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REVIEW ARTICLE

A review of the neurobiological basis of dyslexia in the adult population☆

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Abstract
Introduction: Adult dyslexia affects about 4% of the population. However, studies on the neurobiological basis of dyslexia in adulthood are scarce compared to paediatric studies.
Aim: This review investigates the neurobiological basis of dyslexia in adulthood.
Development: Using PsycINFO, a database of psychology abstracts, we identified 11 studies on genetics, 9 neurostructural studies, 13 neurofunctional studies and 24 neurophysiological studies. Results from the review show that dyslexia is highly heritable and displays polygenic transmission. Likewise, adult neuroimaging studies found structural, functional, and physiological changes in the parieto-occipital and occipito-temporal regions, and in the inferior frontal gyrus, in adults with dyslexia.
Conclusion: According to different studies, aetiology in cases of adult dyslexia is complex. We stress the need for neurobiological studies of dyslexia in languages with transparent spelling systems.

PALABRAS CLAVE
Dislexia;
Adultez;
Genética;
Neuroimagen

Una revisión de las bases neurobiológicas de la dislexia en población adulta

Resumen
Introducción: La dislexia en la edad adulta afecta a alrededor del 4% de la población. Sin embargo, la investigación acerca de los sustratos neurobiológicos de la dislexia en población adulta es relativamente escasa en comparación con la realizada en niños.
Objetivo: El presente estudio ofrece una revisión de las bases neurobiológicas de la dislexia en población adulta.

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Desarrollo: A partir de una búsqueda bibliográfica en la base de datos del *Psychological Abstracts: PsycINFO*, se identificaron 11 trabajos sobre las bases genéticas, 9 estudios que emplearon técnicas de neuroimagen estructural, 13 artículos que emplearon técnicas neurofuncionales, y 24, neurofisiológicas. Los resultados de la revisión señalan la gran heredabilidad de la dislexia, así como la implicación de diferentes genes. Asimismo, los estudios de neuroimagen muestran diferencias estructurales, funcionales y fisiológicas en regiones temporoparietales y occipitotemporales, y en el giro frontal inferior en los adultos con dislexia.
Conclusión: Las investigaciones muestran la gran complejidad etiológica de la dislexia en población adulta. Se destaca la necesidad de realizar estudios neurobiológicos en diferentes lenguas transparentes.

Introduction

Over the years, many terms have been used to name developmental dyslexia, including congenital word blindness, familial congenital word blindness, amnesia visualis verbalis, analphabetia partialias, bradylexia, congenital alexia, constitutional dyslexia, psycholexia, congenital typholexia, congenital dyslexia, developmental reading backwardness, primary or specific reading retardation, and strephosymbolia. In summary, from a cognitive and behavioural viewpoint, developmental dyslexia is a heterogeneous syndrome characterised by unexpected failure to recognise words, leading to the inability to attain a fluid, effortless reading style.[1–4] In addition to difficulty recognising words completely and/or fluently, patients also have problems with spelling, reading comprehension, and mathematical reasoning.[5]

The prevalence of dyslexia is between 5% and 15% of all school-age children, depending on the language and culture.[5] Prevalence estimates for Spain range from 3.2% to 5.9% in primary education,[6] and from 3.2% to 5.1% in secondary education.[7] Although prevalence in adulthood has not been studied, it is thought to be around 4%.[5]

Several longitudinal studies have shown that reading difficulties are chronic since they tend not to resolve in the long term. Therefore, evidence of reading difficulties persisting into adolescence and adulthood has led to considerable advances in research into the manifestations and neurobiological substrate of dyslexia in adulthood. In fact, research in adult subjects represents 5.82% of all research on learning difficulties conducted between 1998 and 2003.[8]

