



# Recent update on reading disability (dyslexia) focused on neurobiology

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Reading disability (dyslexia) refers to an unexpected difficulty with reading for an individual who has the intelligence to be a much better reader. Dyslexia is most commonly caused by a difficulty in phonological processing (the appreciation of the individual sounds of spoken language), which affects the ability of an individual to speak, read, and spell. In this paper, I describe reading disabilities by focusing on their underlying neurobiological mechanisms. Neurobiological studies using functional brain imaging have uncovered the reading pathways, brain regions involved in reading, and neurobiological abnormalities of dyslexia. The reading pathway is in the order of visual analysis, letter recognition, word recognition, meaning (semantics), phonological processing, and speech production. According to functional neuroimaging studies, the important areas of the brain related to reading include the inferior frontal cortex (Broca's area), the midtemporal lobe region, the inferior parieto-temporal area, and the left occipitotemporal region (visual word form area). Interventions for dyslexia can affect reading ability by causing changes in brain function and structure. An accurate diagnosis and timely specialized intervention are important in children with dyslexia. In cases in which national infant development screening tests have been conducted, as in Korea, if language developmental delay and early predictors of dyslexia are detected, careful observation of the progression to dyslexia and early intervention should be made.

**Key words:** Learning disability, Neurobiology, Reading disability (dyslexia)

## Key message

- Neurobiological studies using functional brain imaging have uncovered the reading pathways, brain regions involved in reading, and neurobiological abnormalities of dyslexia.
- An accurate diagnosis and timely specialized intervention are important in children with dyslexia. When national infant development screening tests have been conducted as in Korea, if a language developmental delay and early predictors of dyslexia are detected, the progression to dyslexia should be carefully observed and early intervention provided.

## Introduction

According to the American Individuals with Disabilities Education Act (IDEA),<sup>1)</sup> a specific learning disability, which includes a reading disability, refers to a disorder in one or more of the basic psychological processes involved in understanding or using spoken or written language. It may manifest as an impaired ability to listen, think, speak, read, write, spell, or perform mathematical calculations. This includes conditions such as perceptual disabilities, brain injury, minimal brain dysfunction, dyslexia, and developmental aphasia. Specific learning disabilities exclude learning problems that are primarily the result of the visual, hearing, or motor disabilities, intellectual disability, emotional disturbance, or environmental, cultural, or economic disadvantages. In the Diagnostic and Statistical Manual of Mental Disorders-5,<sup>2)</sup> learning disabilities are classified as impairments in reading, written expression, and mathematics, and 80% of learning disabilities are related to reading disabilities.

In this paper, I describe reading disability by focusing on the underlying neurobiological mechanisms and the importance of early diagnosis in children. In 1877, Adolph Kussmaul reported that, while some patients had no problems with sight, intelligence, or speaking ability, they were unable to read the text.<sup>3)</sup> In 1887, German physician Rudolf Berlin first used the term dyslexia in his research.<sup>4)</sup> The most current definition of dyslexia is codified by U.S. Federal law as follows: "The term dyslexia means an unexpected difficulty in reading for an individual who has the intelligence to be a much better reader, most commonly caused by a difficulty in the phonological processing (the appreciation of the individual sounds of spoken language), which affects the ability of an individual to speak, read, and spell."<sup>5)</sup>

The etiology of dyslexia is familial, occurring in 50% of children who have a parent with dyslexia and in 50% of the siblings of dyslexic persons.<sup>5)</sup> Dyslexia is best explained by the differences in multiple genes, each contributing a small amount to its expression.

