

## Chapter 13

# Learning Disabilities

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Learning disability (LD) refers to a condition in which a child fails to develop adequate academic skills, such as reading, writing, or calculation. LDs involve inadequate development of academic skills, rather than representing a loss of previously acquired function, although brain lesions may certainly result in cognitive deficits that affect reading, writing, and calculation (for a review, see Heilman and Valenstein) [1]. Most research on LDs has involved children, who are the focus of this chapter. For a review of LDs in adults, the interested reader is referred to Mapou [2]. In this chapter, we will first present a conceptual overview of LDs and types of LDs. Second, we will offer recommendations on how to effectively triage children who present with academic skill deficits. Third, we will cover some of the fundamental mechanisms involved in LDs that have been identified in neuropsychological and imaging studies. We will conclude by mentioning some recent interventions that appear promising for remediating academic skill deficits among children with LDs.

### History and Background

LDs should be understood to represent unexpected underachievement in one or more areas of core academic skill [3]. The first part of this term (“unexpected”) means that one or more deficits in academic

skills exist that would not have been anticipated, given the child’s history and present circumstances. For example, children with mental retardation, blindness, or deafness would typically not be expected to achieve reading, writing, and calculation skills to the extent mastered by their unaffected peers. Similarly, a child who has not attended school regularly (for whatever reason), or who has lacked adequate instruction in core academic areas, would also not be expected to demonstrate a typical level of achievement. Historically, a child’s level of intellectual functioning (IQ score) was used as a standard to which his or her level of academic achievement was compared. A child of high average intelligence, for example, might be regarded as having an LD if he or she demonstrated reading abilities within the low average range. In other words, a certain level of academic achievement was expected based on the child’s level of intellectual functioning; deviations from the expected level were regarded as indicative of LD.

Academic achievement deficits that result from primary visual or auditory impairment, mental retardation, or inadequate exposure to quality instruction should not be regarded as LDs; in such instances, academic skill deficits would be expected. Similarly, children with limited exposure to English should not be regarded as having an LD for this reason alone. As reviewed extensively elsewhere [3, 4], we do not view an IQ–achievement disparity as either necessary or sufficient for an LD diagnosis. Briefly, children with IQ–achievement discrepancies do not appear to differ in a meaningful way from their low-achieving peers (who lack such a discrepancy) with respect to cognitive or neurobiological correlates, genetic factors, etiology, course, or, perhaps most importantly, response to intervention [3]. Moreover, the use of cutoff and/or

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discrepancy scores is fraught with unreliability and measurement error. Thus, IQ–achievement discrepancy is no longer tenable as a way to conceptualize or identify LDs.

The second part of the term unexpected underachievement refers to the child's substandard mastery of core academic skills. A question then arises as to what constitutes underachievement: how low must performance be for it to be considered problematic? Some researchers (e.g., Dombrowski and colleagues) [4] have suggested incorporating a combination of national and local norms in making the determination of underachievement. Specifically, these authors argue that LD identification should be based on (1) a standard score of 85 or below on a nationally normed measure of academic achievement and (2) evidence of educational impairment (based on grades, curriculum-based assessment, and teacher reports or ratings). A weakness of this proposed identification method is that the use of a specific cut point (e.g., standard score of 85 or below) is problematic due to measurement error. Nonetheless, the second criterion of Dombrowski et al.'s [4] approach includes consideration of the child's academic performance at a local level. This criterion does not eliminate the measurement error problem associated with measuring academic achievement at a single point in time and with a fixed cut score. However, it does supplement the score with highly relevant data pertaining to the child's academic performance in his or her most immediate environment.

Fletcher and colleagues [3] advocate a hybrid model for identifying LD that combines features of low achievement and response to intervention (RTI) approaches. RTI is not a new concept, but with changes in educational law based on the Individuals with Disabilities Education Act (IDEA 2004), a shift was made to take into consideration the role of instruction and performance over time. This model involves considering a child's response to instruction, serial curriculum-based assessments of the academic domain at issue, and evaluations of instructional quality. A child who demonstrates an inadequate response to instruction would next receive norm-referenced assessments in the achievement domain. A comprehensive evaluation that screens for comorbid conditions and addresses other possible causes of underachievement (e.g., mental retardation, speech/language impairments, and/or behavioral problems) is also conducted.

Assessment and consideration of psychosocial variables (e.g., home environment or native language) occurs as well.

We are in general agreement with Fletcher and colleagues [3] regarding the hybrid model, as it clearly addresses many of the flaws inherent in other models. Our primary concern about the model, though, is that not all schools may have the resources and personnel who are able to carry out assessments and interventions of the type proposed. Moreover, change seems to happen slowly in large bureaucracies, and we are aware at present (September 2009) that many schools continue to operate with outdated models, assessment practices, and intervention techniques. This is not to blame the schools, as many of them likely lack the necessary funding and/or staff training to carry out such programs. It simply means that something must be done in the interim or in situations when the hybrid model cannot be applied. We believe that a low-achievement model is reasonable to be used as a conceptualizing framework in instances when RTI cannot be applied. Utilizing an approach such as that outlined above [4] with appropriate consideration given to potential exclusionary factors (but not IQ) appears to be a reasonable and practical way to identify children at risk for LDs.

### **Prevalence Rates of LD**

Estimates of the prevalence of LDs vary according to the criteria by which they are defined. In some studies, LDs are considered as a disorder category and are not fractionated by type. At a very general level, the 2004 National Survey of Children's Health reported an 8% lifetime prevalence of LD among children 3–17 years of age. In this study, lifetime prevalence of LD was measured by a survey question: "Has a doctor, health professional, teacher, or school official ever told you [name of child] has a learning disability?" Lifetime prevalence rates differed by sex: 9.5% of boys were reported to have an LD compared to 6.3% of girls [5]. An obvious weakness of this study is that LDs were operationalized as a survey question in a parent interview. Nonetheless, this study involved 36,579 households in the United States and 12,424 sample children, thereby reaching a level of population representativeness that is usually impossible except in

studies of this scope. In an analysis of data from the preceding survey year (2003), correlates of LD included living in a household with lower education, male gender, increasing age, speaking English as a primary language, living in poverty, parental unemployment, being adopted, presence of a smoker, living in a two-parent stepfamily situation, higher parental aggravation, and not discussing ideas with the child calmly [6].

Another approach is to examine data on children who receive special education services under the Individuals with Disabilities in Education Act (IDEA). The most recent available data (2006–2007 school year) show that 5.4% of children in the United States received services due to an LD [7]. It should be noted that this value (5.4%) represents a point prevalence figure, i.e., the percentage of children identified as having LD and receiving services under IDEA, as contrasted with the lifetime prevalence data reported above in the 2004 National Survey of Children's Health, which is understandably higher.

Prevalence estimates for specific LD types are difficult to summarize succinctly, as various methods for defining the types have been used. It may be stated with reasonable confidence that dyslexia is the most common type of LD. Prevalence rates range from 5 to 17.5% [8, 9], and dyslexia affects approximately 80% of children identified as having an LD [10]. These figures are derived almost exclusively from studies of word-reading difficulties, as opposed to deficits in reading fluency and/or comprehension. At the present time, no specific prevalence estimates of deficits in reading fluency or comprehension (apart from word-level reading difficulties) are available [3].