Regarding cognitive deficiencies, the meta-analysis conducted by Swanson and Hsieh[9] shows that specific cognitive and language processes in adults with dyslexia differ from those in adults with no reading disabilities due to difficulties in phonological processing persisting since childhood, as well as deficits in verbal memory, vocabulary, and naming speed. In addition, as stated by Swanson,[10] deficiencies in adults with dyslexia are more severe in those with higher IQs. As a consequence, both children and adults with dyslexia devote less time to reading, resulting in more limited vocabulary and severely impaired reading comprehension. Adults with reading disabilities have considerable difficulty understanding complex texts and making inferences.[11] Therefore, adolescents and adults with reading disabilities are frequently unable to keep up with academic demands; the knowledge they exhibit is limited, and this may severely impact their performance on reading tasks. In addition, difficulty reading has a negative effect not only on academic and cognitive performance but also on the personal and motivational levels. Klassen et al.[12] conducted a meta-analysis of 171 articles and concluded that such internalising problems as anxiety and depressive symptoms are frequent among adults with dyslexia. Self-esteem is also lower in adolescents and adults with dyslexia.[13]

Neuroimaging techniques provide neurological evidence about the neural networks involved in reading and its associated difficulties. Thus, the left hemisphere has been found to host neural networks involved in reading: an anterior network located in the inferior frontal gyrus (Broca's area), linked to articulation, silent reading, and naming,[14] and 2 posterior regions in the left hemisphere, one surrounding the parieto-temporal region which is responsible for word processing, and the other in the parieto-occipital region, responsible for word formation.[15–18] On the other hand, numerous studies have shown that dyslexia is highly heritable.[19,20] Other studies have also showed the influence of genetics on different reading disabilities.[20,21] Likewise, advances in molecular genetics have made it possible for researchers to locate several genes on chromosomes 1, 2, 3, 4, 6, 11, 15, 17, 18, and X which are involved in transmitting reading disabilities and various reading-related skills.[15,22] However, research on the neurobiological substrate of dyslexia in adults is relatively scarce compared to research conducted in children.

Objective

Based on the above, the present study aims to offer a general perspective on the neurobiological substrate of developmental dyslexia in adults based on a selective review of articles addressing this topic published in the past years. We aimed to summarise, analyse, and discuss findings reported in the last 10 years on the genetic basis of dyslexia, and

neurological findings in adults with developmental dyslexia, using neuroimaging and neurophysiological techniques.

Methods

We conducted a literature search on the PsycINFO database using the keywords 'dyslexia' and 'reading disabilities' and using the thesaurus application for the concept 'reading learning disabilities'. Our purpose was to identify studies including the selected terms in their title, abstract, or keywords. No time limits were imposed for our literature search. We then undertook an in-depth analysis of peer-reviewed articles on neurobiology published in scientific journals in the past 10 years (2004—2013) and including a population aged over 18. We reviewed article abstracts to select those including adult populations; in doubtful cases, we accessed the article in its full text form. We subsequently classified the articles including adults with developmental dyslexia into: (a) genetic studies, broken down into family studies, heritability studies, and molecular genetic studies; (b) studies using structural and/or functional neuroimaging techniques; and (c) studies using neurophysiological techniques.

Results

We have structured the results of our literature review by creating the following categories: genetic studies, structural and functional neuroimaging studies, and neurophysiological studies.

Genetic studies

According to these studies, dyslexia is genetically determined. Researchers in this field have conducted genealogical studies, studies of the heritability of reading skills, molecular genetics studies, etc. Pioneers in the field of reading disabilities (for example, Orton, Hinshelwood, etc.) had already reported cases of reading difficulties shared by siblings, parents, and other related individuals, that is, they observed that dyslexia was more frequent in families in which a member was affected than in the normal population.[23]

Heritability or quantitative genetics studies aim to ascertain whether or not family associations in dyslexia indicates genetic transmission (heritability), and the potential influence of environmental factors. Many studies of children with reading disabilities suggest that these difficulties are heritable; having reading difficulties is 8 times more likely with one affected parent.[24,25]