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Received: 9 September, 2020, Revised: 6 January, 2021, Accepted: 21 January, 2021

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According to LaBuda and DeFries,<sup>6</sup> the reading limitations of twins with reading disabilities are attributed to the following factors: 40% genetics, 35% shared environmental factors (socio-economic status, parents' reading ability, education method), and 25% to unique environmental factors. The genes that are reportedly most related to dyslexia are DCDC2 (doublecortin domain-containing protein 2) and KIAA0319. The DYX1-9 (dyslexia susceptibility 1-9) and ROBO1 (roundabout 1) genes are also known to be related.<sup>7</sup>

## Neurobiology

### 1. Reading pathway

To understand a written word, it is necessary to look at and interpret it (i.e., the process of extracting meaning from meaning memory) and be able to look at it and read it aloud (i.e., the process of converting it into words, phonological mediation). The process of converting text into words is a model of an independent but interactive dual-pathway system (Fig. 1).

Individuals with dyslexia have difficulty converting spoken words into segmented, smaller elemental units of sound (phonemes). This process is essential for reading because it requires the ability to link the lexicon (visual word) or printed symbols to sounds.

Increasing evidence indicates that disruption of attention mechanisms may also play an important role in reading difficulties.<sup>5</sup> For this reason, many patients with attention-deficit hyperactivity disorder (ADHD) who visited the pediatric neurodevelopmental clinic were also diagnosed with dyslexia.

### 2. Classification

Dyslexia can be classified according to the location of each problem along the reading path (Fig. 1). First, it can be categorized into peripheral dyslexia and central dyslexia. Peripheral

dyslexia refers to a reading disorder that presents as an impaired visual analysis of the word form, and central dyslexia refers to a deficit in the process following visual analysis such as semantic access or phonological mediation. Peripheral dyslexia may present as an inability to distinguish the direction of a sign, such as an arrow pointing left or right.

Central dyslexia can be classified into superficial dyslexia, phonological dyslexia, and deep dyslexia. Superficial dyslexia refers to reading by phoneme-grapheme conversion due to damage to the semantic or visual vocabulary pathway within the reading pathway. During the reading process, nonwords, regular words, or high-frequency words can be read accurately, whereas low-frequency irregular words are prone to errors. Phonological dyslexia uses the semantic pathway because of a faulty phonological pathway. In phonological dyslexia, real words can be read better than nonwords, and nonwords are read as similar real words. Deep dyslexia is characterized by a problematic semantic system and phonological pathway. In this case, real words are read better than nonwords, and reading actual words can also show semantic errors, for example, reading "cat" as "dog."

### 3. Functional neuroimaging research and major brain areas related to reading

Functional brain imaging in both children and adults with dyslexia demonstrates inefficient functioning of the posterior brain systems of the left hemisphere, a pattern referred to as the neural signature of dyslexia.<sup>8</sup> Shaywitz et al.<sup>8</sup> used functional magnetic resonance imaging (fMRI) to study this effect by conducting a tapping task phonological analysis. They found significantly greater activation in posterior reading systems in typical readers than in readers with dyslexia. Readers with dyslexia compensate by developing anterior systems bilaterally, and the right homolog of the left visual word form area (VWFA) enables accurate reading, but it does not support fluent or rapid