Epidemiological studies suggest that males are 1.5–2 times as likely as females to have dyslexia [11]. Math LDs have been found to be present in approximately 4–6% of children [12]. Although data are limited, the prevalence of written expression LDs has been found to range from 6 to 22% as a function of geographic region, gender, and ethnicity [13].

## The Process of Diagnosis

The role of the neuropsychologist is likely to diminish over time as more schools adopt a hybrid low-achievement/RTI model such as that proposed by

Fletcher et al. [3]. During this transitional period, clinical neuropsychologists will almost certainly continue to receive referrals that involve questions of LD. One might imagine that a child is in one's office for evaluation, and his or her parents are concerned about their child's academic achievement; what should the practicing neuropsychologist do in cases when RTI or a hybrid model cannot be utilized? In the future, it is hoped that most issues related primarily to academic skill deficits will be easily and comfortably referred to the local school district for identification and intervention. In instances when well-developed RTI programs already exist, then we would advocate referring suspected LD cases to competent school personnel unless there is a reason to suspect that the child would also benefit from a complete neuropsychological evaluation (such as when a child has a primary medical condition affecting cognitive functioning).

To this point, we have only discussed LDs in their simplest form, i.e., free from comorbidity with medical and mental health conditions that may adversely affect academic functioning. The neuropsychologist practicing in a medical setting is likely to encounter individuals with diseases affecting the central nervous system (e.g., epilepsy), and who have deficits in academic skills in association with their underlying condition. We believe that a clinical neuropsychologist remains the most appropriate professional to assess the cognitive functioning, including academic skills, of individuals with known or suspected disorders of the central nervous system. It is unlikely that school personnel will have the necessary knowledge of medical conditions and brain functioning to conduct an appropriate evaluation. Moreover, such cases are necessarily more complicated since the child's academic skill deficits are likely secondary to acquired brain dysfunction – a disease affecting the brain, as opposed to the developmentally based substrate of a typical LD. Even in such cases, though, children would ideally also be directed to an RTI program in a local educational setting for confirmation of the LD. It remains to be determined if interventions designed to improve academic skills among children with LDs differ in effectiveness for children who have LDs in the context of a primary medical disorder.

It has been our experience that the neuropsychological evaluation in conjunction with a hospital-based school reentry program is an important bridge among parents, the child, and school personnel. For example,

the Lucile Packard Children's Hospital at Stanford offers the HEAL program for children with medical conditions who may have problems transitioning back to school. The results of the neuropsychological evaluation are incorporated into a school plan. Personnel from the HEAL program also visit the school to observe the child and to meet with school personnel as needed. It may not be possible for neuropsychologists in private practice to provide this service, but it demonstrates how the neuropsychological evaluation in a medical setting can be helpful in making appropriate recommendations for school-age children.

### Evaluating Children at Risk for LD

Having considered when to evaluate children with concerns about their academic skills, we now turn to discussing assessment strategies for the five types of LD that have been identified in empirical research. Three of the types involve reading deficits (word recognition, reading fluency, and reading comprehension). The fourth type involves individuals who struggle with mathematics, including calculation and applied mathematical problem solving (e.g., story problems). The fifth type involves children who have significant difficulty with written expression, including spelling, handwriting, and written composition [3].

In the context of outpatient neuropsychological evaluation, direct assessment of the academic domains of interest forms the core of the test battery for identification of child at risk for LD. The term "at risk for LD" is used since one cannot likely diagnose LD with confidence in the absence of an evaluation of RTI, at least among children [14]. The child's level of intellectual functioning may be considered, although we do not consider an IQ test to comprise an essential component of the test battery unless mental retardation is suspected. In such cases, assessment of the individual's level of adaptive behavior should also be undertaken.

At a bare minimum, the individual's level of academic skill should be assessed in each of the five domains identified in the LD literature. The test battery should include measures of word reading, reading fluency, reading comprehension, mathematics, and spelling. There are numerous commercially available test batteries that will satisfy this criterion. We generally prefer the following tests from

the *Woodcock–Johnson Tests of Achievement – Third Edition (WJ-III)*. Another popular achievement battery is the *Wechsler Individual Achievement Test – Second Edition (WIAT-II)*.

Academic skill	WJ-III	WIAT-II alternate
Oral word reading	Letter–Word Identification	Word Reading
Reading fluency	Reading Fluency	–
Reading comprehension	Passage Comprehension	Reading Comprehension
Calculation	Calculation	Numerical Operations
Spelling	Spelling	Spelling
Phonological decoding of print	Word Attack	Pseudoword Decoding

It is commonly believed that the WIAT-II was co-normed with the Wechsler intelligence tests (e.g., WISC-IV and WAIS-III), but this is not the case. Rather, the test publisher administered the WIAT-II and Wechsler intelligence tests to relatively small samples of examinees in order to determine the correlations between the respective tests [15]. In contrast, the WJ-III was completely co-normed with the *Woodcock–Johnson Tests of Cognitive Abilities*. We prefer the WJ-III to the WIAT-II for several reasons. First, the WJ-III normative sample ( $n = 8,818$ ) is nearly twice the size as the WIAT-II normative sample ( $n = 4,879$ ). Second, the WJ-III may be used with individuals ranging in age from 2 to 90+ years (vs. 4–85 years for the WIAT-II). Third, the WJ-III has alternate forms (Forms A and B), as well as a third form that recently became available (Form C). Thus, there are three parallel forms that contain the same core subtests, but with distinct items within each test. Fourth, we have found the WJ-III to be faster and easier to administer than is the WIAT-II. Fifth, the two batteries compare favorably in terms of psychometric properties, with any major disparities favoring the WJ-III.

In addition to the tests listed above, we prefer to include Writing Samples, Quantitative Concepts, and Oral Comprehension from the WJ-III when possible. Writing Samples provides a more thorough assessment of handwriting and quality of written expression than Spelling alone offers. Quantitative Concepts can be helpful to assess the child's mastery of math facts that are less dependent on formal calculation procedures. Oral Comprehension is very similar to Passage

Comprehension in its processing demands, but all inputs occur through the auditory (rather than visual) modality.

In the case of an individual attending high school or college, a more extensive measure of reading comprehension is desirable and will likely be necessary should the individual wish to apply for accommodations on tests such as the Scholastic Aptitude Test (SAT). We have found the Nelson–Denny Reading Test (NDRT) to be most suitable for this purpose. Determination of eligibility for extended time on standardized tests often requires evidence that the individual is disproportionately hindered under standard time constraints. Thus, administration of the NDRT Reading Comprehension Test under both standard and extended time formats provides a direct test of this issue. We would recommend using alternate forms for this comparison. For example, one might administer Form G in standard format early in the test session, and then administer Form H in extended time format toward the end of the test session, or even on a separate day.

In some cases, modifications to the test battery will be necessary. The Peabody Individual Achievement Test – Revised (PIAT-R) may be suitable for children with significant motor deficits, as no writing is required on any of the subtests. Children with expressive language difficulties may also be good candidates for the PIAT-R Reading Comprehension subtest, in which the child reads a sentence and then points to one of the four pictures that best describe the sentence. The PIAT-R also arguably comes closer than other achievement batteries to measuring the individual’s “pure” academic skills, since none of its subtests are timed.