Four studies in adult populations showed a heritability index for reading abilities ranging between 0.45 and 0.74. The study by Astrom et al.[26] shows that up to 70% of all reading deficits have a genetic basis; the incidence of environmental variables is greater in monozygotic twins than in dizygotic twins or other siblings. The influence of heritability was confirmed by Kirkpatrick et al.,[27] who state that genetics has an impact of more than 70% on reading difficulties and skills, whereas environment has little to no effect. Although less robust, the results of the study by Stein et al.[28] are equally significant; these authors found a heritability of 45% for repeating real words with several syllables. According to one interesting study of adults with reading difficulties, the impact of genetic factors was shown to be greater in those with high IQ scores, that is, the genetic impact was more evident in relatives with dyslexia and IQ scores similar to or higher than 100, whereas environmental impact is more marked in those with lower IQ scores.[29] The idea that the impact of genetics is dependent on IQ had already been confirmed by the same research team in children with dyslexia.[30]

Meanwhile, 7 studies of molecular genetics have aimed to identify DNA markers, that is, potential chromosomal polymorphisms/deviations linked to severe reading disabilities. Studies conducted since 1983 in children with dyslexia have found several associations with chromosomes 1,[24,31,32] 2,[33—36] 3,[37] 6,[38—42] 15,[20,40] and 18.[43] The genes identified in the said chromosomes are considered to be functionally involved in neural migration and abnormal axonal growth, which leads to abnormalities in the development of cortico-cortical and cortico-thalamic circuits.[44]

Molecular genetics research in adults with reading disabilities also reveals that several chromosomal locations are involved in dyslexia and reading-related skills. Anthoni et al.[45] have found that the *CYP19A1* gene (5p21.2) is involved in reading, speaking, and talking.

Bates et al.[46] confirmed that *ROBO1* (3p12.3) is involved in short-term recall of arbitrary phonological strings. The study by Newbury et al.[47] found an association between reading-related measures and the gene variants *CNTNAP2* (7q35-q36) and *CMIP* (16q24). According to Marino et al.,[48] *DCDC2* (6p22.2) and *DYX1C1* (15q21), in addition to being involved in transmission of dyslexia, have a pleiotropic role for mathematics but not for language phenotypes. Pagnamenta et al.[49] demonstrate that deletions in *CNTNAP5* (2q14.3) and *DOCK4* (7q31.1) constitute a risk factor for dyslexia, although they may also be involved in autism. Finally, an association between dyslexia and a susceptibility locus at chromosome 15q has also been established.[50]

However, different studies yield contradictory results. For instance, the study by Svensson et al.,[22] which included 62 members of the same family representing 6 different generations, does not confirm the incidence of genetic factors on reading disabilities. Likewise, Newbury et al.[47] could not confirm the influence of the *KIAA0319* (6p22.2) and *DCDC2* genes on dyslexia, although they did find an association between *KIAA0319* and oral language ability.

Functional neuroimaging studies

These studies use neuroimaging techniques that measure brain activity by detecting changes in blood flow. In other words, when a brain area is in use, blood flow to this area also increases. These studies have used different techniques, including functional MRI, which shows images of brain regions which perform a specific activity; functional transcranial Doppler sonography, which measures brain blood flow velocity by emitting low-frequency sound waves (2 MHz) which pass through the cranium; or

positron emission tomography, which detects and analyses the three-dimensional distribution of a radiotracer administered intravenously. The 13 studies included here analyse different cognitive processes and their association with brain activation in people with dyslexia during the performance of certain lexical and non-lexical tasks.

Several studies confirm that patients with dyslexia lack hemispheric specialisation for reading and writing and other linguistic skills.[51–54] However, the study by Park et al.[53] found a marked pattern of right lateralisation in a bilingual patient with dyslexia.

Different studies have found low brain activation in various brain areas in adults with dyslexia. Steinbrink et al.[52] found lower activation in the insular cortex in patients with dyslexia than in controls during phonological and temporal processing tasks. Díaz et al.[55] found less activation of the medial geniculate body (thalamus) and cortical centres during phonological processing and processing of changes in voice characteristics. Peyrin et al.[56] observed decreased activation of the left inferior frontal gyrus during performance of a phonological task in adults with dyslexia. Pecini et al.[57] observed reduced activation in the frontal networks of the left hemisphere related to phonological working memory in patients with dyslexia and a history of language delay. In the study by Conway et al.,[58] patients with dyslexia displayed increased activity in the left posterior superior temporal region and inferior parietal areas during linguistic and non-linguistic auditory working memory tasks, as well as increased activation in the primary auditory cortex during the tones comparison task.

