

Investigating Dyslexia through Diffusion Tensor Imaging across Ages: A Systematic Review

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Abstract: Dyslexia is a neurodevelopmental disorder that presents a deficit in accuracy and/or fluency while reading or spelling that is not expected given the level of cognitive functioning. Research indicates brain structural changes mainly in the left hemisphere, comprising arcuate fasciculus (AF) and corona radiata (CR). The purpose of this systematic review is to better understand the possible methods for analyzing Diffusion Tensor Imaging (DTI) data while accounting for the characteristics of dyslexia in the last decade of the literature. Among 124 articles screened from PubMed and Scopus, 49 met inclusion criteria, focusing on dyslexia without neurological or psychiatric comorbidities. Article selection involved paired evaluation, with a third reviewer resolving discrepancies. The selected articles were analyzed using two topics: (1) a demographic and cognitive assessment of the sample and (2) DTI acquisition and analysis. Predominantly, studies centered on English-speaking children with reading difficulties, with preserved non-verbal intelligence, attention, and memory, and deficits in reading tests, rapid automatic naming, and phonological awareness. Structural differences were found mainly in the left AF in all ages and in the bilateral superior longitudinal fasciculus for readers-children and adults. A better understanding of structural brain changes of dyslexia and neuroadaptations can be a guide for future interventions.

Keywords: dyslexia; diffusion tensor imaging; structural brain changes; structural connectivity



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1. Introduction

Dyslexia is a neurodevelopmental disorder that impairs fluency and/or speed of reading, as well as word recognition; it may also impact spelling. The difficulties should not be explained by other cognitive, health, or socio-economic factors [1]. The lack of accurate and fluent reading is a product of poor recognition and decoding abilities, and despite that, verbal comprehension is not equally affected in dyslexia [2,3].

Developmental dyslexia is classified within the framework of the diagnosis-specific learning disorder of reading [4], and it manifests in a spectrum from mild, to moderate, to severe [5]. It is present in over 80% of people with a learning disability in studied languages, having some variations regarding severity and type of difficulties according to the language structural characteristics [6]. Dyslexia's mean prevalence is estimated at around 7% of the world population, with a predominance in male individuals [2,3]. Still, the incidence and prevalence are unclear due to the heterogeneity of literacy and language cultures with wide variances in terms of definitions, diagnostic instruments, rules, guidelines, and protocols for assessing dyslexic children and adults [1,7].

Two main medical classifications (ICD-11 and DSM-5) define the diagnostic criteria for dyslexia, and the assessment focuses mainly on identifying the reading and spelling

discrepancies compared to the general population performance together with the assessment of other aspects that could confirm or rule out the diagnosis, for example, intelligence, phonological awareness, word and pseudoword reading, verbal fluency, verbal working memory, reading, and naming under stress [8]. This careful and time-consuming evaluation aims to support the clinical exclusion criteria, which contributes to reducing the prevalence by avoiding wrongful diagnoses of individuals struggling to read. Furthermore, there has been an effortful search in different fields for a better understanding of dyslexia's development and neuroimaging contribution in clarifying neuroanatomical forming behind reading and dyslexia.

Clinical neuroimaging has been transformed by Diffusion-Weighted Imaging (DWI) and Diffusion Tensor Imaging (DTI), making it possible to examine the brain's architecture and identify pathology earlier and more accurately than traditional magnetic resonance imaging sequences. Nowadays, diffusion is already used in clinical practice for stroke, trauma, tumors, demyelinating conditions, and neurosurgical planning. In psychiatric and neurological conditions, it is still used mainly in the research context [9].

The foundation of diffusion imaging lies in the behavior of water molecules, which move freely through space equally in all directions when unimpeded by structures. However, when encountering obstacles like cell membranes, water molecules tend to diffuse in alignment with the orientation of those barriers [10]. Magnetic resonance imaging, facilitated by DWI sequences, enables the measurement of water displacement in various directions for a brief duration. This information can then be used to assess tissue integrity, particularly in white matter fiber pathways [9].

Recent advancements in DTI research have expanded the focus beyond the assessment of a straightforward diffusion scalar to emphasize the significance of the more intricate 3D diffusion pattern. Axial diffusivity (AD), radial diffusivity (RD), mean diffusivity (MD), apparent diffusion coefficient (ADC), and others are additional imaging metrics that are increasingly used [11].

A standard DTI metric utilized in evaluating a variety of neuropathologic processes, from traumatic brain injury to demyelinating illness, is fractional anisotropy (FA), which quantifies the degree of this directionality [11]. Despite its promise for identifying subtle illnesses and alterations not discernible with conventional MRI sequences, the clinical applications of DTI have been questioned regarding the specificity of the findings [11].

In developmental neuroscience, DTI metrics have been shown to be a useful biomarker of white matter tract development and tissue injury, being used for treatment monitoring and potentially acting as outcome predictors. Children's normal and pathological brain maturation has been described by the ADC/FA scalars since it is well known that as brain myelination and maturation advance, ADC values fall and FA values rise [12].

The literature has shown that people with dyslexia or reading disability may show brain structural changes with lower FA values in the left frontal and temporoparietal regions that coincide with the majority of studies on the left arcuate fasciculus (AF) and corona radiata (CR). Few studies have suggested a role for the posterior part of the corpus callosum or more ventral tracts like the inferior longitudinal fasciculus (ILF) or the inferior fronto-occipital fasciculus (IFOF) [13]. And more recently, a meta-analysis found no differences between dyslexics and typical readers when observing studies that conducted Voxel-Based Analysis (VBA) of FA and compared it to reading ability [14].

The purpose of this systematic review is to search for a better understanding of the multitude of possible methods for analyzing DTI data while accounting for the characteristics of a clinical population such as developmental dyslexia in the literature in the last 10 years.

2. Materials and Methods

2.1. Search Strategy

The systematic review searched the primary databases, PubMed and Scopus, for publications published within the last ten years, including the period from January 2011 to September 2022. The indexed articles were selected, and their findings were reported, fol-

lowing the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15], and this study was not registered on Prospero. The criteria of interest selected were keywords in the following sequence: ((Dyslexia) AND (Brain connectivity) OR (Diffusion tensor imaging), using the boolean operators (DecS/MeSH):

SCOPUS: ((TITLE-ABS-KEY (dyslexia) OR TITLE-ABS-KEY (“Reading disorder”) OR TITLE-ABS-KEY (“Reading disorders”) OR TITLE-ABS-KEY (“Reading disability”) OR TITLE-ABS-KEY (“Reading disabilities” []) OR TITLE-ABS-KEY (“Developmental reading disability”) OR TITLE-ABS-KEY (“Developmental reading disabilities”) OR TITLE-ABS-KEY (“Developmental reading disorder”) OR TITLE-ABS-KEY (“Developmental reading disorders”))) AND ((TITLE-ABS-KEY (dti) OR TITLE-ABS-KEY (“Diffusion Tensor MRI”) OR TITLE-ABS-KEY (“Diffusion Tensor Magnetic Resonance Imaging”) OR TITLE-ABS-KEY (tractography) OR TITLE-ABS-KEY (“Diffusion Tractography”) OR TITLE-ABS-KEY (“Diffusion Tensor Imaging”) OR TITLE-ABS-KEY (“Diffusion weight imaging”) OR TITLE-ABS-KEY (dwi))) AND (LIMIT-TO (DOCTYPE, “ar”)) AND (LIMIT-TO (LANGUAGE, “English”)) AND (LIMIT-TO (PUBYEAR, 2022) OR LIMIT-TO (PUBYEAR, 2021) OR LIMIT-TO (PUBYEAR, 2020) OR LIMIT-TO (PUBYEAR, 2019) OR LIMIT-TO (PUBYEAR, 2018) OR LIMIT-TO (PUBYEAR, 2017) OR LIMIT-TO (PUBYEAR, 2016) OR LIMIT-TO (PUBYEAR, 2015) OR LIMIT-TO (PUBYEAR, 2014) OR LIMIT-TO (PUBYEAR, 2013) OR LIMIT-TO (PUBYEAR, 2012) OR LIMIT-TO (PUBYEAR, 2011)).