The extent to which it is necessary to include measures of cognitive functioning other than academic skills depends on the reason for evaluation. When deciding whether or not to include additional measures, the primary criterion should be whether performance on the respective measures might reveal strengths or weaknesses that could be useful for intervention planning. For example, it might be useful to assess an individual’s level of receptive word knowledge using the *Peabody Picture Vocabulary Test – Fourth Edition* (PPVT-4). If performance on this measure is markedly above that of oral word reading performance, for example, then such information would point toward a deficit in recognizing printed words, as opposed to a lack of word knowledge per se. Neuropsychologists are advised to be

judicious, though, in selecting the additional measures, since there appears to be little empirical support for the notion that addressing strengths and weaknesses in cognitive skills (apart from academic skills per se) relates to intervention outcomes [3]. For example, an intervention attempting to improve a child’s naming skills would not necessarily be expected to result in improved word reading. As noted by Fletcher et al. [3], “Gains are specific to what is taught. If interventions do not teach academic content, little transfer occurs” (p. 273).

On the other hand, children with academic achievement problems and a known and/or suspected medical condition affecting cognitive functioning may benefit from a comprehensive neuropsychological evaluation in addition to specific measures of academic achievement. Even if the findings from the neuropsychological portion of the evaluation do not clearly inform the academic issues, such findings may be utilized to understand potential dysfunction of the child’s brain. In the case of epilepsy, for example, findings of modality-specific deficits may be helpful for lateralizing the epileptic focus to one cerebral hemisphere. Moreover, findings of academic skill deficits may have implications for inferences regarding lateralized brain dysfunction in epilepsy patients. In one study, for example, epilepsy patients with comorbid reading deficits showed equivalent reductions in verbal and nonverbal memory, regardless of the side of seizure onset [16].

To summarize, circumstances continue to exist in which clinical neuropsychologists may contribute to the assessment and possible identification of children at risk for LD. Although there is a welcome movement toward using a dynamic RTI approach for identifying LDs, not all individuals presenting for assessments will be enrolled in an educational setting, and not all educational settings will have well-developed RTI programs. Furthermore, some individuals will have medical conditions that affect cognitive functioning, including academic skills. It seems reasonable for clinical neuropsychologists to continue to be involved in LD assessment, provided that they are aware of the limitations that non-RTI approaches possess. Individuals who appear to have deficits in core academic skills that are not clearly attributable to causes such as visual impairment, hearing impairment, or mental retardation may be considered “at risk” for having an LD, which then would ideally be confirmed through an

evaluation of RTI. For opposing viewpoints on this issue, the interested reader is referred to two recent papers [17, 18].

## Biological and Neuropsychological Mechanisms

### Genetic Influences

Considerable evidence indicates that genetic factors influence the development of LDs. Dyslexia, for example, tends to run in families, and family history is an important risk factor. In children of parents with dyslexia, rates range from 23 to 65% [19]. The prevalence rate of dyslexia among individuals with an affected sibling is approximately 50% [20]. Twin studies consistently reveal higher concordance rates for dyslexia among monozygotic compared to dizygotic twins [21]. Sizeable heritability estimates have also been obtained for reading comprehension [22], and measures related to reading fluency, such as rapid naming [23]. Nine loci where dyslexia genes are encoded have been identified (*DYX1* through *DYX9*). *DYX2* has been the most replicated locus which is located on the “p” arm of chromosome 6 in band “22” (6p22) [10]. Meng et al. [24] recently proposed that *DCDC2* encoded on 6p22 is a candidate gene for reading disabilities. Math disabilities [25] and disorders of written expression also show evidence of heritability [26], but no specific candidate genes have yet been identified.

### Brain Mechanisms and Correlates of Dyslexia

Though most children with LDs do not show overt evidence of brain damage using standard brain imaging techniques, and these measures have not been shown empirically to be diagnostic of LD, there is a growing body of research substantiating the neural mechanisms of LDs using functional and specialized structural brain imaging methods. While early theories regarding the neural basis of dyslexia, dyscalculia, and dysgraphia were based on lesion studies [27–30], advances in technology have made it possible to investigate brain differences between individuals

with and without LD and extend prior research. By far, most of this work has been in the area of developmental dyslexia, but developmental dyscalculia has also been studied. In contrast, there is a notable lack of research examining the neural mechanisms underlying developmental dysgraphia. This section of the chapter will summarize the relevant research regarding the neural bases of developmental dyslexia, dyscalculia, and dysgraphia based on studies with alphabetic languages.

Reading is a complex skill that must be taught and requires phonological processing (i.e., sensitivity to the sound structure of words), orthographic processing (i.e., visual features of words), and semantic processing (i.e., meaning). Therefore, language systems and visual systems of the brain working interactively are needed for the development of reading. Most researchers agree that developmental dyslexia is a heterogeneous disorder, but there is now a consistent and broad area of research showing that a core deficit in developmental dyslexia is problems with phonological processing. We would like the reader to be aware that there are other theories regarding brain mechanisms contributing to dyslexia, including the magnocellular theory [31, 32], rapid auditory processing theory [33, 34], and the cerebellar theory [35–37]. For a review, see Ramus et al. [38]. There is also research indicating that naming speed plays a role in a child’s ability to become a fluent and automatic reader [39, 40]. However, researchers debate whether the naming speed deficit is part of a phonological factor or whether rapid naming is a unique contributor to reading achievement [41, 42]. Lastly, there is a plethora of research identifying specific subtypes of developmental dyslexia, although there is little empirical evidence that subtyping and targeting the deficits delineated by this process leads to improved outcomes. A variety of functional and structural imaging methodologies, including functional magnetic resonance imaging (fMRI), positron emission topography (PET), magnetic source imaging (MSI), voxel-based morphometry (VBM), diffusion tensor imaging (DTI), and related techniques such as event-related potentials (ERP), have shown differences in activation patterns and brain structure comparing dyslexic and typically achieving children and adults in an anterior left frontal region and two posterior left hemispherical regions. More specifically, the left inferior frontal gyrus (IFG; anterior), the left temporal parietal, the left occipital temporal

regions, and pathways connecting these regions mediate speech production, phonological awareness skills, and orthographic processing. These areas are necessary for the development of skilled reading based on studies of dyslexic and typically achieving readers (for reviews, see Schlaggar and McCandliss [10] and Shaywitz, Gruen, and Shaywitz [43]).

The left IFG has been associated with articulation and naming [44], the left temporal parietal region with the integration of phonological processing and orthography [45, 46], and the left occipital temporal regions with processing the visual features of letters and words [47, 48]. This area has been termed the visual word form area (VWFA) and is activated by visually but not acoustically presented words. It has been hypothesized that a shift occurs from bilateral ventral occipitotemporal cortex to a preponderance of left ventral occipitotemporal involvement in concert with reading development [48, 49].

Cross-sectional studies comparing children and adults with and without dyslexia using PET and fMRI have indicated hyperactivation in the left frontal gyrus and hypoactivation in the left perisylvian regions and left occipital temporal regions in the participants with dyslexia during reading-related and phonological awareness tasks [50, 51], in both age-matched and reading-matched groups [52, 53]. The latter study by Hoft and colleagues also incorporated voxel-based morphometry (VBM) in order to more closely examine the structural brain differences that may underlie the concomitant functional differences in dyslexia. VBM is a method that makes voxel-by-voxel comparisons in the concentration of gray matter between two groups. They found reduced gray matter volume in the left parietal region that corresponded to areas of reduced activation in participants with dyslexia relative to non-dyslexic participants. Atypical gray matter morphology in the left temporal region has also been reported in other studies using VBM [54, 55]. Along these lines, Galaburda's post-mortem microscopic analysis of brains of individuals with dyslexia revealed abnormalities in the form of ectopias, dyslaminations, and scars, which provides evidence for a disruption in gray matter [56, 57].

