Handbook of Clinical Neurology, Vol. 174 (3rd series)
Neurocognitive Development: Disorders and Disabilities, Part II
A. Gallagher, C. Bulteau, D. Cohen and J. Michaud, Editors
https://doi.org/10.1016/B978-0-444-64148-9.00004-1

c0020 Chapter 4

Developmental dyslexia: A new look at clinical features and brain mechanisms

MICHEL HABIB*

Resodys Institute and Department of Neurology, University Hospitals of Marseille, Marseille, France

st0010 **Abstract**

Developmental dyslexia is the commonest "specific learning disorder" (DSM-5) or "developmental learning disorder with impairment in reading" (ICD-11).

This impairment in reading acquisition is related to a defect in the installation of cognitive precursors necessary to master the grapheme–phoneme conversion. Its origin is largely genetic, but many environmental factors seem capable of modulating symptom intensity. Three types of presentation, roughly equal in occurrence, are useful to distinguish according to the associated disorders (language, attentional, and/or motor coordination), thus suggesting, at least in part, potentially different mechanisms at their origin. In adolescence and adulthood the clinical presentation tends to bear a more uniform pattern, covering a large range of severity depending on each person's ability to compensate for their deficit. Research has demonstrated dysfunction of specific brain areas during reading-related tasks (using fMRI), essentially in the left cerebral hemisphere, but also atypical patterns of connectivity (using diffusion imaging), further supplemented by functional connectivity studies at rest. The current therapeutic recommendations emphasize the need for multidisciplinary care, giving priority, depending on the clinical form, to the language, psychomotor, or neuropsychologic aspects of rehabilitation. Various training methods whose effectiveness has been scientifically tested are reviewed, emphasizing those exploiting the hypothesis of a lack of intermodal connectivity between separate cognitive systems.

p0010 Developmental dyslexia (DD), or specific learning disorder of reading, is the commonest form of this category of disorders. The two major international classifications, the DSM-5 (American Psychiatric Association, 2013) and the ICD-11 (still in preparation), have relatively clear diagnostic criteria: a reading acquisition defect resulting in a lag compared with the performance of an average of individuals on standardized reading tests, which has a significant repercussion on school/academic achievement and the use of reading in daily life, the normality of intelligence, and the absence of other pathology likely to interfere with this learning.

p0015 The prevalence of DD and specific learning disorders varies significantly among studies, from 5% to 15%, depending on one hand on the classifications (diagnostic criteria) used and on the other hand on environmental context. Epidemiological studies using the DSM-IV definition demonstrated 5%–8% of dyslexics in the general population in roughly the same manner in all countries. Although not yet available, studies using the more inclusive DSM-5 criteria should yield higher figures. Conversely, the ICD-11 definition includes a criterion not present in DSM-5, the so-called reading-intelligence discrepancy criterion (between actual reading scores and those expected from general intelligence), which could minimize the prevalence rates.

Moreover, socioeconomic background and mother tongue influence reading difficulties, the latter being p0020

*Correspondence to: Michel Habib, M.D., Ph.D., Resodys Institute, 3 square Stalingrad, 13001 Marseille, France. Tel: +33-6-7262-8030, E-mail: michel.habib@univ-amu.fr

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

much more frequent in socially disadvantaged environments (Fluss et al., 2009) and their impact significantly lower for idioms whose phono-orthographic conversion system is transparent (such as Italian or German: Ziegler et al., 2003).

p0025 These different considerations have emerged in the classification of the disorder. There is no longer a specific heading called "dyslexia" or "reading disorder" (versions DSM-IV and ICD-10) but a general heading called "specific learning disorder" (DSM-5) or "developmental learning disability" (ICD-11) also including two other areas that were previously the subject of separate chapters: disorders of written expression and impairment in calculation or math reasoning. This nosographic evolution, while seemingly trivial, represents in fact a radical change in the concepts around these disorders. It is obviously motivated by the widely shared clinical observation that the reading disorder is often associated with other cognitive difficulties, which for the clinician may render artificial its strict individualization. In this respect, the new way of looking at things is much more in line with clinical reality. However, it has the disadvantage of potentially leading to a ban of the term "dyslexia," which, in the current state of practice and knowledge, may seem premature.

s0010 MAIN FEATURES OF CLINICAL PRESENTATION

s0015 The "classical" phonological dyslexia presentation

p0030 The commonest diagnostic situation is undoubtedly that of a child consulting in the first 2 years of primary school for difficulties with written language. A practitioner, whether a teacher or a healthcare professional, can easily notice the lack of understanding in a child of this basic, universal procedure of learning the correspondence between the written forms (graphemes) and their sound equivalents (phonemes). It is clear that the diagnosis of dyslexia cannot be confirmed formally unless there is evidence of at least a few months' delay, but the mere fact of suspecting a shift compared with the progression of the rest of the class is enough to initiate a diagnostic procedure. Speech therapists or specialized teachers demonstrate and quantify, through standardized testing tools, the degree of deviation from the norm and allow specific interventions to be undertaken, generally focused on active manipulation of phonemes and phoneme-to-grapheme instruction. Moreover, the practitioner can reevaluate his/her mode of intervention as soon as he/she has obtained the results of a battery of complementary neuropsychologic tests. This includes general intellectual assessment (e.g., WISC-V), specific language tasks (syllabic and phonemic segmentation, pseudowords repetition, rapid naming of drawings, and fluency), and memory (immediate and long term) and attentional testing.

The main errors are often of a phonological nature, p0035
such as voiced/unvoiced confusions (p/b, t/d, etc.), sometimes associated with symmetrical letter confusions (d/b, p/q) reflecting the child's disability to create an orthographic lexicon from an overall visual representation of readily accessible word forms. The degree of transparency/opaqueness of the maternal language (e.g., German vs English) influences the reading disorder. Altered accuracy and fluency are more prominent in transparent languages whereas phonemic confusions will predominate in opaque ones (see later).

This type of dyslexia is often associated with short- p0040
term (mainly auditory) memory impairment, affecting the learning of counting tables, sometimes as a part of real dyscalculia. In the purest forms, however, working memory as well as long-term memory and attentional processes are found within normal limits. It is also in this classical form of dyslexia that one can find either in the past history or on examination evidence of some degree of oral language delay, beyond the unique scope of phonology. That is also the reason why some authors call this classical phonological dyslexia as the "linguistic" DD.

Inseparable from the reading disorder, the written p0045
expression is very early altered in the orthographic form of the words with multiple errors: phonological confusions, elisions, substitutions of letters, and so on, globally referred to as spelling errors (dysorthographia).

The "visuoattentional" subtype of dyslexia s0020

This form of DD appears in children with a severe p0050
alteration of the grapheme-to-phoneme conversion skill without any linguistic disorder showing in the finest phonological tests. It is specific in that the reading is very slow, hesitant, but with few errors, notably very effortful, and therefore generating a great cognitive fatigue that will potentially impair every single classroom activity. It is also in this type of dyslexia that one encounters the most severe misspelling, because the systematic decoding procedure does not allow the child to construct an orthographic lexicon and thus get automatic access to orthographic production. Some authors have reported specific visual detection tasks being specifically impaired in children with this profile of dyslexia (Valdois et al., 2003). According to our personal experience, this subtype is particularly frequent in those dyslexic individuals with high intellectual potential (HIP).