PubMed: (((((((((Dyslexia*[Title/ Abstract]) OR “Reading disorder”[Title/ Abstract]) OR “Reading disorders”[Title/ Abstract]) OR “Reading disability”[Title/ Abstract]) OR “Reading disabilities”[Title/ Abstract]) OR “Developmental reading disability”[Title/ Abstract]) OR “Developmental reading disabilities”[Title/ Abstract]) OR “Developmental reading disorder”[Title/ Abstract]) OR “Developmental reading disorders”[Title/ Abstract]) AND ((((((DTI[Title/ Abstract]) OR “Diffusion Tensor MRI”[Title/ Abstract]) OR “Diffusion Tensor Magnetic Resonance Imaging”[Title/ Abstract]) OR “Diffusion Tractography”[Title/ Abstract]) OR “Diffusion Tensor Imaging”[Title/ Abstract]) OR Tractography[Title/ Abstract])).

2.2. Inclusion Criteria

The review included only original articles written in English published within the last 10 years, and full text available about dyslexia in structural analyses by DTI. According to the patient/problem, intervention, comparison, and outcome (PICO) criterion, the problem was: the structural brain changes in dyslexia are unclear; the intervention was: structural analysis by DTI; the comparison was: differences between dyslexia and typical readers volunteers; and the outcome was: the structural brain pattern of dyslexia of development.

2.3. Exclusion Criteria

We excluded studies based on the following criteria: (i) reviews or meta-analyses; (ii) publications written in languages other than English; (iii) indexed articles published in more than one database (duplicates); (iv) articles that included dyslexia with other neurological or psychiatric comorbidities such as stroke, brain injury, epilepsy, autism, traumatic brain injury, aphasia, and mood disorders; (v) articles that performed any analysis other than DTI, such as machine learning, graph theory, and only methodological comparison; (vi) articles in which the diagnosis of dyslexia is unclear; (vii) articles without at least one outcome or method of analysis reporting DTI measures and/or correlation with demographic or neuropsychological measures; (viii) case reports; (ix) neonates; and (x) dyslexia with genetic alterations.

2.4. Data Compilation

In this review, seven of the authors (B.M., M.Y.B., E.M.D., L.F.C., A.S.C., K.L., and M.P.N.), in pairs, independently and randomly analyzed, reviewed, and assessed the eligibility of titles and abstracts according to the strategy of established search. The authors B.M., M.Y.B., E.M.D., L.F.C., A.S.C., K.L., and M.P.N. selected the final articles by evaluating the texts that met the selection criteria. The authors B.M., E.M.D., L.F.C., and A.S.C. were responsible for the search for the demographic, clinical, and neuropsychological charac-

teristics of volunteers and dyslexia patients, being checked by the senior authors (K.L. and M.P.N.). The authors B.M., M.Y.B., L.F.C., and A.S.C. searched for the characteristics of structural brain analyses and their outcomes, and all data were checked by the senior authors (K.L. and M.P.N.). All of the authors contributed to writing the entire text of this review.

2.5. Data Extraction

The selected articles were analyzed using two topics, which were represented in tables that addressed the following characteristics: (1) the demographic characteristics of the population sample, their language, their nationality, and the neuropsychological tools used to characterize the reading disorder; and (2) the characteristics of DTI acquisition, the parameters used in the image analyses and corrections, the structural outcomes between groups, and the correlation with clinical data when reported.

2.6. Risk of Bias Assessment

The selection of articles was performed in pairs, and a third independent author decided if the articles should be included. The data selected in the tables were divided by the authors into the groups already described above, and the checking of the data was carried out by the following group. The final inclusion of studies into the systematic review was by agreement of all reviewers.

2.7. Data Analysis

The data from the articles included in the tables were analyzed descriptively using the percentage, mean, and standard deviation; the variation to characterize each factor attributed to the demographic and neuropsychological characteristics of the participants in each study; and the characteristics of the acquisition, analysis, and results of the structural assessment performed by DTI image acquisition.

3. Results

3.1. Overview of the Screening Process of the Included Studies

Following the inclusion and exclusion criteria described above, we found 124 articles in the last ten years throughout the Scopus and PubMed databases, with 116 from Scopus and 8 from PubMed. Of the 116 articles found in Scopus, 64 were excluded after screening, two studies were with participants with alexia, one with aphasia, two with autism, one with mood disorder, two neonates, 20 without dyslexia diagnosis, two with genetic alterations, nine with brain injury (such as stroke, epilepsy, cortical lesion, and TBI), six were case reports, three were meta-analyses, seven were reviews, three were methodological studies, and six only featured morphometric analyses. The eligibility analysis excluded a further four articles. Three studies reported different methodologies of DTI analysis (machine learning, graph theory, and manual and automatic segmentation), and one did not report the DTI results, resulting in 48 studies included in this selection. Out of the eight articles identified in PubMed, five were excluded during screening: two lacked a dyslexia diagnosis, and three were duplicates from Scopus. After the eligibility assessment, an additional two studies were excluded. One study conducted DTI analysis using machine learning, while another did not report DTI results. Consequently, only one study from PubMed was included [16–59] in this systematic review, 48 were included from Scopus, and one was included from PubMed, as shown in Figure 1.

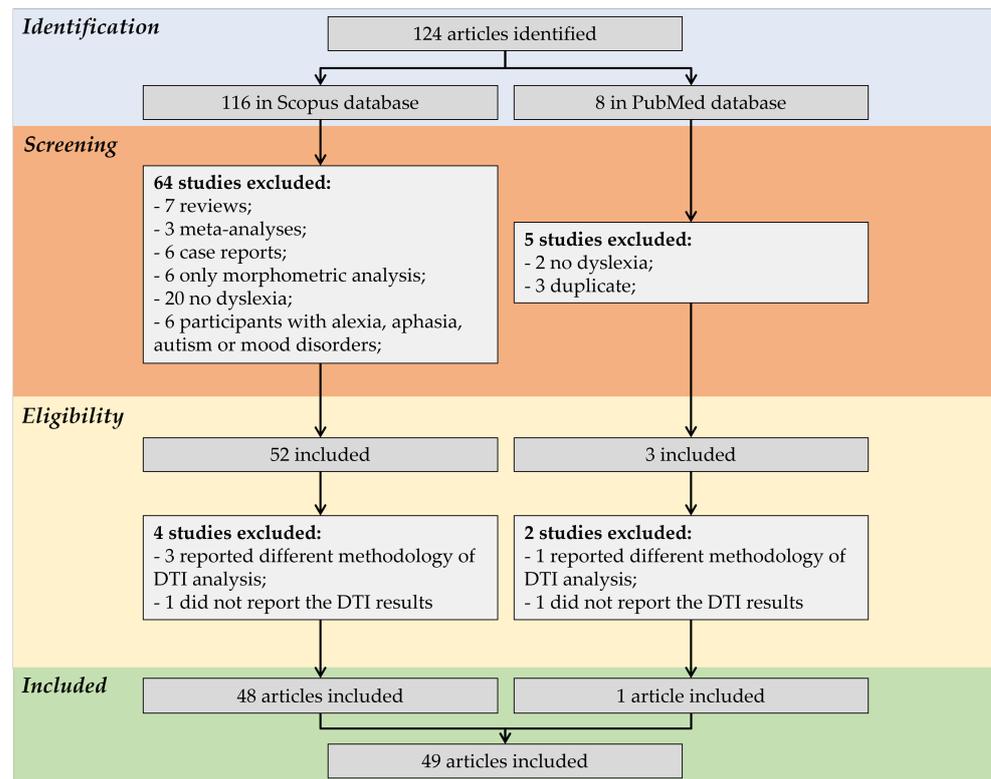


Figure 1. PRISMA flowchart of this systematic review study, identifying at each stage the number of studies included and the reasons for excluding studies until the final stage of inclusion of studies.