Adults with dyslexia have also been found to show increased activation of the left inferior frontal gyrus during phonological tasks.[59,60]

Similarly, McCrory et al.[61] found markedly reduced activation of the left occipitotemporal area during reading. Karni et al.[62] provide more specific results: these authors found a different brain activity pattern in the slow nonwords condition. The left frontal gyrus (Broca's area) and operculum are activated in dyslexic readers whereas control subjects display activation in the visual areas of the left extrastriate cortex. Lastly, Gilger et al.[63] found no functional differences between gifted and non-gifted dyslexic patients.

Structural neuroimaging studies

MRI and diffusion tensor imaging are the structural neuroimaging techniques used to study the anatomy of brain structures in patients with dyslexia. These techniques provide high-resolution three-dimensional images showing alterations in brain structure. We included 9 studies in this category.

Some of these studies aimed to analyse variations in grey matter in a population of adults with dyslexia. According to the study by Casanova et al.,[64] dyslexic adults have a smaller volume of cortical grey matter and less gyrification, especially in the left temporal lobe. Richardson et al.[65] support the hypothesis that grey matter density in the posterior area (left posterior superior temporal sulcus) is a predictor of auditory short-term memory capacity in normal and dyslexic individuals. The study by Frye et al.[66] reported decreased brain surface area and grey matter volume in the frontal lobe in dyslexic patients; this may be related to alterations in prenatal cortical folding.

Pernet et al.[67] found that patients with dyslexia displayed either greater or lesser grey matter volumes in the right cerebellum and right lentiform nucleus than controls, which is linked to the presence of different dyslexia phenotypes. In addition, this study confirms that dyslexic patients with lower grey matter volumes perform poorly on phonological tasks. Steinbrink et al.[68] also report decreased grey matter volume in the superior temporal gyrus of both hemispheres.

On the other hand, other studies have confirmed the presence of alterations in white matter volume in different brain areas in patients with dyslexia. Lebel et al.[69] found reduced white matter volume in both frontal lobes in adults with dyslexia. Steinbrink et al.[68] found decreased fractional anisotropy in bilateral frontotemporal and left temporoparietal white matter. Likewise, the study conducted by Casanova et al.[70] reported greater gyral white matter amplitude in patients with dyslexia.

Lastly, the study by Chang et al.[71] suggests an association between some periventricular grey matter nodules and disruptions in white matter microstructure, and between the degree of white matter integrity and reading fluency in dyslexic patients.

Neurophysiological studies

Several techniques have been used to study brain physiology in patients with developmental dyslexia, especially EEG, evoked potentials, and brain electrical activity mapping. Twenty-four studies using neurophysiological techniques have been published in the last decade.

Mahé et al.[72,73] have conducted several studies with evoked potentials. These authors have found impaired N170 print tuning in dyslexic adults during word recognition, longer latencies, more errors for pseudowords, and a lack of hemispheric specialisation. Similar results have been reported by Shany and Breznitz[74]: N170 activation is lower in the visual association cortex in Hebrew speakers with dyslexia. Korinth et al.[75] found that N170 was absent in around 40% of slow readers who had not been diagnosed with dyslexia.

Lallier et al.[76] detected a decrease in P3b amplitudes; this component is associated with atypical perception in dyslexic individuals. Savill and Thierry[77] also reported decreased P3b amplitude during reading pseudohomophones. Similarly, Dhar et al.[78] found an absence of frontal amplification of P3 in the Nogo condition and reduced inhibitory control in individuals with dyslexia, ADHD, and both disorders. Mayseless and Breznitz[79] conducted a study in Israeli university students and found longer reaction times and shorter latencies of P1 and P2 components; brain activation decreased in the left hemisphere when viewing concrete objects and increased in the right hemisphere when viewing pseudo-objects. In another study,[79] after applying 2 training programmes, the researchers found decreased amplitude and greater latency of the P1 component, which seems to suggest that amplitude and latency compensate after visual training.