Brain activation patterns have been studied longitudinally with fMRI in response to reading intervention programs [49, 58]. These studies further confirm the importance of left temporoparietal regions in reading. They also reveal that some children with dyslexia

evidence normalization of activity, whereas others have more persistent problems.

Cross-sectional studies of children with dyslexia using MSI, which measures the location and time course of brain's magnetic activity, have shown an absence of a left lateralized response in perisylvian regions when reading words [59]. Children with dyslexia showed greater activation in the right temporoparietal area that the authors interpreted as indicating a compensatory role of the right hemisphere. Similar to the fMRI studies showing normalization of activity after intervention, Simos and colleagues have shown that similar areas previously showing timing differences in children with dyslexia were also normalized [60, 61] after a combination of two interventions. The first intervention targeted phonological and decoding skills (*Phono-Graphix*) [62] and the second intervention assisted with reading fluency (*Read Naturally*) [63]. A weakness of these studies, though, is that they did not employ an objective approach to determining the number and location of magnetic sources (cf. Papanicolaou et al. [64]).

While these functional imaging studies have focused on gray matter, a special type of structural MRI scan, diffusion tensor imaging (DTI), allows measurement of white matter. For a review of white matter pathways in reading, see Ben-Shachar [65]. Although conventional MRI is excellent at discriminating white matter from gray matter, it is poor at discriminating the fine tissue structure within the white matter. DTI provides information about the alignment and integrity of white matter axons in the brain by measuring intracellular and extracellular water diffusion. Fractional anisotropy (FA) can be derived from DTI. FA values are a measure of microstructural features within a voxel and reflect the orientation dependence of diffusion; high FA values within a voxel suggest the presence of highly directional diffusion such as that seen in normal white matter fiber tracts. Studies looking specifically at white matter pathways using DTI have shown that the left temporoparietal region in children [66, 67] and adults [68] yields lower FA values among poor readers. In children, this area has been identified within the superior portion of the corona radiata at the level of the corpus callosum. DTI was also used to study fibers from the temporal lobes to the corpus callosum [69]. White matter diffusion was inversely related to phonological awareness performance in the posterior corpus callosum. The authors hypothesized

that the finding may reflect that better phonological awareness performance is related to fewer but larger axons in this region connecting the right and left temporal lobes. Larger axons allow for faster conduction of signals compared to smaller axons. This result is consistent with the temporal processing theory of dyslexia, which purports that good readers are better at processing rapidly changing visual and auditory information [70, 71].

### **Brain Mechanisms and Correlates of Dyscalculia**

Development of quantitative abilities includes an abstract sense of numbers and quantity, counting, and calculation, and has not been studied as extensively as reading. Unlike reading, which must be learned, humans are believed to be born with an innate sense for number estimation and simple calculations [72, 73]. However, there are also higher level math skills that require explicit teaching.

Dehaene and colleagues [74, 75] have postulated that there are three parietal circuits that play a significant role in math skills, including number estimation, calculation, and counting. The three regions are the horizontal segment of the intraparietal sulcus (HIPS) in both hemispheres, the left angular gyrus (AG), and the posterior superior parietal lobule (PSPL). Although some studies have found that prefrontal regions are involved in an ancillary role and are likely required for working memory [76, 77], the HIPS regions have been shown to activate alone during number detection and number comparison tasks regardless of the modality [78, 79].

Both fMRI studies and lesion studies have shown that areas within the HIPS in both hemispheres are critical for number processing (for a review, see Dehaene [75]). The HIPS is activated when performing mental arithmetic (greater activation for subtraction vs. multiplication) and number comparison (right hemisphere greater than left hemisphere). HIPS activation appears to be specific for processing numbers compared to other categories of information even in subliminal conditions.

Activation of the left AG has been demonstrated in fMRI studies using tasks that require number processing and calculation, but may not be a specific

finding as the left AG has connections to the reading and the language system. Dehaene et al. [75] hypothesize that the left AG contributes to the storing of arithmetic facts – rote arithmetic skills such as multiplication tables – but that it is unlike the HIPS in that it does not mediate subtraction tasks, number comparisons, or number representations. Two studies have shown distinct sites along the left AG that subserved subtraction and multiplication in patients with lesions or impairments produced by cortical stimulation [80, 81]. Changes in activation patterns of the left AG have also been associated with math complexity [77].

Finally, the PSPL has shown activation during tasks requiring number comparison [79, 82], number estimation [83], subtraction [84], and counting [85]. This area has also been associated with mediation of visuospatial tasks, attention, eye orientation, and spatial working memory [86, 87]. Dehaene et al. acknowledge a degree of caution in interpreting these findings and the need for further research to substantiate their provisional claims about this region.

Early imaging work exploring the neural basis of impaired arithmetic processing was conducted in females with Turner syndrome (TS) and fragile X, populations in which a deficit in arithmetic skills is present. PET [88] and anatomic MR studies in patients with TS [89, 90] showed glucose hypometabolism in bilateral parieto-occipital regions and reduction in brain volume in bilateral parieto-occipital regions. In an fMRI study, girls and young adult females with fragile X showed activation in the left parietal and bilateral frontal regions during tasks of arithmetic calculations involving two and three operands, while control subjects showed bilateral frontal and parietal activation [91]. Further support of these circuits' involvement in arithmetic processing comes from fMRI studies in children with developmental dyscalculia. The first fMRI study in children with developmental dyscalculia ( $n = 18$ ) compared to control children ( $n = 20$ ) found significantly less activation in the left intraparietal sulcus (IPS), the right IFG, and the right middle frontal gyrus (MFG) during a task of approximate calculation and that activation in the left IPS, the left IFG, and the right MFG correlated with behavioral performance [92]. The same researchers, using VBM, found that children with developmental dyscalculia ( $n = 12$ ) compared to control children ( $n = 12$ ) exhibited significantly less gray matter volume in the right IPS, the anterior cingulum, the left IFG, and the bilateral



MFG, as well as significantly decreased white matter volume in the left frontoparietal lobe and the right parahippocampal gyrus [93].

One study used DTI to investigate white matter integrity in children and adolescents with velocardiofacial syndrome [94], a genetic syndrome. Performance on a mental arithmetic task correlated with FA values in white matter tracts in left inferior parietal regions in children and adolescents with velocardiofacial syndrome. This finding was not present among healthy participants. A second study used DTI to investigate the relationship between white matter and math skills in typically developing children [95]. Performance on two written tests requiring mathematical calculations and application of math principles correlated with FA values in two left hemispherical regions, the left superior corona radiata and the left inferior longitudinal fasciculus [95]. More research is needed to clarify the role of white matter in developmental dyscalculia.

### ***Brain Mechanisms and Correlates of Dysgraphia***

Spelling, composition, and handwriting are the skills needed for writing development [96]. There is less consensus regarding the identification of disorders of written expression compared to reading and math disorders, and many times writing disorders are included with other learning disabilities. Although developmental dysgraphia is defined as impairment in the ability to write, it includes difficulty in handwriting, spelling, and written expression [3]. Components of writing are related to reading (mapping of phonology to orthography), but writing is not the inverse of reading. Berninger and colleagues [97] have demonstrated this notion in their work examining the interrelationships of the development of language by eye and language by hand. Their approach to studying language is based on the assumption that language is composed of four functional systems in the brain, i.e., language by ear (aural), language by mouth (oral), language by eye (reading), and language by hand (writing). Through the use of structural equation modeling, outcomes of interventions, and functional brain imaging, they have shown that the language by eye and language by hand systems share processes but are distinct and separable skills [98]. To date, our understanding of brain regions

involved in writing is based on lesion studies in individuals with acquired agraphia. There have been no functional imaging studies in adults with developmental dysgraphia while they are performing spelling or writing tasks. There is one fMRI study with children who are good and poor writers [3].