The main clinical elements are suggestive of an atten- p0055
tional disorder, sometimes associated with behavioral features such as impulsivity and/or more or less visible motor agitation typical of an attention deficit with or without hyperactivity disorder (ADHD). These children have problems in areas other than reading, for instance,

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

all tasks requiring sustained and/or shared attention, as in dual task situations, such as listening attentively to the teacher while writing.

p0060 This visuoattentional dyslexia presentation refers to disturbances in the bilateral temporoparietal circuits sustaining attention skills (and not in the left hemispheric frontal-temporal circuits of language as shown in phonological dyslexia) (Peyrin et al., 2008).

s0025 The "dyspraxic" form of dyslexia

p0065 For this category of children, it is neither the phonological system nor the attentional processes that are incriminated, but impaired motor coordination and visuospatial abilities. They resemble dyspraxic children in that their handwriting is awkward, as is their copy of geometric drawings, and their visuospatial abilities are inferior, in general, to what is expected according to their age and intellectual levels. Most typically, children's reading abilities, albeit initially a serious matter of concern, will improve within the first 2 years to the point where they do not need support anymore, while, in the same time, the impact of their writing difficulties on their school productivity gradually rises due to increasing demands in speed and exactitude from the curricular system. Written productions most often associate patterns of dysgraphia and multiple spelling errors, due to combined and reciprocal interaction between the linguistic and motor aspects of the process of writing (Roux et al., 2013). Clumsiness of the gesture, the irregularity of the letters' baseline, and ultimately a gradually increasing gap between the academic requirements and the pupil's personal potential for compensation will often lead, more or less rapidly, to the total replacement of handwriting by tapping on a keyboard. In some cases, dyslexia may remain problematic, often then suggesting neuromotor involvement of the ocular apparatus, with eye pursuit defects or abnormal saccades that affect the fluidity of gaze during the act of reading. In these cases, rehabilitation by an orthoptist (or optometrist depending on the country care system) may significantly improve reading.

p0070 Finally, a report made by a psychomotor or occupational therapist will often show the presence of relative difficulties in the field of visual-spatial processes, such as when copying the Rey-Osterreith figure, whose structure is poorly perceived and incorrectly reproduced, as well as difficulties in accessing temporal notions and in finding one's way in time, in all its dimensions, a condition sometimes referred to as dyschronia (Llinas, 1993).

s0030 Comorbidities and associated features

p0075 It is universally recognized that features of dyslexia almost never occur alone and additional diagnoses, whether pertaining to oral language, coordination, attention, or calculation disorders, are most frequently required. Oral language disorders, including so-called specific language impairments (SLIs), have a complex relationship with dyslexia. Children who have had difficulties with oral language are considered to be at risk for dyslexia, but some children with SLI, even in severe cases, will not become dyslexic (Snowling et al., 2000). Nevertheless, it is considered that even a minor defect in the development of oral language, whether a disorder of the articulation of phonemes or of the lexicon or syntax, even if they do not significantly impede the child's intelligibility, are risk factors for subsequent dyslexia.

In the same way, writing difficulties may appear p0080
before the age of reading, in the preschool period, thus serving as a warning signal for subsequent occurrence of dyslexia. The particular case of ADHD, a common comorbidity of dyslexia, poses clinical problems that may remain unrecognized until preadolescence, especially in children with HIP, which allows them to compensate the consequences of the disorder for a long time, or even completely mask them. In this respect, the HIP child is a real challenge for the teacher, who may fail to recognize his/her dyslexia, but also for the clinician, who may be misled by seemingly normal test results.

Finally, another important comorbidity is that p0085
between dyslexia and dyscalculia, which most often poses a challenge for academic progress, as it is well known that a competency in mathematics guarantees better integration and acceptance of the disorder (Willcutt et al., 2013). The prevalence of dyscalculia in school children is around 3.6%–6.5% (Lewis et al., 1994; Gross-Tsur et al., 1996), and the cooccurrence of reading and numeracy disorders in a same child may vary from 17% to 64%, according to studies.

The common underlying mechanism between math p0090
and reading disorders is not completely elucidated (Rourke, 1993; Shalev et al., 1997; Landerl et al., 2004; Butterworth, 2005). Two studies (Moll et al., 2016; Raddatz et al., 2017) of dyslexia/dyscalculia comorbidity reached similar conclusions, namely the existence of cognitive risk factors common to both entities (working memory, attention, executive functions) and a signature specific to each of them, the phonological disorder for dyslexia and temporal sense and number sense deficit for dyscalculia.

ETIOLOGIC FACTORS s0035

Since DD is a partly hereditary condition depending on p0095
the interaction of several different genes, the general pattern that emerges is that of a multifactorial etiology, including polygenic conditions and environmental factors.

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

s0040 Genetics of dyslexia

p0100 The inherited character of dyslexia has been suspected for a long time and refers to the phenomenon of aggregation. The occurrence of dyslexia is up to eight times higher if one of the parents is dyslexic, and the risk of observing one or more dyslexics in the family of a dyslexic is of the order of 60%. But family aggregation does not necessarily mean genetic transmission, because a child and his/her parents also share many elements related to the environment. For example, a father with poor reading abilities can influence his child's reading habits significantly.

p0105 The comparative studies of mono- or dizygotic twins have shown that the second twin of a pair whose first is dyslexic has almost 70% probability of being dyslexic in case of identical twins, while the rate drops to 40% for dizygotes. These results establish that around 50%–60% of the phenotype can be explained by the genotype, thus firmly establishing a genetic contribution to dyslexia. They do not, however, provide much information about the nature of this genetic contribution (Logan et al., 2013).

p0110 Advances in molecular genetics have shown a link between the transmission of certain portions of chromosomes and the transmission of dyslexia observed within families.

p0115 In 2003 Finnish researchers (Taipale et al., 2003) first identified a gene associated with dyslexia (*DYX1C1*) in the q21 region of chromosome 15 involved in neuronal migration (Wang et al., 2006) in the fetal cerebral cortex. Since then, at least eight other chromosomes have been identified, such as ROBO1 implicated in axonal and dendritic migration, as well as in the migration of interneurons. A transnational European study of 900 dyslexic individuals (Becker et al., 2014) has shown the existence of about 10 variants of the *DCD2* gene, which associate differently with the reading deficit level, and in a variable manner depending on the country. Only certain variants are associated with dyslexia and only in some countries.

p0120 Some studies (Eicher and Gruen, 2013; Mascheretti et al., 2017; Xia et al., 2017) have begun to pool data from genetics and brain imaging demonstrating a statistical link between certain genes carrying dyslexia risk and neuroanatomical characteristics such as the neuronal density and white matter structure in specific areas. The results are inconclusive for the moment, but they stand as a promise to reinforce, in a near future, the diagnosis of dyslexia in the clinical setting.

s0045 Effect of socioeconomic status (SES)

p0125 It is widely recognized that dyslexia associated with both accuracy and reading comprehension is more prevalent in economically disadvantaged contexts. In addition, the SES predicts lower reading performance for both entry-level reading and the later trajectory, which improves more slowly in the first few years of schooling (Hecht et al., 2000). Fluss and colleagues, studying more than 1000 children in 20 schools in the city of Paris, demonstrated that the incidence of dyslexia varies from 3.3% to 24.2% depending on socioeconomic background. Systematic reviews and meta-analyses have shown clearly and convergently that SES accounts for 10% of the variance in reading skills (Peterson and Pennington, 2015). This means that 90% of the reading variance is independent of the SES, and therefore many children from disadvantaged backgrounds must learn to read correctly, just like many children who do not learn to read come from ordinary backgrounds.