3.2. Demographic and Neuropsychological Characteristics of Studied Dyslexia Subjects

This systematic review aimed to provide an overview of dyslexia in various stages of life, from early childhood (preschool to kindergarten) with a familiar history of dyslexia to elementary school children, adolescents, and adults, following the structural brain changes involved in this neurobiological disorder. In the selected studies about dyslexia and structural brain analysis by tractography included in this systematic review, 15% of studies [16–23] included only children below 6 years old with the family risk of dyslexia before reading acquisition (classified as pre-readers); followed by 70% of the studies that analyzed older groups, at different stages of reading proficiency (classified as reading children) from 7 years old up to 19, males and females (classified as readers); and 15% of studied male and female adults aged from 20 to 33 years old (classified as reading adults) (Table 1).

Table 1. Demographic and neuropsychological assessment.

| Ref. | Year | Country | Language | Group | N | Sex (F/M) | Age (Years) | Years of Education (or Level) | IQ | A Word Reading/Spelling | Pseudoword Reading | Text Reading | RAN | Phonological Awareness | Language | Attention | Others |
|-------------------------------|------|---------|----------|--|----------------------------------|---|--|--|--|---|---|---|-------------------------------|---|--|---|--|
| Zuk J, et al. [16] | 2021 | USA | English | TR FHD– TR FHD+ RD FHD+ | 39 18 17 | 21:18 7:11 9:8 | 5.5 ± 0.3 5.5 ± 0.3 5.7 ± 0.4 | Pre-Kindergarten; Kindergarten | Non-verbal (KBIT-2) | LWID (WRMT-R/NU and WRMT-R); Letter Sound Knowledge (YARC) | NR | NR | Objects; Colors; Letter | Elision; Blending Words (CTOPP) | Vocabulary Knowledge (PPVT-4); Sentence Comprehension (CELF-4); Speed Accuracy | NR | WM: Nonword Repetition (CTOPP); Sentence Repetition (GAPS) |
| Yu X, et al. [17] | 2020 | USA | English | TR FHD– TR FHD+ RD FHD+ | 34 35 12 | 16:18 17:18 4:8 | 5.4 ± 0.3 5.5 ± 0.4 5.8 ± 0.5 | The end of 1st grade to 4th/ grade | Non-verbal (KBIT-2) | WID (WRMT-R); SWE (TOWRE-2) | PDE (TOWRE-2); WA (WRMT-R) | NR | Objects; Colors | CTOPP | CELF-4 | NR | HLE |
| Langer N, et al. [18] | 2017 | USA | English | FHD+ FHD– | 14 18 | 7:7 10:8 | 0.9 ± 0.3 0.8 ± 0.3 | NR | NR | NA | NA | NA | NA | NA | Expressive and receptive language (MSEL) | NA | Gross and fine motor (MSEL); Visual reception (MSEL) |
| Kraft I, et al. [19] | 2016 | Germany | German | FHD+ FHD– | 25 28 | 11:14 12:16 | 5.7 ± 0.4 5.6 ± 0.4 | Kindergarten | Non-verbal | One minute word reading (SLRT-II); Spelling (DERET) | One minute pseudoword reading (SLRT-II) | NR | Subtest (BISC) | Pseudoword repetition (SETK 3-5), SS and RI (BISC), and PA (BAKO) | NR | Symbol comparison (BISC) | DS (K-ABC) |
| Vandermosten M, et al. [20] | 2015 | Belgium | Dutch | FRD+ FRD– | 36 35 | 13:23 17:18 | 5.1 ± 0.2 5.1 ± 0.2 | The last year of kindergarten | Non-verbal (Raven) | Letter knowledge productive/receptive test | NR | NR | Objects; Colors | End-phoneme and end-rhyme identification task (PA) | NR | NR | NR |
| Van Der Auwera S, et al. [21] | 2021 | Belgium | Dutch | PreR: FRD– FRD+ BR: FRD– FRD+ FR: FRD– FRD+ | 24 16 13 24 10 15 | 14:10 8:8 13:10 12:12 2:8 5:10 | 6 ± 0.1 6 ± 0.1 8 ± 0.1 8 ± 0.1 11 ± 0.1 11 ± 0.2 | Kindergarten1st/ 2nd grades 3rd/4th/5th grades | Non-verbal (Raven and Block Design–WISC-III) | Word Reading List; Letter knowledge; and Spelling | Pseudoword Reading Test | NR | NR | Phoneme Deletion and Spoonerism; PA | NR | NR | NR |
| Wang Y, et al. [22] | 2017 | USA | English | PreR: FHD– FHD+ BR: FHD– FHD+ FR: FHD– FHD+ | 16 24 23 24 10 15 | 8:8 14:10 12:12 13:10 2:8 5:10 | 5.3 ± 0.8 5.4 ± 1.1 7.0 ± 2.2 7.3 ± 2.2 10.0 ± 2.5 10.2 ± 1.8 | Nine single words 1st/2nd grades 3rd/4th/5th grades | Non-verbal (KBIT-2) | WID (WRMT-R (FR); SWE (TOWRE) (BR and FR); and TOSWRF (FR) | PDE (TOWRE) | Gray Oral Reading Test(GORT-5), Reading Fluency WJ-III-TA | Objects (PreR); Colors | CTOPP (FR); PC (WRMT-R, BR) | CELF-4 (BR) | NR | TOMAL2 (FR) |
| Vanderauwera J, et al. [23] | 2017 | Belgium | Dutch | DYX TR FRD+ FRD– | 15 46 34 27 | 7:8 15:31 13:21 9:18 | 7.9 ± 0.1 7.9 ± 0.1 7.9 ± 0.1 7.9 ± 0.1 | PreR—prior 1st grade/ BR—2nd/3rd grade | Non-verbal (WISC) | Word reading, one-minute test (BR); Spelling (BR); and Productive/Receptive Letter Knowledge (PreR) | Pseudoword reading two minute test (BR) | NR | Objects (PreR); Colors | PA (PreR); End-phoneme and end-rhyme identification task | NA | NA | NR |
| Zhao J, et al. [24] | 2022 | France | French | Control DYX | 31 26 | 13:18 13:13 | 12 ± 1:11 ± 2 11 ± 1:12 ± 1 | NR | Verbal (WISC); Non-verbal(WISC) | Word Reading Ability (Odedys); Word Spelling-to-Dictation Test | Nonword Reading Ability (Odedys) | Alouette Test | Digits; Objects | Phoneme deletion and Spoonerism | NR | VAS (Global and Partial Letter Report Task) | Verbal WM (DS- WISC) |
| Meisler SL, [25] | 2022 | USA | English | Control DYX | 582 104 | 195:387 44:60 | 10.8 ± 3.2 10.2 ± 2.5 | NR | Non-verbal (KBIT-2) | SWE (TOWRE-2) | PDE (TOWRE-2) | NR | NR | NR | NR | NR | NR |

Table 1. Cont.

