left posterior area as rapidly as controls. This may be due to a disruption in patients with dyslexia of the white-matter tracts underlying the temporoparietal cortex, which connect brain areas that subserve reading. A correlation was noted between reading skill and the extent of the disturbance of tracts in the left hemisphere.[17]

Since the late 19th century, it has been known that dyslexia runs in families.[18–21] The first formal genetic study was published in 1950.[22] Later genetic studies involving monozygotic and dizygotic twins confirmed the high degree of heritability.[23–25] As the Human Genome Project has moved forward and with the development of sophisticated molecular techniques, a number of loci have been identified as potentially involved in dyslexia: chromosome 1p,[26] chromosome 2p11,[27,28] chromosome 3,[29,30] and chromosome 6p.[25,31–35] A locus on the long arm of chromosome 15 has been identified in a number of studies[36–39] and the *DYXC1* gene has been fine-mapped to the chromosome 15q21 locus.[40] A quantitative trait locus on chromosome 18p11.2, strongly associated with phoneme awareness deficits, has also been reported.[41] It would appear that there is not just one gene that confers the genetic risk for dyslexia, but rather, several different genes may be associated with dyslexia, and whatever the genetic risk, environmental factors also play a role. At this point, it is not clear how specific genes will relate to the underlying cognitive deficits seen in dyslexia (eg, phonologic awareness, sight word reading). A number of studies have focused on these more specific features of the phenotype and have found that some genes may be linked to single-word reading, whereas others may be related to phonologic awareness[41] or other aspects of reading, but this is far from conclusive.[30,36,24,43] There is also the question of how genes associated with dyslexia relate to some of the other comorbidities of dyslexia (eg, language impairment or psychiatric disorder, such as depression, anxiety, or attention-deficit hyperactivity disorder [ADHD]).[25]

Numerous theories of the pathophysiology of dyslexia have been advanced (for a more extensive review of this subject, see Vellutino et al[2]). One prominent theory is the double-deficit hypothesis. This theory postulates that some individuals with reading disability have a deficit in phonologic awareness, whereas others have a rapid naming deficit—the result of disruption in the linking phonologic and orthographic information, which requires precise timing and bears a specific relationship to reading fluency. A third group has both phonologic coding deficits and rapid naming deficits.[44,45] This combined (double deficit) type is the most severe. The double-deficit hypothesis is not without empiric support: children with the double deficit are more impaired than those without it, and rapid naming appears to be correlated with speed related to letter-sound decoding and word identification, whereas phono-

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logic awareness is more involved in decoding and identifying words.[46] Rapid naming accounts for unique variance above and beyond that of phonologic skills.[47] However, given that rapid naming and phonologic skills are significantly correlated and have substantially shared variance in reading performance, the greater severity of the double-deficit group can be the result of a statistical artifact.[48] Torgesen et al showed that when these autocorrelation effects are controlled, the unique variance of rapid naming drops out.[49] Similarly, matching the double- and single-deficit groups on phonologic awareness and rapid naming tasks tended to eliminate the differences in reading measures.[50] Other factors, such as processing speed or attention problems, might be involved as well.[51,52]

Another theory of dyslexia involves a low-level auditory processing deficit that impairs the ability of the patient with dyslexia to perceive rapidly varying sounds and is thus the core deficit underlying phonologic awareness.[53–56] Dysfunction of the cerebellum has also been suggested as a possible basis for dyslexia because of its involvement in automaticity, timing, and a broad spectrum of cognitive and motor performances.[57–60] The theory that visual deficits lie at the basis of dyslexia has been prominent since the first reports of "word blindness"[19] and was reinforced by Orton's suggestion that dyslexic children saw letters and words as reversed.[61] Visual tracking problems have been suggested as an underlying reason for dyslexia but are not supported by research studies.[62,63] When reading text, patients with dyslexia indeed show atypical eye fixation patterns that are also seen in normal readers who encounter difficult words.[64] There is some empiric support for the notion that the magnocellular system, which subserves visual motion processing, is a component of dyslexia.[65,66] Eden and Zeffiro noted that there is a body of evidence from at least four independent sources that point to the temporoparietal junction (which receives input from the magnocellular system) as the site of the impairment in dyslexia,[67] suggesting that this area may be involved in neuronal systems that subserve both phonologic processing and eye movement control, which is also regulated by the cerebellum.

In an enlightening study, Ramus et al evaluated 16 university students with dyslexia and an equal number of controls on an extensive battery of tests that assessed language, phonologic awareness, auditory and visual perception, and motor control referable to the cerebellum.[68] All of the students demonstrated significant phonologic deficits, even after controlling for differences in processing speed. Ten of the students performed more poorly on the auditory tasks, but there was remarkable variability in test performance. Only 2 of the 15 students evaluated on the visual task had difficulty, and one fourth had difficulty on some component of the cerebellar tasks. The conclusion was that the phonologic deficit hypothesis was present in all subjects and was a sufficient cause of dyslexia. The other areas of dysfunction did occur in some of the students but by no means all.