The impact of SES has also been demonstrated in various brain imaging studies. Children genetically at risk for a reading-learning disability are less sensitive to the effect of enriched linguistic interaction with the mother (Powers et al., 2016); nevertheless, intensive reading training modifies the cortical thickness in a more pronounced way in children raised in families with weak SES (Romeo et al., 2017). p0130

Effect of maternal language s0050

The degree of severity of dyslexia is influenced by language transparency. A transparent language is defined by a strong correspondence between the oral (phoneme) and written (grapheme) forms of the alphabetic code, while an opaque language is characterized by a weak oral/written correspondence. For example, in an opaque language such as English, the more or less 40 phonemes constituting the entire range of verbal sounds must be mapped upon about 1120 graphemes, which would explain the low level of achievement of English students at the end of their first year of reading, compared with students in most other European countries. Conversely, Italian is a transparent language with an almost strict correspondence between the oral and written codes, in such a manner that learning the phonemic code allows one to read the large majority of the words (Seymour et al., 2003). Dyslexics coming from countries with a transparent language (such as German or Italian) are therefore more affected for fluency than accuracy (Landerl et al., 1997). Nevertheless, comparative studies of dyslexia across different countries show that, whatever the degree of transparency/opacity of each language, the widely prevalent mechanisms remain that of a phonological disorder (Ziegler et al., 2010). Finally, special mention must be made of dyslexia in Chinese, whose ideographic writing explains the important role of syllabic consciousness as a predictor of dyslexia, beside that of phonology. p0135

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

Recent works in functional imaging have shown that Chinese dyslexic patients share partially common underactivation areas with dyslexics from Western countries (Siok et al., 2004; Cao et al., 2017).

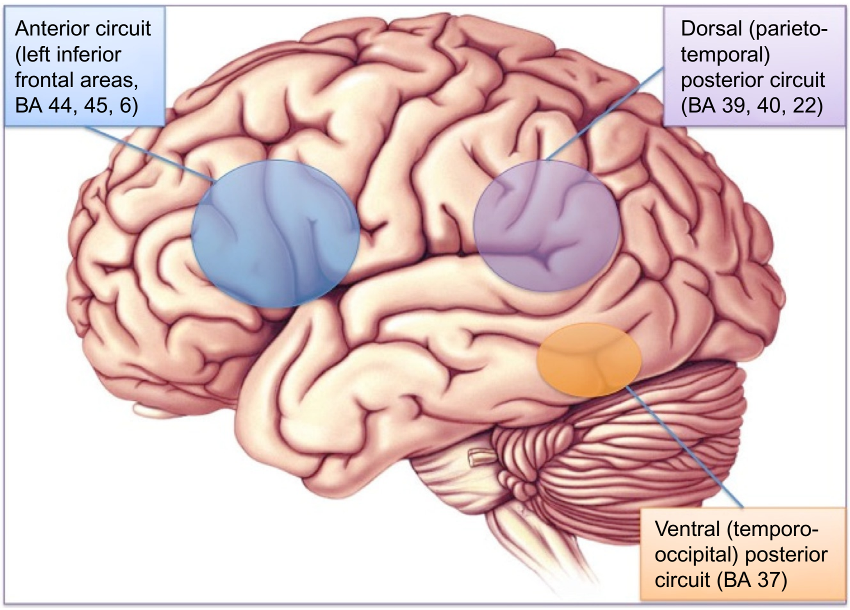
s0055 THE MECHANISM OF DYSLEXIA AND ITS NEUROCOGNITIVE SUBSTRATES

s0060 The history of brain imaging in dyslexia: Early fMRI studies

p0140 Since they became available to the scientific community, in the early 1990s, neuroimaging methods have been used extensively to unravel the mysteries of the dyslexic brain. The first learning came from fMRI techniques studying brain activations during reading and/or oral or visual phonological tasks (e.g., saying whether two read words rhyme or not). Several meta-analyses (Demonet et al., 2004; Norton et al., 2014) pointed out a common cerebral dysfunction in dyslexics. One of these is illustrated in Fig. 4.1, which shows three cortical zones of abnormal activation consistently disclosed across several independent studies: the three regions are located over the left hemisphere; two are involved in language function (Broca's area or inferior prefrontal cortex and Geschwind's area or the temporoparietal junction) and a third is localized in the left fusiform gyrus—the visual word form area (VWFA), in the basal temporooccipital junction, close to the visual cortex. The VWFA has been one of the major revelations in reading research over the past 2 decades. It is considered as the one responsible for the attribution of a linguistic status to the visual stimuli represented by the sequences of letters during the act of reading. It specializes in the early beginning of learning to read (Turkeltaub et al., 2003) and seems to be the most significantly underactive part of the brain in dyslexic children and adults (at least in alphabetic languages).

One of the questions that repeatedly animated researchers in this quest for the brain bases of dyslexia was whether the changes observed were the cause or the consequence of the reading disorder. In the current state of knowledge, there are just as many arguments in favor of both possibilities: for example, it is noteworthy that children with a family history of dyslexia underactivate around the age of 5 1/2, before any learning of reading, a left occipito-temporofrontal network in a typical phonological task (Raschle et al., 2010). It is also clear that limited experience of reading due to dyslexia will amplify, sometimes dramatically, the consequences and intensity of impairment in such a way that the dyslexic child and then adolescent will never reach a sufficient degree of automation of the elementary processes to allow higher-level processing of information to occur. Even in the absence of dyslexia, there is evidence that a limited experience of reading can hamper the development of the same brain circuits (Castro-Caldas et al., 1998). p0145

Finally, significant scientific knowledge comes from two meta-analyses from an Austrian group (Richlan et al., 2009, 2011) that compared functional MRI p0150



f0010 **Fig. 4.1.** The brain reading network: left-hemisphere cortical regions showing consistent structural and functional abnormalities in dyslexic adults and children. From Demonet, J.F., Taylor, M.J., Chaix, Y., 2004. Developmental dyslexia. *Lancet* 363, 1451–1460.

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

findings in nine studies each dedicated to children and adults. They demonstrated that Broca's area was underactive in dyslexic adults but overactive in the dyslexic child. The precise topography of this overactivation is located a little more posterior to the zone of underactivation in the adult, suggesting a different mechanism, the former being the manifestation of a compensatory activity related to an excessive dependence, in the dyslexic child, on the motor aspects of speech known to be controlled by this cortical region.

s0065 Morphological brain studies in dyslexia

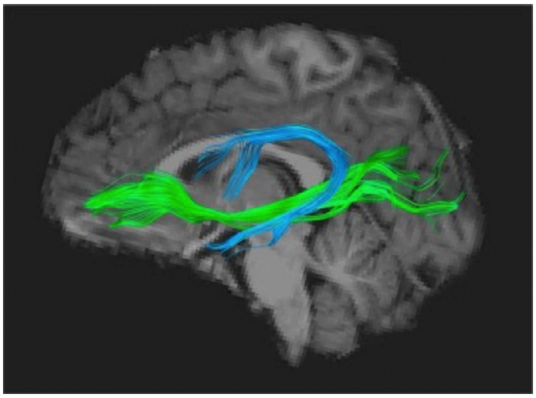
p0155 Besides these functional imaging data, the dyslexic brain also presents structural differences or atypicalities that were demonstrated with various structural imaging techniques.