| Ref. | Year | Country | Language | Group | N | Sex (F:M) | Age (Years) | Years of Education (or Level) | IQ | A Word Reading/Spelling | Pseudoword Reading | Text Reading | RAN | Phonological Awareness | Language | Attention | Others |
|-------------------------------|------|-------------|------------------|-----------------|----------|----------------|---|-------------------------------|----------------------------------|--|----------------------------------|---------------------------------|-----------------|--------------------------------------|----------|---|---|
| Liu T, et al. [26] | 2022 | France | French | Control DYX | 31 16 | 13:18 13:13 | 11 ± 1 12 ± 1 | NR | Verbal and Non-verbal (WISC-IV) | NR; Global and Partial Letter Report Task (VAS) | NR | NR | Digits; Objects | Phoneme deletion and Spoonerism | NR | NR | Verbal WM (DS-WISC) |
| Farah R, et al. [27] | 2022 | USA | English | Control RD | 24 22 | 12:12 10:12 | 8-12 | NR | Non-verbal (TONI); Verbal (PPVT) | SWE (TOWRE); LWID (WJ-III) | PDE (TOWRE); WA (WJ-III) | NR | NR | Elision (CTOPP) | NR | Connors questionnaires and VSA (TEA-Ch) | DS (WISC); Switching/Inhibition (DKEFS, Color-Word Condition); and Overall EF (BRIEF) |
| Partanen M, et al. [28] | 2020 | Canada | English | Control DYX | 22 13 | 11:11 5:8 | Pre-test 8.5 ± 0.4 8.6 ± 0.4 Post-test 8.9 ± 0.4 8.9 ± 0.4 | 3rd Grade | Non-verbal (TONI-4) | Word Recognition Task (KTEA-II) | Decoding Task (KTEA-II) | Reading Comprehension (KTEA-II) | NR | NR | NR | NR | NR |
| Lou C, et al. [29] | 2020 | Canada | English | RD random group | 64 | 33:31:00 | 10.9 ± 1.3 | NR | NR | SWE (TOWRE) | PDE (TOWRE) | Reading Comprehension (WJ III) | Letters | NR | NR | NR | NR |
| Liu T, et al. [30] | 2021 | France | French | Control DYX | 31 26 | 13:18 13:13 | 11 ± 1 12 ± 1 | NR | Verbal and Non-verbal (WISC) | Word Reading Fluency (Odedys); Word Spelling-to-Dictation Test | Nonword Reading Fluency (Odedys) | Alouette Test | NR | NR | NR | NR | NR |
| Koirala N, et al. [31] | 2021 | USA | English | Random group | 244 | 151:34:00 | 10.2 ± 2.8 | NR | FSIQ(WISC) | SWE (TOWRE-2) | PDE (TOWRE-2) | NR | NR | Elision and Blending Words (CTOPP-2) | NR | NR | NR |
| Huber E, et al. [32] | 2021 | USA | English | Control DYX | 41 32 | 16:25 12:20 | 9.4 9.8 | NR | NR | SWE (TOWRE) | PDE (TOWRE) | WJ-RF | NR | NR | NR | NR | WJ-MFF; WJ-CALC; and WJ-BRS |
| Borghesani V, et al. [33] | 2021 | USA | English | Control DYX | 14 26 | 5:9 14:12 | 10.4 ± 1.6 10.4 ± 2.0 | 1st grade and 4th grade | Non-verbal (WASI) | SWE (TOWRE-2) | PDE (TOWRE-2) | Gray Oral Reading Test (GORT-5) | NR | NR | NR | NR | NR |
| Vander Stappen C, et al. [34] | 2020 | France | French | Control DYX | 13 18 | 5:8 9:9 | 10.5 ± 0.8 10.6 ± 1.0 | NR | Non-verbal (WISC-IV) | SWE - BALE | BALE | BALE | Objects; Colors | Syllable and phoneme deletion task | NR | NR | NR |
| El-Sady S, et al. [35] | 2020 | Egypt | Arabic | DYX | 20 | 05:15 | 8.2 ± 1 | NR | SB4 | 1 min reading DAT | nonsense passage reading DAT | 1 min reading DAT | Objects | Phonemic segmentation subtest of DAT | NR | NR | Bead threading; Postural stability; and DS |
| Wang HLS, et al. [36] | 2019 | Taiwan | Mandarin Chinese | Control DYX | 22 24 | NR | 9 ± 0.9 10 ± 1 | Primary school | Non-verbal (WISC-IV) | Chinese character recognition | NR | NR | NR | NR | NR | NR | Lexical tone awareness; auditory identification of FM test |
| Vanderauwera J, et al. [37] | 2019 | Netherlands | Dutch | TR and RD | 34 | 19:15 | 13.7 ± 0.5 | grade 8 (28), 7 (3) and 9 (3) | WISC-III-NL | One-minute word reading test | Klepel test | NR | NA | NA | NA | NA | NR |

Table 1. Cont.

| Ref. | Year | Country | Language | Group | N | Sex (F:M) | Age (Years) | Years of Education (or Level) | IQ | A Word Reading/Spelling | Pseudoword Reading | Text Reading | RAN | Phonological Awareness | Language | Attention | Others |
|---------------------------------|------|-------------|------------------|--|----------------|-----------------------|--|----------------------------------|-------------------------------------|---|----------------------------------|---------------------------------|----------------------------------|--|--|-----------------------------|---|
| Lou C, et al. [38] | 2019 | France | French | Control DYX | 31 26 | 13:18 13:13 | 11.5 ± 1.4 11.6 ± 1.3 | NR | Verbal and Non-verbal (WISC) | Word reading test (Odedys) | Nonword reading test (Odedys) | Alouette test | Digits; Objects | Phoneme deletion and spoonerism | Word spelling-to-dictation test | NR | Verbal WM (DS- WISC) |
| Lebel C, et al. [39] | 2019 | USA | English | Dysfluent inaccurate Dysfluent accurate Non-impaired | 20 36 14 | 5:15 13:23 8:6 | 10.0 ± 1.2 9.4 ± 1.3 9.2 ± 1.2 | NR | WASI FSIQ | SWE (TOWRE); LWID (WJ) | PDE (TOWRE); WA (WJ) | Gray Oral Reading Test (GORT-4) | NR | Phonological Decoding (TOWRE) | NR | NR | NR |
| Banfi C, et al. [40] | 2018 | Austria | German | TR DYX SD | 27 21 21 | 12:15 9:12 6:15 | 9 ± 0.1 9 ± 0.3 10 ± 0.6 | The end of 3rd and 4th grade | Verbal and Non-verbal (WISC) | (SRLT-II); Spelling (DRT-3) | (SRLT-III) | Sentence reading fluency(SLS) | Digits; Objects | PA | Vocabulary standard score (WISC-IV) | Parental questionnaire ADHD | Verbal WM and processing speed (DS, Symbol search WISC-IV) |
| Žarić G, et al. [41] | 2018 | Netherlands | Dutch | TR DYX | 13 15 | 8:5 7:8 | 9 ± 0.8 9 ± 0.6 | 2–3 years of reading instruction | Non-verbal (WISC) | Word reading subtest (3DM) | Pseudoword reading subtest (3DM) | NR | Letters; Digits; Objects | Phoneme deletion; Spelling; and Letter speech sound matching | NR | NR | Memory span (syllables) |
| Su M, et al. [43] | 2018 | China | Mandarin Chinese | Control DYX | 22 18 | 11:11 7:11 | 11 ± 0.8 11 ± 1.0 | Primary school | Non-verbal and Verbal (C-WISC) | Word list reading; Chinese character recognition | NR | NR | Digits | Phoneme deletion | Lexical decision; Morphological production | NR | Verbal WM (Digit recall) |
| Yagle K, et al. [42] | 2017 | USA | English | TR DYG DYX | 10 9 10 | NR | 9–14 | 4–9 grades | Non-Verbal (Wechsler) | Word reading (TOSWRP); word spelling (TOC) | Nonword reading | NR | NR | NR | NR | NR | NR |
| Christodoulou JA, et al. [44] | 2016 | USA | English | TR DYX | 26 26 | NR | 7.8 ± 0.6 7.8 ± 0.6 | NR | Non-verbal (KBIT-2) | WID (WRMT-III); SWE (TOWRE-2) | WA (WRMT-III); PDE (TOWRE-2) | NR | NR | NR | NR | NR | NR |
| Zhao JT, et al. [45] | 2016 | France | French | Control DYX | 31 26 | 13:18 13:13 | 11.5 ± 1.3 11.6 ± 1.3 | NR | Verbal and Non-verbal (WISC) | Word reading fluency (Odedys); Word spelling | Nonword reading fluency (Odedys) | Alouette Test | Digits; Objects | Word spelling-to-dictation test, Spoonerism | NR | NR | DS (WISC) |
| Koerte IK, et al. [46] | 2015 | Germany | German | Control DYX | 24 16 | 0:24 0:16 | 9.9 ± 0.3 9.7 ± 0.4 | 3rd and 4th grades | Non-verbal (CFT-20R) | SLRT-II | SLRT-II | NR | Digits, Letters, Colors, Objects | Phoneme deletion | NR | NR | DS (K-ABC); Verbal WM (Wechsler); Arithmetic test (HRT 1-4); and Number line task (WRT 1-4) |
| Garcia-Zapirain BC, et al. [47] | 2016 | Spain | Spanish | TR DYX MVR | 19 20 18 | 8:11 8:12 8:10 | 10.0 ± 0.9 10.5 ± 1.1 10.4 ± 0.9 | NR | Verbal and Non-verbal (WISC-IV) | Word reading (PROLEC-R) | Pseudoword reading (PROLEC-R) | ELFE 1-6 | NR | NR | NR | NR | WM |
| Fernandez VG, et al. [48] | 2016 | USA | English | TR DYX | 27 29 | 15:12 14:15 | 10.1 ± 2.1 12.1 ± 2.5 | 6–8 grades | Verbal and non-verbal (KBIT-2, SB4) | LWI (WJ-III); WRAT-3; and SWE (TOWRE) | PDE (TOWRE) | PC (WJ-III-TA) | NR | NR | NR | NR | NR |
| De Moura LM, et al. [49] | 2016 | Brazil | Portuguese | TR RD | 23 17 | 12:11 9:8 | 9.7 ± 0.9 9.2 ± 0.9 | NR | Verbal and Non-verbal (WISC-III) | Aloud reading (TDE) | NR | NR | NR | NR | NR | NR | NR |
| Richards TL, et al. [50] | 2015 | USA | English | Control DYX DYG | 9 17 14 | 5:4 7:10 3:11 | mean of 12.25 (from 9 to 15.6) | 4–9 grades | Verbal (WISC-IV) | Spelling dictated words (WIAT III); Sight Spelling (TOC) | NR | NR | NR | NR | NR | NR | Best and Fast writing (DASH) |