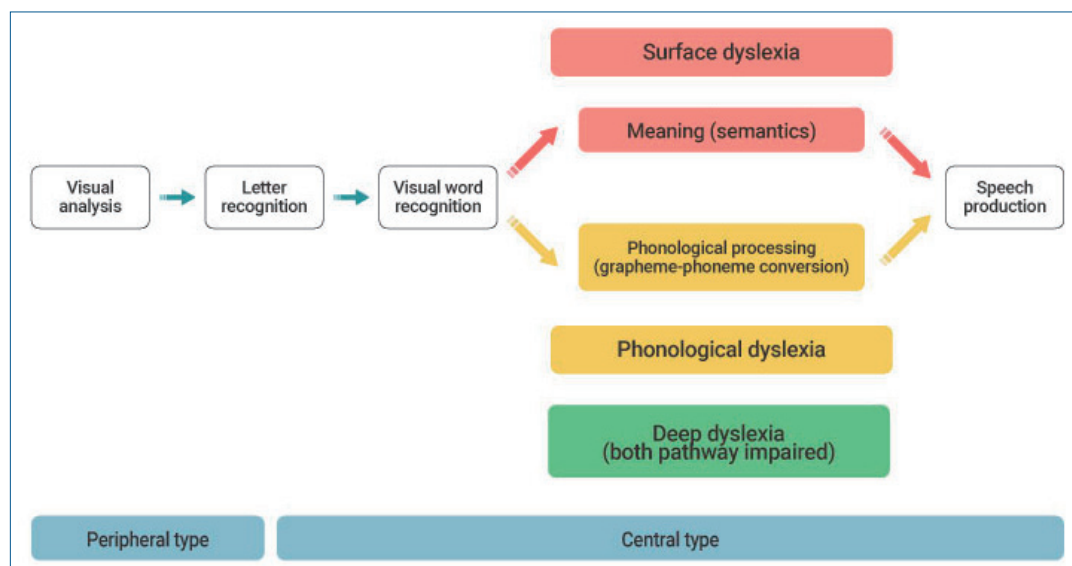


Fig. 1. Reading pathway of dual-route model and subsequent classification of dyslexia.

reading.<sup>9)</sup>

According to functional neuroimaging studies, the important areas of the brain related to reading include the left occipital-temporal region (VWFA), the inferior frontal cortex (Broca's area), the midtemporal lobe region, and the inferior parietotemporal area (Fig. 2).<sup>8)</sup>

1) Inferior frontal lobe (Broca's area)

When reading irregular low-frequency words, Broca's area displays more activation on fMRI, which plays an important role in grapheme-phoneme conversion.<sup>10,11)</sup> It is also thought that blood oxygen level-dependent activation reflects increased meaning processing.<sup>12)</sup> Heim et al. suggested that both functions for reading are interrelated and that the Brodmann area 45 is related to meaning retrieval, while BA44 is related to grapheme-phoneme conversion.<sup>11,13)</sup>

2) Inferior parietotemporal lobe

The inferior parietotemporal lobe consists of 2 anatomical regions: the supramarginal gyrus adjacent to the superior temporal lobe and the angular gyrus. The supramarginal gyrus is related to Wernicke's area (phonological processing), while the angular gyrus is related to the process of combining verbal working memory and semantic concepts or meaning.<sup>14,15)</sup> In particular, it has been suggested that the left supramarginal gyrus is related to grapheme-phoneme conversion. When excitatory

transcranial magnetic stimulation (TMS) was applied to this area, nonword reading was promoted, and inhibitory TMS interfered with the phonological process for visually presented words.<sup>16,17)</sup>

3) Anterior, middle temporal lobe

This area is mainly associated with semantic memory. In reading, these areas are related to the semantic pathway (converting letters to phonemes through meaning).<sup>18)</sup> In fMRI studies, they show more activation in semantics relative to phonological processing of written words.<sup>18)</sup> Patients with semantic memory loss-type dementia and superficial dyslexia show damage to this area.<sup>19)</sup>

4) Left occipitotemporal sulcus

The VWFA is a functional area of the left fusiform gyrus and surrounding cortex that is involved in identifying words and letters.<sup>20)</sup> This area is essential to a rapid reading ability because it enhances the perception of words by becoming specifically tuned to recognizing the recurring properties of a writing system.<sup>20)</sup> VWFA impairment causes pure alexia, a selective deficit in word recognition.<sup>21)</sup>

These 4 brain regions are systematically connected to perform reading. Phonological processing, a key matter in dyslexia, is related to the inferior parietotemporal area. The anterior, middle temporal lobe, and inferior frontal lobe are responsible for understanding reading meaning, while the left occipitotemporal area (VWFA) is involved in fast reading.