p0160 Initially, the studies focused on the asymmetry of the surface anatomy of the temporal regions (for a review, see Vanderauwera et al., 2018) and the corpus callosum (Robichon and Habib, 1998). Such atypical cortical features were ascribed to developmental deviations from a standard pattern of cortical organization, namely early maturational abnormalities, most probably occurring during the migrational phase of cortical maturation (Habib and Galaburda, 1990). However, measures of regional gray matter thickness using voxel-based morphometry disclosed decreased cortex density in the same areas that reported underactivation with fMRI (Linkersdörfer et al., 2012).

p0165 These structural alterations were also found in prereader children, suggesting that these regions are already abnormally organized before any influence of learning to read (Clark et al., 2014; Kraft et al., 2015).

p0170 However, the most robust and informative studies are those reporting not cortical but subcortical abnormalities.

p0175 Using the diffusion imaging method, several groups independently found convergent evidence of impaired organization of the long white matter fascicles connecting anterior and posterior parts of the brain, chiefly in the left hemisphere. One of the mainly impaired organizations is about the arcuate fasciculus. It is a horseshoe-shaped bundle joining together the auditory areas and the posterior sensory cortex and the lower frontal regions, including Broca's area (Fig. 4.2). Several studies have shown that impaired fiber organization of this tract is a robust predictor of dyslexia, including in preschool children, and could be correlated to these children's scores on phonological tasks (Vandermosten et al., 2012; Langer et al., 2017), strongly suggesting a genetic origin rather than the influence of poor reading experience. In agreement with such a view, Wang et al. (2017) have followed longitudinally a cohort of children with and without familial history of dyslexia and demonstrated that children at familial risk of dyslexia have altered white matter microstructure of the arcuate fasciculus as well as protracted developmental trajectory between ages 5 and 12.



f0015 **Fig. 4.2.** The two main white matter tracts usually reported as abnormally organized in the dyslexic brain: arcuate fasciculus (AF, in *blue*) and inferior fronto-occipital fasciculus (IFOF, in *green*), respectively, associated with phonological and orthographic scores on standardized tests. From Vandermosten, M., Boets, B., Poelmans, H., et al., 2012. A tractography study in dyslexia: neuroanatomic correlates of orthographic, phonological and speech processing. *Brain* 135 (3), 935–948; Vandermosten M., Cuynen L., Vanderauwera J., et al., 2017. White matter pathways mediate parental effects on children's reading precursors. *Brain Lang* 173, 10–19. https://doi.org/10.1016/j.bandl.2017.05.002.

Another white matter bundle, the inferior fronto-occipital fasciculus, mostly involved in the orthographic aspects of reading, has also been repeatedly found to be miswired and could be further influenced by the level of paternal reading (Vandermosten et al., 2017). p0180

Finally, in terms of atypical hemispheric lateralization, stronger connections in right-lateralized white matter tracts, such as the superior longitudinal fasciculus, have been found in dyslexic children who showed greater improvements in reading (Hoeft et al., 2011), as well as in those children with a family history of dyslexia who went on to become nondyslexic (Vandermosten et al., 2012). These results suggest that right-lateralized white matter pathways may support an alternative or compensatory role of the right-hemisphere network in reading in children with dyslexia. p0185

In conclusion, the neuroimaging studies summarized earlier were mainly motivated by the idea that reading is a function closely related to language and refer to the widely held position that the origin of dyslexia is tightly linked to a fundamental defect in the processing of phonology by structures in the left hemisphere, which, for various—mainly genetic—reasons, are inappropriately organized, resulting in a fundamental inability for the beginner reader to start the process of reading. p0190

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

s0070 Toward alternative, nonphonological explanations of dyslexia

p0195 Exclusive phonological explanations of dyslexia are increasingly questioned with regard to the heterogeneity of the clinical presentation. Several alternative tracks have thus been explored, seeking to account for some dyslexic patients never experiencing language disorder as well as other patients combining reading impairment with other cognitive disorders.

p0200 One of the most famous theories, called the "temporal processing impairment" theory of dyslexia (Tallal and Piercy, 1973), was very successful in the mid-1990s by demonstrating that the artificial slowing of speech sounds could have a curative effect on the oral and written language deficits of these children (Tallal et al., 1996). These new insights were prompted by repeated observation that dyslexics often are poor in tasks requiring a temporal analysis such as the perception of duration (Nicolson et al., 1995), the production of ordered phonemes or letters (Rey et al., 2002), and the ability to synchronize simple movement with a beat arbitrarily given by a metronome (Wolff, 2002). However, Thomson and Goswami (2008) demonstrated that the deficit in such tempo reproduction task was proportional to reading difficulties and that it predicted better than most other variables the level of reading and spelling.

p0205 In this context, a cerebellar theory of dyslexia was proposed by Nicolson et al. (2001) as the primum movens of the wide range of clinical observations in patients. A faulty development of cerebellum functions, during early childhood, could be responsible for difficulties in the automation of learning procedures (i.e., motor engrams corresponding to phonemes) and could also clarify the frequent association of motor and writing disorders, which cannot be explained by a purely phonological theory.

p0210 There is finally a growing literature pointing to a deficit in attentional processes—mainly visual attention—compromising the early stages of learning to read (Lobier et al., 2014; Ruffino et al., 2014). It has even been shown that the children's scores on visuospatial attention tasks performed in the prereading period predicted their reading performance 3 years later (Franceschini et al., 2012).

s0075 Impaired cross-modal integration: A new direction with multiple applications

p0215 A theory was developed based on research focused on the incapacity of the dyslexic patient to achieve reciprocal mapping of different types of stimuli, such as the visual image of a letter (grapheme) and its sound correspondent (phoneme) depending on cross-modal integration mechanisms.

This theoretical background relies on studies using MRI during various perception tasks (Blau et al., 2009): auditory alone (sound), visual alone (letter), and two-letter/sound conditions—either congruous (the sound and the letter correspond) or incongruous. p0220

The associative auditory cortex was specifically involved in these tasks and its activation was defective in dyslexics in all tasks except for incongruous pairs, where controls had less activation than dyslexics, reflecting the inability of the latters' associative system to process the incongruence of letter/sound correspondence. This physiologic phenomenon, which occurs in the majority of subjects, is reminiscent of the famous "Mac Gurk effect." It happens when an erroneous visual feedback (video clip of the face of a person pronouncing "ga" while listening to the syllable "ba") induces an auditory illusion where the subject hears a third syllable (da) corresponding to the fusion of the two consonants into a third. Dyslexic individuals, on the contrary, do not experience the fusion (Hayes et al., 2003) and thus will answer having heard either "ba" (the syllable actually pronounced) or "ga" (the syllable recorded visually on the video). p0225

A Swiss group (van der Mark et al., 2011) likewise investigated the connectivity between the VWFA and various cortical areas, using fMRI during an orthographic task. The researchers showed that dyslexics fail to activate Broca's area in response to the activation of the VWFA, realizing an authentic functional disconnection. These findings were corroborated by a study (Boets et al., 2013) using the combination of three MRI methods in adult dyslexics, which demonstrated the integrity of the representation of each individual phoneme. Dyslexia is therefore viewed as a specific failure of the left inferior frontal region (Broca's area) to use otherwise intact information from phonemes stored in the temporal cortex, thus realizing a sort of decoupling between phonemic perception and phonological production. Converging results were obtained by magnetoencephalography in a study exploring the coherence of neural oscillations between different brain regions: there were inadequate connections in dyslexia between the right auditory cortex and left Broca's area. This could be directly involved in the production of the phonological disorder due to a lack of phase coherence between the low frequency of auditory stimuli (1–5 Hz) and the corresponding Delta band oscillatory activity (0.5–1 Hz) of the brain (Molinaro et al., 2016). p0230