Neuropsychological studies of focal brain lesions mostly implicate left perisylvian and left superior parietal regions [99]. These studies have demonstrated that lesions to the left AG, the posterior MTG, the inferior temporal gyrus, and the inferior occipitotemporal region may produce lexical agraphia (greater difficulty in spelling irregular words). Damage to the anterior supramarginal gyrus and/or the insula may yield phonological agraphia (greater difficulty in spelling unfamiliar words or nonwords) (for a review, see Henry and colleagues [100] and Roeltgen [101]). As Fletcher et al. [3] report, it is not known whether these same locations are essential for the development of writing, or if they are compromised in individuals with developmental dysgraphia.

In the few fMRI studies that have examined either children or adults performing spelling tasks in English, healthy participants were used [102–104]. Increased activation was exhibited in the left IFG and the left fusiform gyrus in children. When adults were compared to children, greater activation in bilateral AG and bilateral superior SPL areas was demonstrated. Richards et al. [105] attempted to isolate brain regions that mediated writing skills during an fMRI task contrasting finger sequencing and finger tapping in children at the end of fifth grade who had participated in a longitudinal writing study. Both poor and good writers were included in the study. They identified 11 brain regions with an activation pattern that correlated with both handwriting and spelling. They also found a gender difference in the left superior parietal region with boys showing hypoactivation in this area compared to girls. More studies are needed, especially in children and adults who have been diagnosed with developmental dysgraphia.

### **Treatment**

Information regarding specific intervention programs for LDs is outside the scope of the chapter, but we would like the reader to be aware of some background information and resources for additional information.

It is clear that LDs do not resolve without intervention. Most emphasis in this area has focused on treatment for developmental dyslexia. Within this area, most interventions have been aimed at improving single-word reading. There is consistency across different studies in that children need to have explicit training in phonological awareness skills as a foundation for reading, but there are a variety of treatment types, including classroom intervention, pull-out resource services, computer training, and tutoring, as well as combinations of these approaches. However, common school-based interventions are more likely to stabilize reading rather than remediate it [106]. There are many commercial programs available, some of which are research based. Interventions need to be intense, systematic, explicit, and delivered in small groups [107]. Gains have been maintained for about half of the children for at least 1 year once they have returned to their standard curriculum [106]. Shaywitz [108] advocates for intervention at any age or grade level, but early intervention (6–8 years of age) is key and may prevent further reading problems [109].

Interventions focusing on reading comprehension and fluency are less prevalent than interventions that target phonological awareness and word reading skills. There is some carryover from improvement in phonological awareness and single-word reading to reading comprehension, particularly in the early grades [108, 110], but it is important to continue to assist with vocabulary development so as not to hinder reading comprehension, particularly as children advance past the third grade. Despite improvements in word reading and reading comprehension, one of the most difficult areas to remediate is fluency; older children and adults often remain slow and effortful readers [110, 111]. The National Reading Panel [112] reports that effective reading instruction requires the incorporation of phonemic awareness, phonics, fluency, vocabulary, and comprehension.

Interventions for developmental dyscalculia have focused on number sense, math facts, calculations, conceptual knowledge, and procedural knowledge. Unlike developmental dyslexia, in which there is consensus of research over the past 30 years pointing to a core deficit in phonological awareness, there has been no core deficit identified in developmental dyscalculia until recently. Wilson and colleagues [113] have recently postulated that number sense is a core deficit in developmental dyscalculia, which they define as

a deficit in both the ability to represent numerical magnitude and the ability to connect quantity and symbolic representations of numbers [113, 114]. They have developed a computerized adaptive intervention program (“The Number Race”) that is just beginning to be investigated. There is some evidence from a meta-analysis of 15 studies that were either well-controlled experimental or quasi-experimental studies of low-achieving math students or students at risk for failure [115] showing that the following led to improvements in mathematics: (1) providing data or recommendations to teachers and students, (2) peer-assisted learning, (3) providing clear, specific feedback to parents on their children’s successes, and (4) explicit teacher-led and contextualized teacher-facilitated approaches.

Even less is known about interventions for developmental dysgraphia, with most interventions focusing on spelling and written expression. In a recent review of 19 studies examining both spelling and reading interventions on spelling outcomes, the authors identified five key factors that contributed to improved spelling: 1) instructional delivery (error correction procedures in which the teacher reproduced the student’s error prior to presentation of the correct response), 2) limiting the number of words sequentially learned, 3) computer-assisted instruction, 4) multisensory training, and 5) systematic study and practice [116]. Another recent review of handwriting remediation from an occupational therapy perspective compared 11 studies with a variety of treatment approaches, including perceptual–motor, visual–motor, motor control, individualized interventions/exercises, and supplementary handwriting instruction [117]. The authors found that overall interventions were effective mostly with regard to legibility, but not speed.

For more specific information regarding interventions for LDs, see Fletcher et al. [3, 118] and Hale and Fiorello [118]. The latter book has appendices of interventions along with references for each type of LD. For interventions more specifically targeted for adults, the work of Mapou [2] may be consulted.

## Summary and Future Directions

In this chapter, we have discussed LDs as unexpected underachievement in one or more academic skills. LDs are best identified through an approach that

considers low achievement and failure to respond to instruction. Such a process is likely (now or in the future) to occur primarily through the child's school. Neuropsychologists may continue to screen for academic skill deficits in children; provided that such deficits are not due to mental retardation, sensory impairment, or inadequate exposure to quality instruction, such children may be identified as being at risk for LD. Neuropsychologists also need to be aware of medical disorders (such as epilepsy) that may result in academic skill deficits and remain the most appropriate professionals to consult regarding a child's cognitive functioning in the context of a known or suspected medical disorder.

Screening for LD should, at a minimum, include measures of word reading, reading fluency, reading comprehension, calculation, and written expression. Approximately 5.4% of children in the United States received special education services due to LD in the most recent year for which data are available. Dyslexia remains the most common LD, followed by dyscalculia and dysgraphia. Family history is a significant risk factor for all LDs, and some candidate genes have recently been identified.

Brain-imaging studies have revealed that the left IFG, the left temporoparietal, and the left occipitotemporal regions tend to be hypoactive in children with dyslexia. Among children with dyscalculia, the horizontal segment of the IPS (bilaterally), the left AG, and the left posterior SPL have been implicated as critical for mathematical operations. The left perisylvian region and the left IFG appear to be important for spelling and writing operations.

Treatment for LDs is necessary, as they do not remit without intervention. Numerous approaches have demonstrated evidence of improvement in the academic skill(s) targeted, with phonological awareness training being a key area for dyslexia interventions. Increasing attention needs to be given to interventions for dyscalculia and dysgraphia.