Table 1. Cont.

| Ref. | Year | Country | Language | Group | N | Sex (F:M) | Age (Years) | Years of Education (or Level) | IQ | A Word Reading/Spelling | Pseudoword Reading | Text Reading | RAN | Phonological Awareness | Language | Attention | Others |
|-----------------------------|------|-------------|----------|--|----------------------|---------------------------|--|--|-------------------------------------|---|-----------------------------|--|--|--|----------|------------------|---|
| Marino C, et al. [51] | 2014 | Italy | Italian | TR FRD+ TR FRD− DYX FRD+ DYX FRD− | 10 16 11 10 | 5:5 6:10 6:5 4:6 | 19.1 ± 1.9 18.7 ± 2.4 17.5 ± 2.4 16.4 ± 1.0 | 12.8 ± 1.5 12.0 ± 1.1 10.2 ± 1.8 10.8 ± 1.2 | Full-scale IQ (WISC-R) | Word reading(BVDDE); Spelling (BVDE) | Non-word reading (BVDDE) | Sentences containing homophones | NR | Spoonerism, phonemic blending, and syllable displacement (PA) | NR | NR | ADC, letter and number forward/backward span (TEMA) |
| Fan Q, et al. [52] | 2014 | USA | English | Control DYX | 20 19 | 9:11 8:11 | 12.0 ± 0.7 12.0 ± 0.7 | NR | Verbal and Non-verbal (WISC-IV) | LWID (WJ-III); SWE (TOWRE); and FLI and spelling (WIST) | WA (WJ-III); PDE (TOWRE) | PC and basic reading (WJ-III); TOSCRF | Color Digit Objects (CTOPP) | NR | NR | NR | NR |
| Fan Q, et al. [53] | 2014 | USA | English | TR RD | 16 20 | 8:8 8:12 | 11.7 ± 0.7 12.1 ± 0.7 | NR | Verbal and Non-verbal (WISC-IV) | LWID (WJ-III); SWE (TOWRE); and FLI (WIST) | WA (WJ-III); PDE (TOWRE) | NR | NR | WJ-III-PC | NR | NR | NR |
| Hasan KM, et al. [54] | 2012 | USA | English | TR DYX CFP | 11 24 15 | 3:8 11:1 39:6 | 12.8 ± 1.7 13.7 ± 1.0 13.5 ± 0.8 | NR | Composite IQ (KBIT-2, SB4) | LWID (WJ-III); SWE (TOWRE) | PDE (TOWRE) | PC (WJ-III) | NR | NR | NR | NR | NR |
| Gebauer D, et al. [55] | 2012 | Austria | German | Control SI SRI | 11 11 9 | NR | 12.3 ± 1.9 11.7 ± 1.6 11.3 ± 0.7 | 4th–5th 5–9 graders | Non-verbal (Raven) | SLS 1-4 or 5-8; Spelling (HSP) | SLS 1-4 or 5-8 | ELFE 1-6 | NR | NR | NR | NR | Personality assessment FFQ (Asendropf) |
| Hoefl F, et al. [56] | 2011 | USA | English | Control DYX (rg) DYX (nrg) | 20 13 12 | 14:6 6:7 7:5 | 11.0 ± 2.6 14.5 ± 1.6 13.5 ± 2.2 | NR | Non-verbal (WASI) | (WRMT) *; SWE (TOWRE); and Spelling and writing fluency (WJ) | WA (WRMT); PDE (TOWRE) | Gray Oral Reading Test(GORT); PC (WRMT) | Colors; Objects; Numbers; and Letters | NR | PPVT | NR | MD (CTOPP) |
| Sihvonen AJ, et al. [57] | 2021 | Finland | Finnish | Control DYX | 21 23 | 11:10 12:11 | 29.9 ± 6.0 31.3 ± 8.6 | 16.1 ± 4.4 15.7 ± 5.2 | Verbal (WAIS-III); PIQ (WAIS-IV) | Word List Reading | Pseudoword List Reading | Text Reading | Test not specified | Fig Latin; PA; phonological short-term memory; and rapid access of information | NR | ASRS v1.1 | ARHQ; Verbal WM (Non-word Span Length, WMS-III) |
| Tschentscher N, et al. [58] | 2019 | Germany | German | Control DYX | 12 12 | 0:12 0:12 | 23.7 ± 2.6 24.2 ± 2.3 | NR | Nonverbal (Raven) | Spelling | NR | Reading speed and comprehension | Letters and Numbers | NR | NR | NR | NR |
| Moreau D, et al. [59] | 2018 | New Zealand | English | Control Dyscalc DYX Comorbid | 11 11 11 12 | 4:7 5:6 5:6 5:7 | 27.7 ± 1.7 32 ± 2.2 29.4 ± 1.9 33.2 ± 1.7 | 15.2 ± 0.60 14.6 ± 0.56 15.6 ± 0.51 14.8 ± 0.61 | FSIQ (WASI) | WID (WJ) | WA (WJ) | NR | NR | WRAT spelling | NR | WRAT mathematics | |
| Müller-Axt C, et al. [60] | 2017 | Germany | German | Control DYX | 12 12 | 0:12 0:12 | 23.7 ± 2.6 24.2 ± 2.4 | Undergraduate students ** | Non-verbal (Raven) | Spelling | NR | NR | Numbers; Letters | NR | NR | NR | NR |
| Vandermosten M, et al. [61] | 2013 | Belgium | Dutch | TR DYX | 20 20 | 12:8 13:7 | 21.4 ± 3.0 22.1 ± 3.1 | NR | Non-verbal (WAIS-III) | Word reading; Spelling | Pseudoword reading | NR | NR | NR | NR | NR | NR |
| Lebel C, et al. [62] | 2013 | USA | English | RLD | 136 | 64:1300 | 20.1 ± 3.1 | NR | FSIQ (WASI) | WID (WJ) | WA (WJ) | Fluency (GORT) | NR | NR | NR | NR | NR |