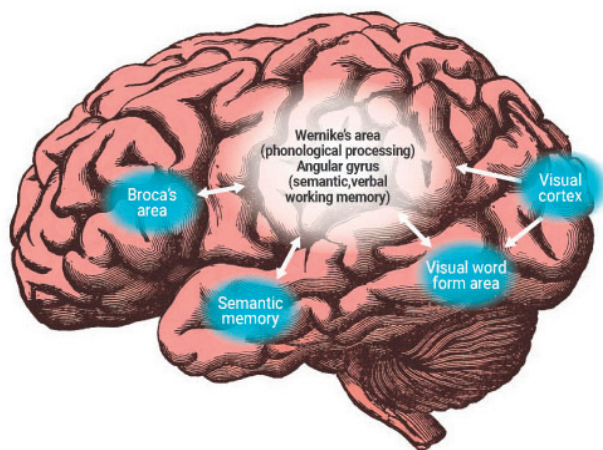


Fig. 2. The major brain regions and interconnectivity involved in reading.

### Clinical features

The epidemiology of dyslexia reveals that it is perhaps the most common neurobehavioral disorder affecting children, with a prevalence of 3%–17.5% (Table 1).<sup>22-30)</sup> Dyslexia is a dimensionally diagnosed disease that belongs to the lower part of the total population on a continuous line. Dyslexia refers to difficulty in reading appropriately according to an individual's cognitive function and age. While genetic and neurobiological causes have been identified, there are no specific markers or imaging tests for diagnosis. The diagnosis considers medical history, observation, psychological evaluation, and reading test results.

Children with dyslexia can read, although their reading speed

Table 1. Prevalence of dyslexia by region and language

Study	Year	Region	Language	Prevalence
Lindgren et al. <sup>23)</sup>	1985	Italy	Italian	8.5% (Gross-national comparisons of prevalence in Italy and the United States)
Shaywitz et al. <sup>22,24)</sup>	1997	US	English	5%–17.5%
Hulme and Snowling <sup>25)</sup>	2011	UK	English	10.3% (1,324 UK primary school children)
Wilcke et al. <sup>26)</sup>	2016	Germany	German	About 5%
Kim et al. <sup>27)</sup>	2018	Korea	Korean	3.2%–8.5%
Verpalen et al. <sup>28)</sup>	2018	Netherlands	Dutch	About 5%
Kita et al. <sup>29)</sup>	2019	Japan	Japanese	3.0%–11.2%
Lin et al. <sup>30)</sup>	2020	China	Chinese	3.0%–12.6%

is slower than that of nonreading impaired children of the same age, and more effort is required.<sup>31,32)</sup> Children with dyslexia have more difficulty with vocabulary and syntax compared to controls at approximately 36 and 42 months.<sup>33,34)</sup> Children diagnosed with dyslexia at 3–4 years of age have a poor sense of prosody (sound stress, fluctuations, pitches, or repetition of homonyms). When singing nursery rhymes, they have difficulty recognizing rhyming words. Children with dyslexia have less knowledge of letters, phonology, and vocabulary at the age of 5 compared to non-reading-impaired children.<sup>33)</sup>

In kindergarten, children have difficulty recognizing the names and pronunciations of letters (phonemes).<sup>31)</sup> Most of the words are not spoken in order, and the first sound of the word may be omitted or the sounds of the word group be inverted. Additionally, the order of the syllables may change, and there may be problems with articulation.

It is important for pediatricians to know the clinical features of preschool children that can predict dyslexia because of early diagnosis and intervention before school age (Table 2).