Our knowledge of LDs has dramatically expanded over the past two decades, particularly with the advent of sophisticated brain-imaging techniques, but there continues to be a lack of evidence-based research identifying effective interventions for individuals with LDs. One reason for this is the heterogeneous nature of LDs and the difficulty in defining and classifying individuals with LDs. Furthermore, many studies have not isolated important demographic variables, intervention

delivery methods, and types of intervention. In addition, there is a lack of randomized controlled trials comparing interventions. Nonetheless, the move toward operationalizing LDs as failure to respond to instruction holds promise, as it puts attempts at treatment in the forefront. We look forward to continued research that highlights the importance of interventions that work.

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## References

1. Heilman KM, Valenstein E. *Clinical neuropsychology*, vol. xv. 4th ed. Oxford: Oxford University Press; 2003. 716p.
2. Mapou, RL. *Adult learning disabilities and ADHD: research-informed assessment*. New York, NY: Oxford University Press; 2009.
3. Fletcher JM, Lyon GR, Fuchs LS, Barnes MA. *Learning disabilities: from identification to intervention*. New York, NY: Guilford Press; 2007. p. 324.
4. Dombrowski SC, Kamphaus RW, Reynolds CR. After the demise of the discrepancy: proposed learning disabilities diagnostic criteria. *Prof Psychol Res Pr*. 2004;35:364–72.
5. Bloom B, Dey AN. Summary health statistics for US children: National Health Interview Survey, 2004. *Vital Health Stat 10*. 2006;227:1–85.
6. Altarac M, Saroha E. Lifetime prevalence of learning disability among US children. *Pediatrics*. 2007;119 (Suppl 1):S77–83.
7. US Department of Education OoSEaRSO, Office of special education programs (OSEP), data analysis system (DANS), 1976–2006. Percentage of children and youth ages 3–21 served under the Individuals with Disabilities Education Act (IDEA), by disability: selected years, 1976–77 through 2006–07. Vol. 2008; 2008
8. Shaywitz SE. Current concepts: dyslexia. *N Engl J Med*. 1998;338:307–12.
9. Disabilities ICoL. *Learning disabilities: a report to the US Congress*. Washington, DC: US Printing Office; 1987.
10. Shaywitz SE, Gruen JR, Shaywitz BA. Management of dyslexia, its rationale, and underlying neurobiology. *Pediatr Clin North Am*. 2007;54:609–23, viii.
11. Rutter M, Caspi A, Fergusson D, et al. Sex differences in developmental reading disability: new findings from 4 epidemiological studies. *J Am Med Assoc*. 2004;291:2007–12.
12. Lyon GR, Fletcher JM, Barnes MC. *Learning disabilities*. In: Mash EJ, Barkley RA, editors. *Child psychopathology*. 2nd ed. New York, NY: Guilford Press; 2003. p. 468–500.

13. Hooper SR, Swartz CW, Montgomery JW, et al. Prevalence of writing problems across three middle school samples. *School Psychol Rev.* 1993;22:610–22.
14. Fletcher JM, Francis DJ, Morris RD, Lyon GR. Evidence-based assessment of learning disabilities in children and adolescents. *J Clin Child Adolesc Psychol.* 2005;34:506–22.
15. Strauss E, Sherman EMS, Spreen O. A compendium of neuropsychological tests: administration, norms, and commentary, vol. xvii. 3rd ed. Oxford, NY: Oxford University Press; 2006. 1216p.
16. Breier JI, Brookshire BL, Fletcher JM, et al. Identification of side of seizure onset in temporal lobe epilepsy using memory tests in the context of reading deficits. *J Clin Exp Neuropsychol.* 1997;19:161–71.
17. Mather N, Gregg N. Specific learning disabilities: clarifying, not eliminating, a construct. *Prof Psychol Res Pr.* 2006;37:99–106.
18. Silver CH, Blackburn LB, Arffa S, et al. The importance of neuropsychological assessment for the evaluation of childhood learning disorders NAN Policy and Planning Committee. *Arch Clin Neuropsychol.* 2006;21:741–4.
19. Scarborough HS. Very early language deficits in dyslexic children. *Child Dev.* 1990;61:1728–43.
20. DeFries JC, Fulker DW, LaBuda MC. Evidence for a genetic aetiology in reading disability of twins. *Nature.* 1987;329:537–9.
21. Grigorenko EL. Developmental dyslexia: an update on genes, brains, and environments. *J Child Psychol Psychiatry.* 2001;42:91–125.
22. Byrne B, Samuelsson S, Wadsworth S, et al. Longitudinal twin study of early literacy development: preschool through grade 1. *Read Writ.* 2007;20:77–102.
23. Petrill SA, Deater-Deckard K, Thompson LA, et al. Genetic and environmental effects of serial naming and phonological awareness on early reading outcomes. *J Educ Psychol.* 2006;98:112–21.
24. Meng H, Smith SD, Hager K et al. DCDC2 is associated with reading disability and modulates neuronal development in the brain. *Proc Natl Acad Sci USA.* 2005;102:17053–8.
25. Alarcon M, DeFries JC, Light JG, Pennington BF. A twin study of mathematics disability. *J Learn Disabil.* 1997;30:617–23.
26. Bates TC, Castles A, Coltheart M, et al. Behaviour genetic analyses of reading and spelling: a component processes approach. *Aust J Psychol.* 2004;56:115–26.
27. Dejerine J. Sur un cas de cecite verbale avec agraphie, suivi d'autopsie. *Mémoires de la Société Biologique.* 1891;3:197–201.
28. Gerstmann J. Syndrome of finger agnosia, disorientation for right and left, agraphia, and acalculia. *Arch Neurol Psychiatry.* 1940;44:398–408.
29. Hecaen H, Angelergues R, Houillier S. Les varietes cliniques des acalculies aucours des lesions retro-rolandiques: approche statistique du probleme. *Revue Neurologique.* 1961;105:85–103.
30. Hecaen H, Marcie P. [Agraphia in the course of conduction aphasia]. *Wien Z Nervenheilkd Grenzgeb.* 1967;25:193–203.
31. Demb JB, Boynton GM, Heeger DH. Brain activity in visual cortex predicts individual differences in reading performance. *Proc Natl Acad Sci USA.* 1997;94:13363–6.
32. Stein J, Walsh V. To see but not to read; the magnocellular theory of dyslexia. *Trends Neurosci.* 1997;20:147–52.
33. Tallal P. Auditory temporal perception, phonics, and reading disabilities in children. *Brain Lang.* 1980;9:182–98.
34. Tallal P, Stark RE, Kallman C, Mellits D. Developmental dysphasia: relation between acoustic processing deficits and verbal processing. *Neuropsychologia.* 1980;18:273–84.
35. Nicolson R, Fawcett AJ, Dean P. Dyslexia, development and the cerebellum. *Trends Neurosci.* 2001;24:515–6.
36. Nicolson RI, Fawcett AJ, Berry EL, et al. Association of abnormal cerebellar activation with motor learning difficulties in dyslexic adults. *Lancet.* 1999;353:1662–7.
37. Nicolson RI, Fawcett AJ, Dean P. Developmental dyslexia: the cerebellar deficit hypothesis. *Trends Neurosci.* 2001;24:508–11.
38. Ramus F, Rosen S, Dakin SC, et al. Theories of developmental dyslexia: insights from a multiple case study of dyslexic adults. *Brain.* 2003;126:841–65.
39. Wolf M, Bowers P. The double-deficit hypothesis for the developmental dyslexias. *J Educ Psychol.* 1999;91:415–38.
40. Wolf M, O'Rourke AG, Gidney C, Lovett MW, Cirino P, Morris R. The second deficit: an investigation of the independence of phonological and naming-speed deficits in developmental dyslexia. *Read Writ.* 2002;15:43–72.
41. Vukovic RK, Siegel LS. The double-deficit hypothesis: a comprehensive analysis of the evidence. *J Learn Disabil.* 2006;29:25–47.
42. Katzir T, Kim YS, Wolf M, Morris R, Lovett W. The varieties of pathways to dysfluent reading: comparing subtypes of children with dyslexia at letter, word, and connected text levels of reading. *J Learn Disabil.* 2008;41:47–66.
43. Schlaggar BL, McCandliss BD. Development of neural systems for reading. *Annu Rev Neurosci.* 2007;30:475–503.
44. Fiez JA, Petersen SE. Neuroimaging studies of word reading. *Proc Natl Acad Sci USA.* 1998;95:914–21.
45. Brunswick N, McCrory E, Price CJ, et al. Explicit and implicit processing of words and pseudowords by adult developmental dyslexics: a search for Wernicke's Wortschatz? *Brain.* 1999;122(Pt 10):1901–17.
46. Paulesu E, Frith U, Snowling M, et al. Is developmental dyslexia a disconnection syndrome? Evidence from PET scanning. *Brain.* 1996;119(Pt 1):143–57.
47. Cohen L, Dehaene S, Naccache L, et al. The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain.* 2000;123(Pt 2):291–307.
48. McCandliss BD, Cohen L, Dehaene S. The visual word form area: expertise for reading in the fusiform gyrus. *Trends Cogn Sci.* 2003;7:293–99.
49. Shaywitz BA, Shaywitz SE, Blachman BA, et al. Development of left occipitotemporal systems for skilled reading in children after a phonologically-based intervention. *Biol Psychiatry.* 2004;55:926–33.