These findings are in agreement with the repeated observations of a weak capacity of adults as well as children with dyslexia to perform a motor gesture in synchrony or in prediction of a regular sound, that is to say, to adapt the oscillatory activity of the neuronal circuits to the rhythmicity of an external stimulus, whether p0235

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

it is the beat of a metronome or the temporal frequency of a speech signal. There is even some degree of proportionality between the difficulties experienced by dyslexics in this type of task and their performance in reading (Flaugnacco et al., 2014). Finally, a relationship between the rhythmic perception abilities of 6-year-olds and their performance at syntactic tasks was demonstrated; this suggests a strong link between the oscillatory activity of the language cortical areas and the linguistic function itself (Gordon et al., 2015). As we shall see in the next section, therapeutic applications of these concepts have begun to be tested, with encouraging results (Slater et al., 2013; Bedoin et al., 2016).

s0080 THERAPEUTIC CONSIDERATIONS

p0240 To conclude this chapter, we shall consider briefly the vast literature about dyslexia therapy by deliberately focusing our purpose on scientifically robust results, mainly those obtained by using imaging methods as a probe of therapy efficacy.

s0085 The "classical" phonological approach

p0245 As previously pointed out, the hitherto dominant position that dyslexia is almost exclusively due to altered phonological brain mechanisms has motivated a great majority of works. The effectiveness of phonological training in improving reading in general has been tested in a variety of settings, mostly educational ones: prevention in at risk children in kindergarten, early intervention at the beginning of learning for students identified as at risk, in poor readers of various ages, from primary to secondary school, or in students with severe dyslexia using more intensive training (Torgesen, 2001). Results have been reviewed in several seminal papers, such as those of Ehri et al. (2001) or Vellutino et al. (2004), reaching the similar conclusion that so-called phonic intervention, coupling phonological awareness exercises and training of grapho-phonemic correspondence, is the "gold standard" of dyslexia therapy. In France, as in most European countries, this kind of intervention is typically carried out either by teachers, with variable levels of specialization, or by speech therapists or "logopedists."

p0250 Neuroimaging studies have largely confirmed such efficacy, mainly showing changes in brain activation between pre- and postintervention scans.

p0255 A meta-analysis (Ylinen and Kujala, 2015) combined the results of almost 20 functional and structural studies that address the main consequences of dyslexia training. Two-thirds of the studies have used functional MRI while only two used morphological MRI and the others exploited electrophysiologic methods, mainly evoked response potentials. The training methods were mainly based on phonological training and grapho-phonemic exercises (but some used specific procedures, such as FastForword (Temple et al., 2003), or nonverbal audio-visual integration). The duration of training was quite variable, mostly around 8 weeks. The improvements observed were generally reported in both clinical and neurofunctional measures, more rarely morphological changes.

In one such study (Krafnick et al., 2011), 8 weeks of p0260
intervention yielded an increase in volume of left fusiform gyrus and precuneus, bilateral hippocampus, and right cerebellum, while these structures remained unchanged for a period of 8 weeks following the end the training period.

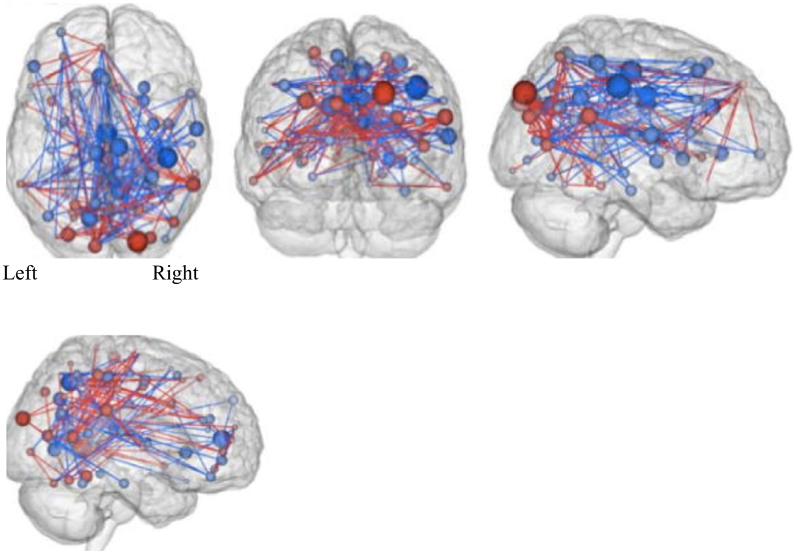
The effects of attention and executive function remediations on dyslexia s0090

Resting state fMRI, which measures the degree of p0265
functional connectivity between different brain regions at rest, has shown in one study (Fig. 4.3) that the dyslexic brain, during the learning period, has atypical connectivity within visual circuits (Finn et al., 2014).

The effect of training on this connectivity was studied p0270
by Koyama et al. (2013) in two regions of interest: the VWFA and the intraparietal sulcus in three groups of 12-year-old dyslexic children according to whether they were trained only in reading, were trained in reading and spelling, or received no remediation. They found weaker functional connectivity in the three groups of dyslexics compared with controls between the intraparietal sulcus and the left middle frontal cortex, suggesting a major role of attention deficit common to dyslexics regardless of their training status. However, those who had undergone rehabilitation, either partial or complete, had a greater increase of connectivity between the right occipital cortex and the left temporooccipital region but a decreased connectivity between this same visual region and the right middle prefrontal cortex, which the authors interpret as two different manifestations of compensation induced by rehabilitation.

Another resting-state fMRI study (Horowitz-Kraus p0275
et al., 2015) has measured connectivity in dyslexic children who had benefited from a particular treatment that was supposed to stimulate executive processes, called the "Reading Acceleration Program" (RAP); this is a computer program designed to improve fluency in reading by forcing subjects to gradually improve their word decoding speed, with proven positive consequences on fluency and reading comprehension. This training is supposed to involve remediation of executive functions since it is based on the improvement of error detection capabilities during reading, attributed to the activity of the cingulate region. The authors

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004



f0020 **Fig. 4.3.** Study of connectivity using resting MRI in dyslexics (children, top three images; adult, bottom image). In *blue*, the stronger connections in dyslexics than in normal readers. In *red*, the stronger connections in controls. Connections are deficient between the visual regions and the frontal (in particular, left) attentional networks in dyslexic children, and abnormally persistent with the anterior language region in adults (Finn et al., 2014; ref. 92).

demonstrated that, compared with normal readers, children with dyslexia (average age 10 years) who also had significant impairment in several domains of executive functions (Wisconsin test, flexibility, Stroop test, etc.) show a pretraining functional connectivity defect in the pathway connecting the cingulate gyrus to the frontal opercular regions. This defect was moreover normalized after a training of 20 sessions, spread over 4 weeks, 5 days a week (Fig. 4.4). In addition, the improvement in reading was proportional to the improvement in executive functions, particularly tasks of sustained attention.