In children with dyslexia, characters are often recognized backward, especially before the age of 7 years.<sup>35)</sup> Preschool-aged children with vocabulary and syntax difficulties and a family history of dyslexia are at risk of being diagnosed with dyslexia later on, but it is difficult to differentiate between dyslexia and normal reading during development.<sup>33,36)</sup> Therefore, it is necessary to check for a family history of dyslexia in children with language delays and monitor possible progression to dyslexia during school age.<sup>31)</sup>

In the first grade, children may present with difficulties reading sight words, experience slow progress with reading, or have illegible handwriting. Children with dyslexia are poorly fluent at grade level and frequently experience pronunciation errors when reading unfamiliar words. When learning letters, children with dyslexia memorize them differently in the logographic stage. The character memorization method entails recognizing

characters as pictures using visual cues without using the phonics of the letters. In elementary school, first, second, and third graders learn to read to prepare for learning, after which they learn through reading.<sup>36,37)</sup>

Even after reading interventions and learning decoding skills, children may continue to be slow and more laborious readers.<sup>33)</sup> In elementary school, children with dyslexia have poor academic performance, accompanied by various behavioral problems such as refusal to attend school, low self-esteem, and somatic complaints.<sup>31)</sup>

Since reading is a skill in the opposite direction of the writing process, it is highly associated with dyslexia. It is more difficult for children with dyslexia to learn a second language than the general population because it is more difficult to process phonology in a second language as well as in their first language.<sup>38)</sup> Dyslexia symptoms continue into adulthood. Brain imaging studies have revealed that the automated reading pathway, which is essential to reading fluency, fails to activate in the mind of a dyslexic person. A common misconception is that children can “outgrow” dyslexia. Dyslexia persists through adulthood, and while reading accuracy can be achieved, fluency is still lacking.<sup>31)</sup>

## Evaluation and diagnosis

Dyslexia should be considered for differential diagnosis if there are concerns about academic achievement and/or reading.<sup>37)</sup> The assessment of children with learning disabilities routinely requires multidisciplinary collaboration between professionals, including psychologists, educators, audiologists, and occupational and speech therapists. Pediatricians should remain vigilant for symptoms of dyslexia when conducting developmental screening tests such as the Korean Developmental Screening Test in patients up to the age of 6 years.

**Table 2. Predictors of dyslexia in preschool children**

Clinical features	Family history of dyslexia (one of the most strongest risk factor)
	Delayed language development
	delayed onset of talking
	short mean length of utterances
	low complexity of syllables produced
	poor receptive or expressive vocabulary
	Poor home literacy environment
	Poor processing of rhythm, prosody and beat synchronization
	Poor ability to pronounce spoken nonsense words (pseudoword)
	Difficulty in report the sound that a letter make
20% to 40% of ADHD have dyslexia, and children with autism spectrum disorder, other behavioral disorders are also at increased risk of having dyslexia	
Findings of dyslexia-related test	Rapid automatized naming: poor ability to automatically retrieve the names of objects, letters, colors
	Poor phonological awareness for spoken word (blending sounds together to make a word or segmenting words into parts)
	Lower working memory
	Lower level auditory or visual processing
	Poor performance of preschool early literacy indicators assessment

ADHD, attention-deficit hyperactivity disorder.

Because early intervention before entering school is effective and can prevent learning deterioration due to dyslexia, it is necessary to provide the appropriate test for early diagnosis.

Dyslexia should be considered among patients who seek treatment due to learning difficulties or ADHD symptoms. It is important to review reading milestones based on age to understand comparisons with same-age peers.<sup>37)</sup> Pediatricians should enquire about the child's ability to recognize letters in kindergarten, read words in the first grade, and read and understand short picture books in the second grade.<sup>37)</sup> Because dyslexia has a large genetic predisposition, and reports indicate that 65% of children have parents with dyslexia, it is important to obtain a comprehensive family history.<sup>39)</sup>

The direct observation of a child's writing and spelling capabilities can be useful in clinical assessments. The practitioner may require the child to write his or her name or simple words using paper and pencils using provided examples. The child should identify the relevant letter, make the corresponding letter sound, and read the word aloud.<sup>31)</sup> A definitive diagnosis of dyslexia is made by pediatricians after evaluating assessments are made by speech pathologists, psychologists, reading experts, and educational experts.

In the United States, the IDEA law allows children with dyslexia to be evaluated in the public school system and receive appropriate education and intervention.<sup>40)</sup> The evaluation might include testing language and reading abilities, cognitive or IQ testing, speech and language evaluation, and/or social-emotional evaluations.