50. Shaywitz SE, Shaywitz BA, Pugh KR, et al. Functional disruption in the organization of the brain for reading in dyslexia. *Proc Natl Acad Sci USA*. 1998;95:2636–41.
51. Temple E, Poldrack RA, Salidis J, et al. Disrupted neural responses to phonological and orthographic processing in dyslexic children: an fMRI study. *NeuroReport*. 2001;12:299–307.
52. Hoeft F, Hernandez A, McMillon G, et al. Neural basis of dyslexia: a comparison between dyslexic and nondyslexic children equated for reading ability. *J Neurosci*. 2006;26:10700–8.
53. Hoeft F, Meyler A, Hernandez A, et al. Functional and morphometric brain dissociation between dyslexia and reading ability. *Proc Natl Acad Sci USA*. 2007;104:4234–9.
54. Brown WE, Eliez S, Menon V, et al. Preliminary evidence of widespread morphological variations of the brain in dyslexia. *Neurology*. 2001;56:781–3.
55. Steinbrink C, Vogt K, Kastrop A, et al. The contribution of white and gray matter differences to developmental dyslexia: insights from DTI and VBM at 3.0 T. *Neuropsychologia*. 2008;46:3170–8.
56. Galaburda AM, Kemper TL. Cytoarchitectonic abnormalities in developmental dyslexia: a case study. *Ann Neurol*. 1979;6:94–100.
57. Galaburda AM, Sherman GF, Rosen GD, et al. Developmental dyslexia: four consecutive patients with cortical anomalies. *Ann Neurol*. 1985;18:222–33.
58. Temple E, Deutsch GK, Poldrack RA, et al. Neural deficits in children with dyslexia ameliorated by behavioral remediation: evidence from functional MRI. *Proc Natl Acad Sci USA*. 2003;100:2860–5.
59. Simos PG, Breier JJ, Fletcher JM, et al. Brain mechanisms for reading words and pseudowords: an integrated approach. *Cereb Cortex*. 2002;12:297–305.
60. Simos PG, Fletcher JM, Sarkari S, et al. Altering the brain circuits for reading through intervention: a magnetic source imaging study. *Neuropsychology*. 2007;21:485–96.
61. Simos PG, Fletcher JM, Sarkari S, et al. Intensive instruction affects brain magnetic activity associated with oral word reading in children with persistent reading disabilities. *J Learn Disabil*. 2007;40:37–48.
62. McGuinness C, McGuinness D, McGuinness G. Phonographix: a new method for remediating reading difficulties. *Ann Dyslexia*. 1996;46:73–96.
63. Ilnot C, Mastoff J, Gavin J, Hendrickson L. *Read naturally*. St. Paul, MN: Read Naturally; 2001.
64. Papanicolaou AC, Pazo-Alvarez P, Castillo EM, et al. Functional neuroimaging with MEG: normative language profiles. *NeuroImage*. 2006;33:326–42.
65. Ben-Shachar M, Dougherty RF, Wandell BA. White matter pathways in reading. *Curr Opin Neurobiol*. 2007;17:258–70.
66. Beaulieu C, Plewes C, Paulson LA, et al. Imaging brain connectivity in children with diverse reading ability. *NeuroImage*. 2005;25:1266–71.
67. Niogi SN, McCandliss BD. Left lateralized white matter microstructure accounts for individual differences in reading ability and disability. *Neuropsychologia*. 2006;44:2178–88.
68. Klingberg T, Hedehus M, Temple E, et al. Microstructure of temporo-parietal white matter as a basis for reading ability: evidence from diffusion tensor magnetic resonance imaging. *Neuron*. 2000;25:493–500.
69. Dougherty RF, Ben-Shachar M, Deutsch GK, et al. Temporal–callosal pathway diffusivity predicts phonological skills in children. *Proc Natl Acad Sci USA*. 2007;104:8556–61.
70. Tallal P, Merzenich MM, Miller S, Jenkins W. Language learning impairments: integrating basic science, technology, and remediation. *Exp Brain Res*. 1998;123:210–9.
71. Stein J. The magnocellular theory of developmental dyslexia. *Dyslexia*. 2001;7:12–36.
72. Dehaene S. *The number sense*. New York, NY: Oxford University Press; 1997.
73. Temple E, Posner MI. Brain mechanisms of quantity are similar in 5-year-old children and adults. *Proc Natl Acad Sci USA*. 1998;95:7836–41.
74. Dehaene S, Piazza M, Pinel P, Cohen L. Three parietal circuits for number processing. *Cogn Neuropsychol*. 2003;20:487–506.
75. Dehaene S, Molko N, Cohen L, Wilson AJ. Arithmetic and the brain. *Curr Opin Neurobiol*. 2004;14:218–24.
76. Chochon F, Cohen L, van de Moortele PF, Dehaene S. Differential contributions of the left and right inferior parietal lobules to number processing. *J Cogn Neurosci*. 1999;11:617–30.
77. Menon V, Rivera SM, White CD, et al. Dissociating prefrontal and parietal cortex activation during arithmetic processing. *NeuroImage*. 2000;12:357–65.
78. Eger E, Sterzer P, Russ MO, et al. A supramodal number representation in human intraparietal cortex. *Neuron*. 2003;37:719–25.
79. Pinel P, Dehaene S, Riviere D, LeBihan D. Modulation of parietal activation by semantic distance in a number comparison task. *NeuroImage*. 2001;14:1013–26.
80. Duffau H, Denvil D, Lopes M, et al. Intraoperative mapping of the cortical areas involved in multiplication and subtraction: an electrostimulation study in a patient with a left parietal glioma. *J Neurol Neurosurg Psychiatry*. 2002;73:733–8.
81. Whalen J, McCloskey M, Lesser RP, Gordon B. Localizing arithmetic processes in the brain: evidence from transient deficit during cortical stimulation. *J Cogn Neurosci*. 1997;9:409–17.
82. Pesenti M, Thioux M, Seron X, De Volder A. Neuroanatomical substrates of Arabic number processing, numerical comparison, and simple addition: a PET study. *J Cogn Neurosci*. 2000;12:461–79.
83. Dehaene S, Spelke E, Pinel P, et al. Sources of mathematical thinking: behavioral and brain-imaging evidence. *Science*. 1999;284:970–4.
84. Lee KM, Kang SY. Arithmetic operation and working memory: differential suppression in dual tasks. *Cognition*. 2002;83:B63–8.
85. Piazza M, Mechelli A, Butterworth B, Price CJ. Are subitizing and counting implemented as separate or functionally overlapping processes? *NeuroImage*. 2002;15:435–46.
86. Corbetta M, Kincade JM, Ollinger JM, et al. Voluntary orienting is dissociated from target detection in