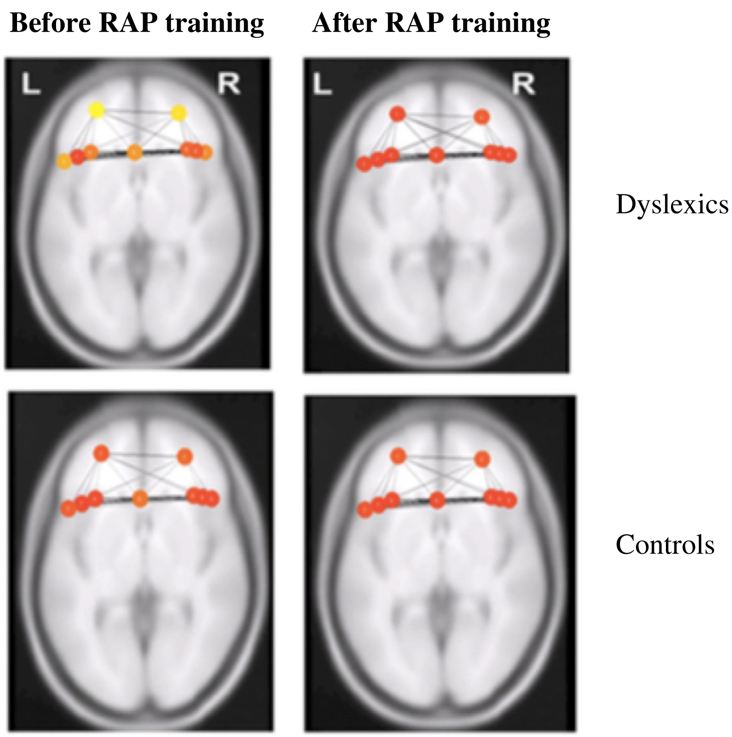
p0280 Finally, a particularly intriguing result has been obtained in a study by Heim et al. (2015) comparing three different kinds of training centered on phonology, reading, or attention. The authors divided the dyslexic children in their study into three groups according to their cognitive profiles and assigned them semirandomly to a type of training. Whatever the type of training, the three groups of dyslexics improved their reading abilities in a similar manner with an increased posttraining activity in the VWFA on functional MRI during a reading task (Fig. 4.5). The three groups of patients also experienced an increased activation in the same left Broca's area during a classical computerized visual attention paradigm. By contrast, other regions of the cortex were activated differently depending on the group. Dyslexics trained in reading and phonology increased their activity in both parietal cortices, while those who had benefited from attention training increased their activity in the left superior temporal cortex. Thus, this work demonstrates that different types of training can have a global or more specific effects on some neurocognitive mechanisms; however, only clinical analysis of improvements would not be enough to establish the effects.

To summarize, the earlier-reported neuroimaging p0285
studies of the effect of training in dyslexia collectively challenge the traditional view of almost exclusive phonological explanations of dyslexia. The most robust effects observed are linked to the attentional component of the training methods, whatever the method employed. This nonspecific effect is surprising and strongly encouraged for future research to explore new avenues using more transversal intervention tools, rather than focusing on a restricted area such as phonology. One of these is the use of musical training as structured intervention to prevent or remediate reading disorders.

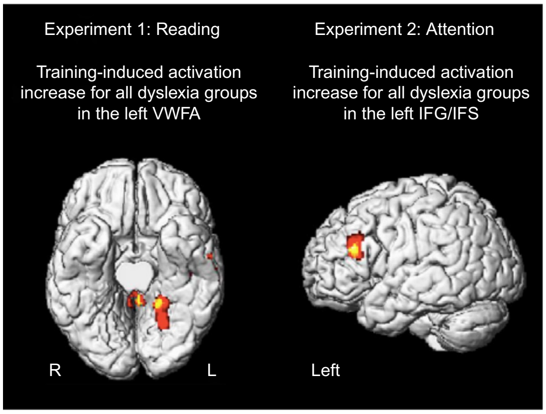
EPILOG: MUSIC TRAINING AS A TOOL FOR THE REMEDIATION OF DYSLEXIA s0095

At least two studies have shown that dyslexic musicians p0290
perform better than dyslexic nonmusicians on phonological and reading tasks and even than nondyslexic controls on certain rhythmic tasks (Bishop-Liebler et al., 2014; Weiss et al., 2014). Difficulties in processing temporal information, such as reproducing a tempo or a rhythm, have been found repeatedly in dyslexic children (Goswami et al., 2013), which could contribute to difficulties in acquiring phonological awareness by altering the perception of the syllabic segmentation of speech.

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004



f0025 **Fig. 4.4.** Normalization of resting-state functional connectivity in dyslexic children, compared with normal readers, after 4 weeks of intensive RAP (rapid reading training called the "Reading Acceleration Program"). Improved frontal cingulo-opercular connectivity. From Horowitz-Kraus T., DiFrancesco M., Kay B., et al., 2015. Increased resting-state functional connectivity of visual- and cognitive-control brain networks after training in children with reading difficulties. *Neuroimage Clin* 8, 619–630.



f0030 **Fig. 4.5.** Three groups of dyslexics, each receiving a different training, either phonological, reading, or attentional, reactivate the same areas after training—the VWFA during a reading task and the left Broca's area during a visual attention task. From Heim, S., Pape-Neumann, J., van Ermingen-Marbach, M., et al., 2015. Shared vs. specific brain activation changes in dyslexia after training of phonology, attention, or reading. *Brain Struct Funct* 220, 2191–2207.

p0295 An additional argument is provided by the demonstration in adult professional musicians of a measurable effect of the practice of music and singing on the anatomy of the arcuate fasciculus, which is of considerable magnitude (up to one and a half times the size of the structure in nonmusician controls: Halwani et al., 2011). As described earlier, the arcuate fasciculus is the most consistently impaired white matter bundle in dyslexic subjects, likely compromising the connectivity between areas whose interaction is crucial to ensure such basic processes as learning to read. In our group, we hypothesized that an intensive training requiring an intermodal integration would have the best chance of improving variables supposed to reflect dysfunction in dyslexics (Habib and Commeiras, 2014). In collaboration with the laboratory headed by Dr. Mireille Besson, at CNRS Marseille, we developed innovative remediation based on repeated and synchronous tasks associating auditory and visual stimulations and motor actions (such as playing the keyboard, performing rhythmic movements of the body, or dancing) to complement more traditional speech-therapy approaches. The results are promising (Habib et al., 2016), prompting us to use music and rhythm in clinical settings and advocating a more widespread use of music in schools to prevent dyslexia.

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

References

American Psychiatric Association (2013). DSM-5®. Diagnostic and Statistical Manual of Mental Disorders, fifth edn American Psychiatric Association, Washington, DC.

Becker J, Czamara D, Scerri TS et al. (2014). Genetic analysis of dyslexia candidate genes in the European cross-linguistic NeuroDys cohort. Eur J Hum Genet 22: 675–680.

Bedoin N, Brisseau L, Molinier P et al. (2016). Temporally regular musical primes facilitate subsequent syntax processing in children with specific language impairment. Front Neurosci 10: 245.

Bishop-Liebler P, Welch G, Huss M et al. (2014). Auditory temporal processing skills in musicians with dyslexia. Dyslexia 20: 261–279.

Blau V, Van Atteveldt N, Ekkebus M et al. (2009). Reduced neural integration of letters and speech sounds links phonological and reading deficits in adult dyslexia. Curr Biol 19: 503–508.

Boets B, Op de Beeck HP, Vandermosten M et al. (2013). Intact but less accessible representations in adults with dyslexia. Science 342: 1251–1254.