What about the treatment of dyslexia? In this issue, Schatschneider and Torgesen present evidence as to why early intervention is so effective.[69] To become efficient readers, children must have adequate phonologic awareness so that they can decode unfamiliar words with sufficient ease[70] to be able to practice reading skills during the first 6 years of formal education. Children with dyslexia find reading laborious and frustrating, and so avoid it. As a result, they are not exposed to the multitude of words that normal readers encounter in the first 6 years of school and do not add new words to their sight word lexicons at the same rate as their normally reading peers,[71] and the gap between the number of sight words that they can readily recognize compared with normally reading peers becomes wider with each passing month. The gap is already substantial by the end of second grade. Training phonologic awareness is very helpful, but by the time the child with dyslexia is in fourth grade, he or she cannot read as fluently as peers. To close the fluency gap, the child with dyslexia must be exposed to more text than classmates, which is hard to accomplish. Information to date indicates that the younger the child is at the age that phonologic treatment starts and the more intensive the treatment, the better the child is likely to fare. Unfortunately, standard school-based learning disability interventions usually do not start until relatively late, and at best, maintain the reading level of a child with dyslexia but will not accelerate it so that the child can catch up and read at a grade-appropriate level.[72–77]

In this issue, Alexander and Slinger-Constant review the research supporting the efficacy of various treatments for dyslexia.[78] In young children, treatment focusing on phonologic awareness is highly effective because it enables them to break the phonologic code in time to become relatively fluent readers. The older child also becomes a better decoder but is very slow to improve reading fluency. The challenge for the older child is to develop programs that enhance reading fluency.

Given the fact that dyslexia is genetic, that parents are usually aware of their own reading difficulties, and that there is incontrovertible evidence that early treatment is of great benefit, why are parents, pediatricians, and preschool teachers so reluctant to consider evaluation and possibly treatment of the young child before he or she enters school? One answer is that the underlying phonologic deficit is subtle, requiring specific assessments to identify, and the child is developing normally and appears bright and verbal. Second, the prevailing belief is that this will be adequately dealt with by special education, although this is not supported by longitudinal studies. Financial considerations may be paramount, but only if one is thinking in the short term. Finally, unless a parent has personally experienced the pain and academic stress associated with dyslexia, it is difficult to understand its impact on the school-aged child or its impairing persistence into adulthood.[79–84] It is hard for young parents to clearly envision the risks for psychiatric disorders, such as depression and ADHD, or the more severe disruptive behavior disorders that can be associated with dyslexia.[85] One young mother, herself not dyslexic, could not understand why her husband with dyslexia and his family (who had multiple members who were dyslexic) were so concerned about her young child's development, long before he had entered school. This is, in some ways, similar to preventive screenings, such as checking newborns for devastating but treatable metabolic conditions. Once the symptoms are obvious, it is much more difficult to treat effectively. Moreover, dyslexia has a range of severity: some children are very severely involved, whereas others appear to be functioning well, although formal testing often picks up deficits that are not apparent. Some children become symptomatic in first grade, whereas some do not get overwhelmed until they are in postgraduate courses with heavy demands on reading.

I have seen several medical students who were able to navigate high school and college with only mild difficulty but could not manage the reading demands of medical school.

What have we learned about early identification? It has been known for some time that atypical early language development is one of the predictors of poor reading in the second grade.[86] However, infants who are destined to become dyslexic appear to process speech sounds (measured by auditory event-related potentials) differently than those who are not at risk. These differences can be observed in the newborn period and at various points in the first year of life, long before the baby starts to talk.[87–89] There are also atypical developmental features that are seen in the at-risk children in preschool. Although these children may not differ in motor, cognitive, or early language development, subtle deficits in language start to emerge around 2 years of age and become more pervasive, albeit still subtle, as the child develops.[90] By age 5 years, weak letter-sound knowledge, naming, and phonemic awareness are apparent.[24,91–96] Young children (less than 2 years of age) who show a combination of delayed language and motor milestones are at enhanced risk of dyslexia.[97]

The good news is that not all children who come from families with dyslexia are destined to be impaired readers, but the risk is significantly increased.[98] Factors that tend to buffer the risk and help potential patients with dyslexia compensate are a high IQ and strong language skills.

Environmental factors also play an important role in the way in which patterns of connectivity occur during postnatal brain development. Children who come from disadvantaged environments, with impoverished language and no exposure to books, face additional challenges when they learn to read. A neuroimaging study compared illiterate Portuguese women (who had stayed home to raise their younger siblings and did not attend school) with their younger sibling who had learned to read and write. The illiterate older sisters were able to repeat real words as well as the literate controls, and there was little difference in the pattern of brain activity, but when the illiterate women repeated nonwords, they made more errors and showed a much more restricted pattern of brain activation.[99] This would suggest that lack of exposure to spoken and written language results in restricted neuronal development in brain areas underlying phonologic processes, which, in turn, makes the acquisition of adequate reading skills even more difficult. The genetic makeup of the individual appears to increase the sensitivity to environmental factors in the patient with dyslexia.[100]

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