Table 1. Cont.

| Ref. | Year | Country | Language | Group | N | Sex (F:M) | Age (Years) | Years of Education (or Level) | IQ | A Word Reading/Spelling | Pseudoword Reading | Text Reading | RAN | Phonological Awareness | Language | Attention | Others |
|-----------------------------|------|---------|----------|--------------|----------|--------------|--------------------------|-------------------------------|--------------------|-------------------------|--------------------|-------------------------------|--|-------------------------------------|---|--|--------|
| Vandermosten M. et al. [63] | 2012 | Belgium | Dutch | TR DYX | 20 20 | 12:8 13:7 | 21.4 ± 3.0 22.1 ± 3.1 | NR | Non-verbal (WAIS) | Word reading; Spelling | Pseudoword reading | NR | NR | PA; Phoneme deletion and Spoonerism | Speech-in-noise perception (Dutch LIST) | NR | NR |
| Frye RE. et al. [64] | 2011 | USA | English | TR DYX/PR | 20 10 | 10:10 5:5 | 23.7 ± 0.7 23.9 ± 1.6 | NR | Non-verbal (CTONI) | LWI (WJ-III); Spelling | WA (WJ-III) | Gray Oral Reading Test (GORT) | Colors (CTOPP); Digits (CTOPP); Objects (CTOPP); Letters (CTOPP) | PA (CTOPP); APA (CTOPP) | NR | Test of variables of attention: commissions, omissions | NR |

Note: Bold font indicates significant group differences. * time effect in DYX group, ** only 1 control had a high school diploma. Abbreviations: NA: Not Applicable; NR: Not Reported; FRD+: Children with Familial Risk for Dyslexia; FRD−: Children without Familial Risk for Dyslexia; TR: Typical reading; rg: reading gain; nrg: no rg; m: months; RAN: rapid automatized naming tasks; DYX: children with dyslexia; RD: Reading Disorder; RI: Reading Impairment; PreR: pre-reader children; BR: older reader children; FR: fluent reader children; PIQ: Performance IQ; FSIQ: Full-Scale Intelligence Quotient; CFT 20-R: Cattell's Fluid Intelligence Test, Scale 2; TrR: Treatment Responders; EF: Executive Functions; MD: Mood Disorders; WRD: word recognition deficits; RLD: reading and learning disabilities; SI: spelling impaired children; SRI: children with spelling and reading impairment; CFP: readers with comprehension or fluency problems; PA: Phonological awareness; PPVT: Peabody Picture Vocabulary Test; TONI or TONI-4: Test of Nonverbal Intelligence; CTONI: Comprehensive TONI; CTOPP: Comprehensive Test of Phonological Processing; TOWRE or TOWRE-2: Test of Word Reading Efficiency; WJ: the Reading Fluency subtest of the Woodcock-Johnson Test; WISC or WISC-IV: Wechsler Intelligence Scale for Children, 4th edition; WASI: Wechsler Abbreviated Scale of Intelligence; WAIS: Wechsler Adult Intelligence Scale, 3rd edition; WIAT: Wechsler Individual Achievement Test; BRIEF: Behaviour Rating Inventory of Executive Function; KBIT or KBIT-2: Kaufman Brief Intelligence Test; WRMT-R NU: Woodcock Reading Mastery Tests-Revised, Normative Update; WA: Word attention; SLRT-II: The Salzburg Reading and Spelling Test; YARC: York Assessment of Reading for Comprehension; GAPS: Grammar and Phonology Screening; CELF or CELF-4: Clinical Evaluation of Language Fundamentals; KTEA-II: Kaufman Test of Educational Achievement-Second Edition; CVLT: California Verbal Learning Test; WID: word identification; LWID: letter and WID; VAS: Visual Attention Span; SB4: Stanford-Binet Intelligence Scales-Fouth Edition; HLE: Home Literacy Environment; HOME: the Home Observation for Measurement of the Environment; DAT: Dyslexia Assessment Test; ASRS: Adult Self Report Scale for ADHD clinical assessment; TOC: Test of Orthographic Competence; TOMAL2: Test of Memory and Learning - Second Edition; MSEL: Mullen Scales of Early Learning; ARHQ: Adult Reading History Questionnaire; ADC: Adult Dyslexia Checklist; HSP: Hamburger-Schreibprobe; SLS: Salzburger-Lese-Sreening; FFQ: five factor questionnaire; DAWBA: Diagnostic and Well-Being Assessment; SWE: Sight Word Efficiency; DS: digit span; VSA: visual spatial attention; BISC: Bielefeld screening of literacy precursor abilities; DERET: German spelling test; SETK 3-5: a developmental German language test for children between 3 and 5 years of age; BAKO: Test of basic reading and spelling skills; PDE: Phonemic Decoding Efficiency; TOSWRF or TOSWRF-2: Test of Silent Word Reading Fluency, Second Edition; GORT: Grey Oral Reading Test; PC: Passage comprehension; ODEDYS: dyslexia screening tool; DKEFS: Delis-Kaplan Executive Function System; BALE: Analytic Battery of Written Language; DRT-3: Spelling percentile; 3DM: differential diagnostics for dyslexia; HRT: Heidelberger Rechentest; WRT: Weingartener Grundwortschatz Rechtschreibtest; PROLEC: Text Comprehension task; WRAT: Wide Range Achievement Test; TDE: test for School Achievement; DASH: Detailed Assessment of Speed of Handwriting; FLI: Fundamental Literacy Index; WIST: Word Identification and Spelling Test; ELFE: standardized achievement tests; TEMA: Test di Memoria e Apprendimento; BVDDE: Battery for the Assessment of Developmental Reading and Spelling Disabilities; and WM: working memory.

Another important aspect is that dyslexia can manifest similarly across languages, but the characteristics and challenges may vary based on the language's structure, writing system, and phonological rules. Because of this, we include the demographic characteristics of the country and the language participants spoke. The pre-reader studies were done mainly in the United States with English language speakers (50%) [16–18,22], followed by 40% [20,21,23] in Belgium with Dutch speakers, and 10% [19] in Germany with German speakers, including young children under 6 years old male and females and balanced distribution (a total of 193 females to 215 males) and with a sample variation of 10 to 46 children in each comparison group. In studies with reading-stage children, 47% spoke English—from the USA (45%) [25,27,31–33,39,42,44,48,50,52–54,56] and Canada (2%) [28,29]; 17% spoke French (the study was carried out in France [26,30,34,38,45]); 11% spoke Dutch—the studies were carried out in Belgium and Netherlands [37,41]; 8% were German; 6% spoke Mandarin—the studies were carried out in China [43] and Taiwan [36]; and 3% of studies were done with speakers of Arabic (Egypt) [35], Spanish (from Spain) [47], Portuguese (from Brazil) [49], or Italian (from Italy) [51]. In adults, the language of studies was less varied: 38% spoke English, and the studies were carried out in New Zealand [59] and the USA [62,64]; 25% spoke German (Germany) [58,60], 25% Dutch (Belgium) [61,63], and 12% Finnish (Finland) [57] (Table 1).