Butterworth B (2005). The development of arithmetical abilities. J Child Psychol Psychiatry 46: 3–18.

Cao F, Yan X, Wang Z et al. (2017). Neural signatures of phonological deficits in Chinese developmental dyslexia. Neuroimage 146: 301–311.

Castro-Caldas A, Petersson KM, Reis A et al. (1998). The illiterate brain. Learning to read and write during childhood influences the functional organization of the adult brain. Brain 121: 1053–1063.

Clark KA, Helland T, Specht K et al. (2014). Neuroanatomical precursors of dyslexia identified from pre-reading through to age 11. Brain 137: 3136–3141.

Demonet JF, Taylor MJ, Chaix Y (2004). Developmental dyslexia. Lancet 363: 1451–1460.

Ehri, L.C., Nunes, S.R, Willows, D.M., Schuster, D.M., Yaghoub-Zadeh, Z., & Shanahan, T. (2001). Phonemic awareness instruction helps children learn to read: evidence from the National Reading Panel's meta-analysis. Read Res Q, 36, 250–287.

Eicher JD, Gruen JR (2013). Imaging-genetics in dyslexia: connecting risk genetic variants to brain neuroimaging and ultimately to reading impairments. Mol Genet Metab 110: 201–212.

Finn ES, Shen X, Holahan JM et al. (2014). Disruption of functional networks in dyslexia: a whole-brain, data-driven analysis of connectivity. Biol Psychiatry 76: 397–404.

Flaugnacco E, Lopez L, Terribili C et al. (2014). Rhythm perception and production predict reading abilities in developmental dyslexia. Front Hum Neurosci 4: 392.

Fluss J, Bertrand D, Ziegler J et al. (2009). Troubles d'apprentissage de la lecture: rôle des facteurs cognitifs, comportementaux et socio-économiques. Dévelopments 1: 21–33.

Franceschini S, Gori S, Ruffino M et al. (2012). A causal link between visual spatial attention and reading acquisition. Curr Biol 22: 814–819.

Gordon RL, Shivers CM, Wieland EA et al. (2015). Musical rhythm discrimination explains individual differences in grammar skills in children. Dev Sci 18: 635–644. https://doi.org/10.1111/desc.12230.

Goswami U, Huss M, Mead N et al. (2013). Perception of patterns of musical beat distribution in phonological developmental dyslexia: significant longitudinal relations with word reading and reading comprehension. Cortex 49: 1363–1376.

Gross-Tsur V, Manor O, Shalev RS (1996). Developmental dyscalculia: prevalence and demographic features. Dev Med Child Neurol 38: 25–33.

Habib M, Commeiras C (2014). "Mélodys": Remédiation cognitivo-musicale des troubles de l'apprentissage, DeBoeck, Paris.

Habib M, Galaburda AM (1990). Intrauterine factors and sinistrality: a review. In: S Coren (Ed.), Left-handedness: behavioral implications and anomalies. Elsevier (North Holland Book Series), New York.

Habib M, Lardy C, Desiles T et al. (2016). Music and dyslexia: a new musical training method to improve reading and related disorders. Front Psychol 7: 26.

Halwani GF, Loui P, Rüber T et al. (2011). Effects of practice and experience on the arcuate fasciculus: comparing singers, instrumentalists, and non-musicians. Front Psychol 2: 156.

Hayes E, Tiippana K, Nicol T et al. (2003). Integration of heard and seen speech: a factor in learning disabilities in children. Neurosci Lett 351: 46–50.

Hecht SA, Burgess SR, Torgesen JK et al. (2000). Explaining social class differences in growth of reading skills from beginning kindergarten through fourth-grade: the role of phonological awareness, rate of access, and print knowledge. Read Writ 12: 99–127.

Heim S, Pape-Neumann J, van Ermingen-Marbach M et al. (2015). Shared vs. specific brain activation changes in dyslexia after training of phonology, attention, or reading. Brain Struct Funct 220: 2191–2207.

Hoeft F, McCandliss BD, Black JM et al. (2011). Neural systems predicting long-term outcome in dyslexia. Proc Natl Acad Sci U S A 108: 361–366.

Horowitz-Kraus T, DiFrancesco M, Kay B et al. (2015). Increased resting-state functional connectivity of visual- and cognitive-control brain networks after training in children with reading difficulties. Neuroimage Clin 8: 619–630.

Koyama MS, Di Martino A, Kelly C et al. (2013). Cortical signatures of dyslexia and remediation: an intrinsic functional connectivity approach. PLoS One 8: e55454.

Krafnick AJ, Flowers DL, Napoliello EM et al. (2011). Gray matter volume changes following reading intervention in dyslexic children. Neuroimage 57: 733–741.

Kraft I, Cafiero R, Schaadt G et al. (2015). Cortical differences in preliterate children at familiar risk of dyslexia are similar to those observed in dyslexic readers. Brain 138: e378.

Landerl K, Wimmer H, Frith U (1997). The impact of orthographic consistency on dyslexia: a German-English comparison. Cognition 63: 315–334.

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

Landerl K, Bevan A, Butterworth B (2004). Developmental dyscalculia and basic numerical capacities: a study of 8-9-year-old students. Cognition 93: 99–125.

Langer N, Peysakhovich B, Zuk J et al. (2017). White matter alterations in infants at risk for developmental dyslexia. Cereb Cortex 27: 1027–1036. https://doi.org/10.1093/cercor/bhv281.

Lewis C, Hitch GJ, Walker P (1994). The prevalence of specific arithmetic difficulties and specific reading difficulties in 9- to 10-year-old boys and girls. J Child Psychol Psychiatry 35: 283–292.

Linkersdörfer J, Lonnemann J, Lindberg S et al. (2012). Gray matter alterations co-localize with functional abnormalities in developmental dyslexia: an ALE meta-analysis. PLoS One 7: e43122. https://doi.org/10.1371/journal.pone.0043122.

Llinas R (1993). Is dyslexia a dyschronia? Ann N Y Acad Sci 682: 48–56.

Lobier MA, Peyrin C, Pichat C et al. (2014). Visual processing of multiple elements in the dyslexic brain: evidence for a superior parietal dysfunction. Front Hum Neurosci 8: 479.

Logan JAR, Cutting L, Schatschneider C et al. (2013). Reading development in young children: genetic and environmental influence. Child Dev 84: 2131–2144.

Mascheretti S, De Luca A, Trezzi V et al. (2017). Neurogenetics of developmental dyslexia: from genes to behavior through brain neuroimaging and cognitive and sensorial mechanisms. Transl Psychiatry 7: e987.

Molinaro N, Lizarazu M, Lallier M et al. (2016). Out-of-synchrony speech entrainment in developmental dyslexia. Hum Brain Mapp 37: 2767–2783.

Moll K, Göbel SM, Gooch D et al. (2016). Cognitive risk factors for specific learning disorder: processing speed, temporal processing, and working memory. J Learn Disabil 49: 272–281.

Nicolson RI, Fawcett AJ, Dean P (1995). Time estimation deficits in developmental dyslexia: evidence of cerebellar involvment. Proc R Soc Lond B Biol Sci 259: 43–47.

Nicolson RI, Fawcett AJ, Dean P (2001). Developmental dyslexia: the cerebellar deficit hypothesis. Trends Neurosci 24: 508–511.