- human posterior parietal cortex. *Nat Neurosci.* 2000;3:292–7.
87. Simon O, Mangin JF, Cohen L, et al. Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. *Neuron.* 2002;33:475–87.
  88. Clark C, Klonoff H, Hayden M. Regional cerebral glucose metabolism in Turner syndrome. *Can J Neurol Sci.* 1990;17:140–4.
  89. Reiss AL, Freund L, Plotnick L, et al. The effects of X monosomy on brain development: monozygotic twins discordant for Turner's syndrome. *Ann Neurol.* 1993;34:95–107.
  90. Reiss AL, Mazzocco MM, Greenlaw R, et al. Neurodevelopmental effects of X monosomy: a volumetric imaging study. *Ann Neurol.* 1995;38:731–8.
  91. Rivera SM, Menon V, White CD, et al. Functional brain activation during arithmetic processing in females with fragile X Syndrome is related to FMR1 protein expression. *Hum Brain Mapp.* 2002;16:206–18.
  92. Kucian K, Loenneker T, Dietrich T, et al. Impaired neural networks for approximate calculation in dyscalculic children: a functional MRI study. *Behav Brain Funct.* 2006;2:31.
  93. Rotzer S, Kucian K, Martin E, et al. Optimized voxel-based morphometry in children with developmental dyscalculia. *NeuroImage.* 2008;39:417–22.
  94. Barnea-Goraly N, Eliez S, Menon V, et al. Arithmetic ability and parietal alterations: a diffusion tensor imaging study in velocardiofacial syndrome. *Brain Res Cogn Brain Res.* 2005;25:735–40.
  95. van Eimeren L, Niogi SN, McCandliss BD, et al. White matter microstructures underlying mathematical abilities in children. *NeuroReport.* 2008;19:1117–21.
  96. Abbott R, Berninger V. Structural equation modeling of relationships among developmental skills and writing skills in primary and intermediate grade writers. *J Educ Psychol.* 1993;85:478–508.
  97. Berninger VW, Abbott RD, Jones J, et al. Early development of language by hand: composing, reading, listening, and speaking connections; three letter-writing modes; and fast mapping in spelling. *Dev Neuropsychol.* 2006;29:61–92.
  98. Berninger VW, Abbott RD, Abbott SP, et al. Writing and reading: connections between language by hand and language by eye. *J Learn Disabil.* 2002;35:39–56.
  99. Basso A, Taborelli A, Vignolo LA. Dissociated disorders of speaking and writing in aphasia. *J Neurol Neurosurg Psychiatry.* 1978;41:556–63.
  100. Henry ML, Beeson PM, Stark AJ, Rapcsak SZ. The role of left perisylvian cortical regions in spelling. *Brain Lang.* 2007;100:44–52.
  101. Roeltgen D. Agraphia. In: Valenstein KMHE, editor. *Clinical neuropsychology*, vol. 4. New York, NY: Oxford University Press; 2003. p. 75–96.
  102. Booth JR, Burman DD, Meyer JR, et al. Development of brain mechanisms for processing orthographic and phonologic representations. *J Cogn Neurosci.* 2004;16:1234–49.
  103. Booth JR, Cho S, Burman DD, Bitan T. Neural correlates of mapping from phonology to orthography in children performing an auditory spelling task. *Dev Sci.* 2007;10:441–51.
  104. Richards T, Berninger V, Nagy W, Parsons AC, Fields KM, Richards A. Brain activation during language tasks activation contrasts in children with and without dyslexia: inferring mapping processes and assessing response to spelling instruction. *Educ Child Psychol.* 2005;22:62–80.
  105. Richards TL, Berninger VW, Stock P, et al. Functional magnetic resonance imaging sequential-finger movement activation differentiating good and poor writers. *J Clin Exp Neuropsychol.* 2009;31:1–17.
  106. Torgesen JK. *Recent discoveries on remedial interventions for children with dyslexia.* Maiden, MA: Blackwell; 2006.
  107. Shaywitz SE, Morris R, Shaywitz BA. The education of dyslexic children from childhood to young adulthood. *Annu Rev Psychol.* 2008;59:451–75.
  108. Shaywitz S. *Overcoming dyslexia: a new and complete science-based program for reading problems at any level.* New York, NY: Vintage Books; 2003. p. 414.
  109. Foorman BR, Francis DJ, Shaywitz SE, Shaywitz BA, Fletcher JM. The case for early reading intervention. In: Blachman BA, editor. *Foundations of reading acquisition and dyslexia: implications for early intervention.* Mahwah, NJ: Lawrence Erlbaum Associates, Publishers; 1997. p. 243–64.
  110. Torgesen JK, Alexander AW, Wagner RK, et al. Intensive remedial instruction for children with severe reading disabilities: immediate and long-term outcomes from two instructional approaches. *J Learn Disabil.* 2001;34(33–58): 78.
  111. Hecht SA, Torgesen JK, Wagner RK, Rashotte CA. The relations between phonological processing abilities and emerging individual differences in mathematical computation skills: a longitudinal study from second to fifth grades. *J Exp Child Psychol.* 2001;79:192–227.
  112. Langenbereg DN. *Report of the National Reading Panel.* Washington, DC: National Institute of Child Health and Human Development; 2000.
  113. Wilson AJ, Dehaene S, Pinel P, et al. Principles underlying the design of “The Number Race”, an adaptive computer game for remediation of dyscalculia. *Behav Brain Funct.* 2006;2:19.
  114. Wilson AJ, Revkin SK, Cohen D, et al. An open trial assessment of “The Number Race”, an adaptive computer game for remediation of dyscalculia. *Behav Brain Funct.* 2006;2:20.
  115. Baker S, Gersten R, Lee D. A synthesis of empirical research on teaching mathematics to low-achieving students. *Elem School J.* 2002;103:51–73.
  116. Wanzek J, Vaughn S, Wexler J, et al. A synthesis of spelling and reading interventions and their effects on the spelling outcomes of students with LD. *J Learn Disabil.* 2006;39:528–43.
  117. Feder KP, Majnemer A. Handwriting development, competency, and intervention. *Dev Med Child Neurol.* 2007;49:312–7.
  118. Hale JB, Fiorello CA. *School neuropsychology: a practitioner's handbook.* New York, NY: Guilford Press; 2004.