The neuropsychological characterization of the studied subjects followed the specificity of dyslexia diagnostic criteria, that the neuropsychological tests that were used included assessment of intelligence quotient (IQ); word and non-word reading and spelling tests; reading comprehension tests; rapid automatized naming (RAN); phonological awareness; and language, attention, and executive functions (description in Table 1). The primary purpose of the neuropsychological evaluation was to compare the performance of the dyslexic groups with the control group.

In the pre-reader, the intelligence was evaluated only by non-verbal tests, and only one study [16] showed a significant difference, with a worse performance of a risk of dyslexic children compared to the typically developing ones. One study did not report an intelligence assessment, possibly due to the very early age of participants [18]. In the reader children group, almost all studies evaluated the IQ (94.6%) with 51.4% by non-verbal and verbal IQ tests [25–27,30,31,38–40,45,47–49,52–54], 40.5% with only non-verbal tests [25,28,33,34,36,41,44,46,55,56], and 2.7% with only the verbal tests [50]. The significant difference between groups occurred in 34.3% of studies in verbal IQ tests and only 5.9% in non-verbal IQ tests. In the adult readers, 57.1% of the studies were administered non-verbal IQ tests [57,60,61,63,64] and only 28.6% showed significant differences with worse outcomes for dyslexic adults.

Concerning reading skills, in pre-readers, 89% [16,17,19–23] of studies assessed the children by word, letters, or pseudoword reading, and out of these 44% [16,17,19,21–23] had significantly lower outcome compared to the control group. In this age range, the RAN was also generally employed (78%) [16,17,19,20,22,23], with objects and colors being the most commonly used items (56%). A significant difference was found in naming speeds, mainly for slower naming of objects by dyslexic children in 44% of studies of this population. The phonological awareness was also mostly assessed (75%) [16,17,19–23], and in 25% of studies performance was lower in dyslexic groups. As for the other cognitive functions, attention was assessed in just one study [19], and the findings on working memory, digit span, visual reception, and gross and fine motor were also seldom reported.

Regarding the reader children, in all of the studies the reading skills were assessed by the word reading, and as would be expected lower performance of children with dyslexia compared to controls was found in 79% of studies [24,27,30–34,38–56]. Other significant between-group differences with worse outcomes for dyslexic children were reported for pseudoword reading (70% [24,27,28,30–34,38–41,44–48,51–56] out of 85% assessed studies) and text reading (39% [24,30,32,34,39,40,45,46,51,52,54–56] out of 64% assessed studies). In 45% of all studies, the phonological awareness was assessed [24,26,27,31,34,35,38–41,43,45,46,51,53], and 39% of studies [24,26,27,31,34,38–41,43,45,46,51,53] produced significant results when compared between

groups. When assessing RAN, 39% of studies evaluated this ability [24,26,29,34,35,38,40,41,43,45,46,52,56], and 33% found a significantly worse outcome for the dyslexic children when compared between groups [24,26,34,38,40,41,43,45,46,52,56]. A small number of studies (9%) assessed language [38,43,56] and attention [24,27,40]; however, almost all of these studies showed worse performance of subjects with dyslexia when compared to the controls. Half of the studies reported results of other cognitive functions in different aspects of short-term memory (digit span 33.3%) [24,26,27,38,40,45,46], verbal working memory (33.3%) [24,26,38,40,43,46], working memory (17%) [41,47], and arithmetic or mood behavior (11%) [46,56]. Almost all of these assessments also reported significant between-group differences and lower outcomes for participants with dyslexia.

For the reading adults, 100% of studies assessed volunteers for the word and/or pseudoword reading [57–64]. In 37.5% of the studies [57,58,62,64], text reading was tested, and all tests produced significant findings that allowed the groups to be distinguished based on the lower performance of the dyslexic group. Only 50% of these studies that tested RAN and phonological awareness showed significant group differences [57,59,63,64], and 25% assessed language and attention domains [57,59], without significant group differences.

Considering the neuropsychological outcome of reading children in the three language groups most represented in this revision (English, French, and Dutch), there was no difference in the cognitive skills found impaired in dyslexic volunteers compared to the controls.

3.3. Brain Structural Connectivity Characteristics on Acquisition, Process, and Outcomes of Dyslexia

The structural analysis through the DTI acquisition was performed in 88% of studies in high-field MRI equipment (3T) (scanner by manufacturers: Siemens (Berlin, Germany) (49%) [16–19,22,24–26,30–32,34,36,38,40,41,43–46,55,57,58,60], Philips (Eindhoven, Netherlands) (35%) [20,21,23,27,33,37,47,48,50–54,61,63,64], General Electric (GE, New York, United States of America) (4%)) [28,56] and 10% in low-field (1.5T) (scanner by manufacturers: Siemens (6%) [39,59,62], Philips or GE (2%)) [35,49]) used in the acquisition of older participants such as reader children (more than 7 year old) and adults (more than 18 year old), as shown in Table 2.

Table 2. DTI acquisition, image processing, and outcomes.

| Ref | MRI Field | Sequence | TR/TE (ms) | DTI Acquisition | | | | | N. of Diffusion Gradients | Time | Software | Corrections | DTI Processing | | Atlas | ROIs/ TRACTS | Tracts Difference between Groups | DTI Outcomes | |
|-------------------------------|------------|----------|------------|-----------------|----------------------|----------|------------------------------|----|---------------------------|--|--|------------------|------------------|--------------------|---|--|---|-----------------------|--|
| | | | | Slice Number | Slice Thickness (mm) | FOV (mm) | b-Value (s/mm ²) | | | | | | Type of Analyses | DTI Metrics | | | | Clinical Correlations | |
| Zuk J, et al. [16] | Siemens 3T | DTI | NR | 30 | 2 | 128x128 | 0; 700 | NR | NR | DTIprep, VISTALab | EC, HM (>2 mm or >0.5°) | ROI | FA | NR | AF, SLF | ↑FA in r-SLF of FHD+ TR compared to FHD− TR and FHD+ RD | r-SLF FA, age, gender, parent education, occupation, and phonological awareness significantly predicted decoding skills among children FHD+ | | |
| Yu X, et al. [17] | Siemens 3T | DTI | NR | NR | 2 | NR | 0; 700; 1000 | NR | NR | DTIprep, VISTALab, AFQ | EC, HM (>2 mm/0.5°), bed vibration, pulsation, venetian blind artifacts, and slice and gradient-wise intensity inconsistencies | Whole brain; ROI | FA | MNI, Native space | Right of SLF, ILF, and AF, sCC, CC2 | ↑FA in r-sCC of FHD+ TR compared to FHD− TR | R-sCC FA had positive correlation with r-IFG activation for FHD−/+ TR | | |
| Langer N, et al. [18] | Siemens 3T | DTI | 8320/88 | 64 | 2 | 256x256 | 1000 | 30 | 5:59 min | DTIprep, FSL (DTIFIT), Trackvis (Diffusion Toolkit), Trackvis, AFQ | EC and HM (>2 mm and 0.5°) | Whole brain; ROI | FA RD AD | MNI | Bilateral AF and CS | ↓FA in l-AF (central portion) FHD+ compared with FHD−, corrected by age | l-AF FA has positive correlation with age, expressive language | | |
| Kraft I, et al. [19] | Siemens 3T | DTI | 8000/NR | 66 | 1.9 | NR | 1000 | 60 | 32 min | FSL (Topup tool), FSL (DTIFIT), MRTrix | EC, HM, and susceptibility-induced distortions | ROI | FA | Destrieux Atlas | SMG, ITG (anterior, long, and posterior AF), SOS/TOS, IFoG, IFobG | No group difference | l-aAF was the best predictor of DYX | | |
| Vandermosten M, et al. [20] | Philips 3T | DTI | 7600/65 | 58 | 2.5 | 200x240 | 1300 | 60 | 10 min 32 s | Explore DTL, Trackvis | EC, HM (6 parameters) Reorientation of the b-matrix Motion as covariate | Whole brain; ROI | FA | TrackVis | AF (dorsal FTP, dorsal post TP), ventral IFOF | ↓FA in l-IFOF of FHD+ | Phonological awareness positive correlation with FA of l-AF(TP) and bilateral IFOF/AF-FTP, as also left ventral tracts in FHD+ | | |
| Van Der Auwera S, et al. [21] | Philips 3T | DTI | 7600/65 | NR | 2.5 | NR | 1300 | 60 | 10:32 min | FSL, VISTALab, AFQ | EC, HM by root mean square | Whole brain; ROI | FA MD | NR | AF | ↓FA in the l-AF in pre-reader RDs | aAF FA was a significant predictor for scores on word reading tests from 2nd grade | | |
| Wang Y, et al. [22] | Siemens 3T | DTI | 8320/88 | NR | NR | 256x256 | 1000 | 30 | 5:59 min | DTIprep, VISTALab, AFQ | EC, HM (>2 mm and >0.5°) | Whole brain; ROI | FA AD RD | white matter atlas | Left of AF, SLF, ILF | ↓l-AF FA at pre-reader FHD+ versus FHD− and for poor versus good readers all ages; FHD+ good readers had faster WM development in r-SLF compared to poor readers | l-AF and ILF FA positive correlations with word identification skill | | |
| Vanderauwera J, et al. [23] | Philips 3T | DTI | 7600/65 | NR | 2.5 | NR | 1300 | 60 | 10:32 min | ExploreDTL, Trackvis | EC, HM | ROI | FA | native space | Long, anterior and posterior dorsal AF, and ventral IFOF | ↑FA in all groups over time. ↓ long AF FA in DYX prior to reading onset, right also kept in early reading. Influence of FHD+ in l-IFOF and long r-AF | FHD+ and rapid naming predicted 80.3% of cases; the l-longAF FA values predicted 84.4% of DYX cases | | |