On the other hand, the study by Fosker and Thierry[80] failed to find significant differences in P2, N2, P3a, and P3b in dyslexic individuals. The only difference between dyslexic patients and controls was a deficit in N1 modulation during phonological discrimination.

Horowitz-Kraus and Breznitz[81,82] report lower ERN/Ne amplitudes and latencies in a group of Israeli university students with dyslexia; these individuals were less skilled than controls and had a different error-detection activity level. Likewise, in a study by Horowitz-Kraus,[83] dyslexic adolescents displayed lower ERN amplitudes than adults with dyslexia, as well as a smaller N400 difference between correct and erroneous responses.

Another recent study[84] found reduced and diffuse interhemispheric coherence of alpha activity in the central-parietal cortex during a visuospatial attention task.

Several studies have found decreased amplitude and latency in mismatch negativity in the left hemisphere during syllable,[85] phoneme,[86] and tone discrimination.[87] However, other studies have found no differences in mismatch negativity for speech discrimination.[88]

Some researchers report lower cerebral activity, gamma oscillations in the left hemisphere during phonological processing,[51] increased activation in perisylvian language areas,[89] and reduced auditory M100 asymmetry in dyslexic adults.[90] Likewise, other studies report atypical components of auditory evoked potentials which reveal the presence of anomalies in cortical auditory processing and a lack of brain lateralisation for acoustic cues.[91,92]

Conclusions

Our literature review of the genetic and neurological basis of dyslexia in adults shows the aetiological complexity of this disorder.[15] Evidence of the genetic basis of dyslexia is sufficient; the condition is highly heritable and involves several genes, although the full genotype of dyslexia in adults is still to be determined.[22] Many of these genes play a fundamental role in neural migration.[20] As stated by Galaburda et al.,[44] these genes may be responsible for subtle cortical malformations affecting neuronal migration and axon growth, thereby causing abnormalities in the development of cortico-cortical and cortico-thalamic circuits. These anomalies would negatively affect cognitive, perceptual, and sensory-motor processes, which are crucial for learning.

The past years have significantly increased our knowledge of the causes of reading disabilities thanks to progress in neuroscience. Neuroimaging techniques have provided a deeper understanding of the neurological differences present in adults with dyslexia. For example, we now know that dyslexics display less activation of the frontal networks, temporoparietal area, and especially the visual word form area (occipitotemporal dysfunction) of the left hemisphere. Likewise, diffusion tensor imaging has shown differences in grey and white matter volume in those areas. Heterogeneity of the results may be due to differences in participant selection criteria, disproportional numbers of men or women in study samples, the lack of adjustment for potential comorbidities, orthographic depth, and methodological differences between studies. However, this heterogeneity is indicative of the aetiological complexity of reading disabilities.

Research in the fields of cognitive and molecular neuroscience may provide the common point between behavioural and genetic findings. Characterising the neural circuits involved in learning to read and identifying the brain areas where grey and white matter activates in dyslexic adults while they read is essential to understand the complexity of brain function and the interactions between genes in adults with dyslexia. Although applying the advances in neuroscience research to classrooms has long been demanded by researchers, some authors consider this idea to be a 'bridge too far'. However, other studies provide empirical support to the cognitive theories that explain reading difficulties.[93] At the same time, some intervention studies have used neuroimaging techniques to assess brain activity in children with reading disabilities and report changes after a number of short interventions.[94,95] These changes in brain activation provide firm support for the validity of these interventions; however, neuroscience cannot solve the problem of how teachers should teach their pupils to read and spell.[96] Given the differences between languages and spelling systems, and their impact on reading disabilities, research on this topic should be conducted on a language-specific basis to determine the difficulties and neurobiological universals of reading and specific functional differences between languages.

Conflict of interest

The authors have no conflict of interest to declare.

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