Norton ES, Beach SD, Gabrieli JD (2014). Neurobiology of dyslexia. Curr Opin Neurobiol 30C: 73–78.

Peterson RL, Pennington BF (2015). Developmental dyslexia. Annu Rev Clin Psychol 11: 283–307.

Peyrin, C., Lallier, M., & Valdois, S. (2008). Visual attention span brain mechanisms in normal and dyslexic readers. Baciu M, éds. Neuropsychology and cognition of language behavioural, neuropsychological and neuroimaging studies of spoken and written language. Kerala: Research Signpost, 22-43.

Powers SJ, Wang Y, Beach SD et al. (2016). Examining the relationship between home literacy environment and neural correlates of phonological processing in beginning readers with and without a familial risk for dyslexia: an fMRI study. Ann Dyslexia 66: 337–360.

Raddatz J, Kuhn JT, Holling H et al. (2017). Comorbidity of arithmetic and reading disorder. J Learn Disabil 50: 298–308.

Raschle NM, Chang M, Gaab N (2010). Structural brain alterations associated with dyslexia predate reading onset. Neuroimage 57: 742–749.

Rey V, De Martino S, Espesser R et al. (2002). Temporal processing and phonological impairment in dyslexia. Effect of phoneme lengthening on order judgement of two consonants. Brain Lang 80: 576–591.

Richlan F, Kronbichler M, Wimmer H (2009). Functional abnormalities in the dyslexic brain: a quantitative meta-analysis of neuroimaging studies. Hum Brain Mapp 30: 3299–3308.

Richlan F, Kronbichler M, Wimmer H (2011). Meta-analyzing brain dysfunctions in dyslexic children and adults. Neuroimage 56: 1735–1742.

Robichon F, Habib M (1998). Abnormal callosal dyslexics: relationships to handedness and phonological abilities. Brain Lang 62: 127–146.

Romeo RR, Christodoulou JA, Halverson KK et al. (2017). Socioeconomic status and reading disability: neuroanatomy and plasticity in response to intervention. Cereb Cortex 7: 1–16. https://doi.org/10.1093/cercor/bhx131.

Rourke BP (1993). Arithmetic disabilities, specific and otherwise. A neuropsychological perspective. J Learn Disabil 26: 214–226.

Roux S, McKeeff TJ, Grosjacques G et al. (2013). The interaction between central and peripheral processes in handwriting production. Cognition 127: 235–241.

Ruffino M, Gori S, Boccardi D et al. (2014). Spatial and temporal attention in developmental dyslexia. Front Hum Neurosci 8: 331.

Seymour PH, Aro M, Erskine JM (2003). Foundation literacy acquisition in European orthographies. Br J Psychol 94: 143–174.

Shalev RS, Manor O, Gross-Tsur V (1997). Neuropsychological aspects of developmental dyscalculia. Math Cogn 3: 105–120.

Siok WT, Perfetti CA, Jin Z et al. (2004). Biological abnormality of impaired reading is constrained by culture. Nature 431: 71–76.

Slater J, Tierney A, Kraus N (2013). At-risk elementary school children with one year of classroom music instruction are better at keeping a beat. PLoS One 8: e77250.

Snowling M, Bishop DV, Stothard SE (2000). Is preschool language impairment a risk factor for dyslexia in adolescence? J Child Psychol Psychiatry 41: 587–600.

Taipale M, Kaminen N, Nopola-Hemmi J et al. (2003). A candidate gene for developmental dyslexia encodes a nuclear tetratricopeptide repeat domain protein dynamically regulated in brain. Proc Natl Acad Sci U S A 100: 11553–11558.

Tallal P, Piercy M (1973). Defects of non-verbal auditory perception in children with developmental aphasia. Nature 241: 468–469.

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004

Tallal P, Miller SL, Bedi G et al. (1996). Language comprehension in language-learning impaired children improved with acoustically modified speech. Science 271: 81–83.

Temple E, Deutsch GK, Poldrack RA et al. (2003). Neural deficits in children with dyslexia ameliorated by behavioral remediation: evidence from functional MRI. Proc Natl Acad Sci U S A 100: 2860–2865.

Thomson JM, Goswami U (2008). Rhythmic processing in children with developmental dyslexia: auditory and motor rhythms link to reading and spelling. J Physiol 102: 120–129.

Torgesen JK (2001). The theory and practice of intervention: comparing outcomes from prevention and remediation studies. In: AJ Fawcett (Ed.), Dyslexia: Theory and Good Practice. Whurr Publications, London, pp. 185–202.

Turkeltaub PE, Gareau L, Flowers DL et al. (2003). Development of neural mechanisms for reading. Nat Neurosci 6: 767–773.

Valdois S, Bosse ML, Ans B et al. (2003). Phonological and visual processing deficits can dissociate in developmental dyslexia: evidence from two case studies. Read Writ 16: 541–572.

van der Mark S, Klaver P, Bucher K et al. (2011). The left occipitotemporal system in reading: disruption of focal fMRI connectivity to left inferior frontal and inferior parietal language areas in children with dyslexia. Neuroimage 54: 2426–2436.

Vanderauwera J, Altarelli I, Vandermosten M et al. (2018). Atypical structural asymmetry of the temporary planum is related to family history of dyslexia. Cereb Cortex 28: 63–72.

Vandermosten M, Boets B, Poelmans H et al. (2012). A tractography study in dyslexia: neuroanatomic correlates of orthographic, phonological and speech processing. Brain 135: 935–948.

Vandermosten M, Cuynen L, Vanderauwera J et al. (2017). White matter pathways mediate parental effects on children's reading precursors. Brain Lang 173: 10–19. https://doi.org/10.1016/j.bandl.2017.05.002.

Vellutino FR, Fletcher JM, Snowling MJ et al. (2004). Specific reading disability (dyslexia): what have we learned in the past four decades? J Child Psychol Psychiatry 45: 2–40.

Wang Y, Paramasivam M, Thomas A et al. (2006). DYX1C1 functions in neuronal migration in developing neocortex. Neuroscience 143: 515–522.

Wang Y, Mauer MV, Raney T et al. (2017). Development of tract-specific white matter pathways during early reading development in at-risk children and typical controls. Cereb Cortex 27: 2469–2485.

Weiss AH, Granot RY, Ahissar M (2014). The enigma of dyslexic musicians. Neuropsychologia 54: 28–40.

Willcutt EG, Petrill SA, Wu S et al. (2013). Comorbidity between reading disability and math disability: concurrent psychopathology, functional impairment, and neuropsychological functioning. J Learn Disabil 46: 500–516.

Wolff PH (2002). Timing precision and rhythm in developmental dyslexia. Read Writ 15: 179–206.

Xia Z, Hancock R, Hoeft F (2017). Neurobiological bases of reading disorder part I: etiological investigations. Lang Ling Compass 11: e12239.

Ylinen S, Kujala T (2015). Neuroscience illuminating the influence of auditory or phonological intervention on language-related deficits. Front Psychol 6: 137.

Ziegler JC, Perry C, Ma-Wyatt A et al. (2003). Developmental dyslexia in different languages: language-specific or universal? J Exp Child Psychol 86: 169–193.

Ziegler JC, Bertrand D, Toth D et al. (2010). Orthographic depth and its impact on universal predictors of reading: a cross-language investigation. Psychol Sci 21: 551–559.

ISBN: 978-0-444-64148-9; PII: B978-0-444-64148-9.00004-1; Author: M. Habib; 00004