Because dyslexia is an underlying deficit in phonological processing, neuropsychological testing should focus on assessing phonological processing. Apart from phonological processing, word decoding, comprehension, and fluency are all assessed by these tools to varying degrees.

The evaluations for dyslexia used in Korea include basic academic skills assessment (BASA)-reading, comprehensive learning test-reading (CLT-R), test of reading achievement and reading cognitive processes ability (RARCP), and Korean language base reading assessment (KOLRA). Test methods mainly comprise detailed evaluation items such as word recognition, reading fluency/reading comprehension, letter knowledge, rapid automatic naming test, and phonological memory.

Some conditions that frequently occur with dyslexia include ADHD, which can have a 20%–40% co-occurrence, certain learning disabilities with math disorders (40% co-occurrence), and autism spectrum disorder (~30% co-occurrence).<sup>41)</sup> It is key to conduct an audiological evaluation and a vision assessment to understand whether impairments in hearing or vision compound or exacerbate the child's difficulties.

Dyslexia requires a differential diagnosis, such as intellectual disability, hearing, visual impairment, and history or diagnosis of ADHD.

## Management

The early diagnosis of dyslexia in children is pertinent to achieving successful early interventions in the reading process, which can improve reading results.<sup>37)</sup> The management of dyslexia often requires a lifespan approach because it is a chronic condition.<sup>37,42,43)</sup> There is no effective medicinal or nutritional method for treating dyslexia.<sup>44)</sup> The effects of visual training, music education, and chiropractic interventions on dyslexia are doubtful.<sup>45)</sup> In the case of dyslexia presenting alongside ADHD, treatment of comorbid ADHD is important for improving dyslexia, and atomoxetine is effective in this regard.<sup>46)</sup> If children respond well to interventional reading trials, then they may not require any additional reading instruction, which may indicate that they have a developmental lag in reading skills and not dyslexia.

Evidence-based interventions focus on building phonemic awareness (e.g., speech is manipulated into syllables and then into words). Interventions should be performed by a teacher/reading expert, preferably in small groups with other children of a similar level.<sup>47)</sup> Interventions should systematically target education on 1 or 2 phonemes at a time, build skills sequentially, and include a multisensory approach.<sup>42,43)</sup> Reading skills improve meaningfully when these interventions are implemented.<sup>42)</sup>

Phoneme recognition training is followed by phonics training to recognize the correspondence between letters and sounds.<sup>48)</sup> After mastering phonics, the focus should be to read rapidly and accurately, and then practice automatic comprehension while reading.<sup>49,50)</sup> Using audiobooks, reading storybooks, and repeated exposure to words outside of school provides opportunities for increasing vocabulary complexity and vocabulary enrichment.<sup>31,37)</sup>

During the senior education phase, such as in high schools and universities, it is necessary to provide accommodations for students with dyslexia, such as granting additional test time, using audiobooks instead of written texts, or taking oral tests.<sup>51)</sup>

## Conclusions

Reading is a complex cognitive skill that involves various areas of the brain. Dyslexia is related to problems such as poor word recognition, limited decoding ability, and impaired automatic word recognition. Clinical symptoms of dyslexia vary by age, and the main diagnostic factor is that the patient's reading ability is insufficient compared to their cognitive ability and chronological age. Furthermore, there is a central problem in phonological processing.

Interventions for dyslexia can affect reading ability by causing changes in brain function and structure.<sup>52)</sup> An accurate diagnosis and timely specialized intervention are important in children with dyslexia. Successful management includes early childhood intervention and the provision of suitable accommodations after adolescence.

## Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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**How to cite this article:** Kim SK. Recent update on reading disability (dyslexia) focused on neurobiology *Clin Exp Pediatr* 2021;63:497-503. <https://doi.org/10.3345/cep.2020.01543>