Table 2. Cont.

| Ref | MRI Field | Sequence | TR/TE (ms) | DTI Acquisition | | | | b-Value (s/mm ²) | N. of Diffusion Gradients | Time | Software | Corrections | DTI Processing | | Atlas | ROIs/ TRACTS | Tracts Difference between Groups | DTI Outcomes | |
|-------------------------|-------------|----------|---------------|-----------------|----------------------|-------------|------------------|------------------------------|---------------------------|--|--|------------------|------------------|-----------------------------------|--|--|---|--------------|--|
| | | | | Slice Number | Slice Thickness (mm) | FOV (mm) | Type of Analyses | | | | | | DTI Metrics | Clinical Correlations | | | | | |
| Zhao J. et al. [24] | Siemens 3T | DTI | 14,000/91 | 70 | 1.7 | 218 | 1400 | 60 | 18 min | Explore DTI, Trackvis, FSL | NR | Whole brain | FA | TrackVis MNI-152 | UF, FAT | Males DYX had a ↓HMOA in the UF compared with males TR | HMOA of the UF showed a positive correlation with VAS in DYXs | | |
| Meisler SL, [25] | Siemens 3T | DKI | 3320/100.2 | NR | 1.8 | NR | 0; 1000; 2000 | 64 | NR | QSIprep, MRtrix, FSL, and TractSeg | Gibbs unringing, EC, HM, and AP-PA field | Whole brain | FA | FSL and MNI | AF, SLF (I, II, and III), ILF, IFOF, UF, SCP, ICP, MCP, and sCC | No group difference | Age and sex with gFA positive correlation; in older children, FA in r-SLF and I-ICP related to nonword reading skills | | |
| Liu T. et al. [26] | Siemens 3T | DTI | 14,000/91 | 70 | 1.7 | 218 | 1400 | 60 | 18 min | PANDA, FSL, and Trackvis | EC | Whole brain | FA | MNI and AAL atlas | 90 ROIs of AAL | NR | Positive correlation between node FA for I-SOG and VAS score, I-MTG and I-ORBSupmed and phonological score | | |
| Farah R. et al. [27] | Phillips 3T | DTI | 6652.446/82.6 | 160 | 2 | 224x120x224 | 1000 | 61 | 7 min 25 s | VISTALab, AFQ | EC, HM | Whole brain; ROI | FA | NR | AF, SLE, ILF | ↓ FA in the left of AE, ILF, and SLF in RD | ↓ FA in the I-SLF positive correlated with reading and working memory score in DYX | | |
| Partanen M. et al. [28] | GE 3T | DTI | 7000/60 | 60 | 2 | 256x256 | 0; 1000 | 60 | 7.5 min | TORTOISE, FDT (FSL), DTIFIT (FSL), and PROBRACKX (FSL) | EC, HM | Whole brain; ROI | FA MD | MNI305 and Desikan–Killiany atlas | bilateral IFG, Ins, STG, SMG, AnG, and FFG | ↑MD in bilateral Ins; I-IFG, I-STG, and r-SMG in DYX | SMG, r-IFoG, and I-Ins MD had negative correlation with reading gains and decoding, respectively | | |
| Lou C. et al. [29] | Siemens 3T | DTI | 3000/50.6 | 64 | 2 | 256x256 | 0; 1000 | 56 | NR | ExploreDTI | EC, HM, EPI distortions | Whole brain; ROI | FA | AAL and MNI152 | 90 ROIs of AAL | NR | IFoG and IfoG, Ins, FFG, IPL, SMG, AnG, HG, STG, MTG, ITG, IOG, PreCG, ROI, and thalamus in the left hemisphere positive correlated with reading efficiency and phonemic decoding, mainly for girls DYX | | |
| Liu T. et al. [30] | Siemens 3T | DTI | 14,000/91 | 70 | 1.7 | 218x218 | 0; 1400 | 60 | 18 min | PANDA, FSL | EC, HM | Whole brain; ROI | FA | AAL and MNI | 90 ROIs of AAL | NR | Negative correlation between READACC (pseudoword/word reading) and the r-FFG FA in DYX | | |
| Koirala N. et al. [31] | Siemens 3T | DTI | NR | NR | 1.8 | NR | 0; 1000; 2000 | 64 | NR | FSL (QUAD), FSL (DTIFIT), and FSL (BEDPOSTX), XTRACT | Susceptibility, EC, and HM | Whole brain; ROI | FA MD RD ODI NDI | Native space | 23 tracts (including SLE, which seeds were central sulcus, SFG, ACG, MFG, and AnG) | NR | Positive correlation between phonological processing and the left IFOF, MDL, SLF2, VOF, CBD and FX FA, and the I-UF MD | | |
| Huber E. et al. [32] | Phillips 3T | DKI | NR | NR | 2 | NR | 0; 800; 2000 | 32 and 64 | NR | FSL, DIPY, MRtrix, and AFQ | AP-PA, EC, Mean slice-by-slice displacement > 3 mm | Whole brain | FA MD AWF Da MDc | NR | AE, CS, UF, SLE, ILF, ThR, FMj, FMn, and IFOF | I-AF MD difference for Group x time interaction | Positive correlation between MD of I-AF, UF, I-ILF, I-HFOF, FMj, MDc of left of AE, UF, ILF, IFOF, and FMj with word reading and negative correlation between AWF of right ILF, IFOF, and FMn with word reading | | |

Table 2. Cont.

| Ref | MRI Field | Sequence | TR/TE (ms) | DTI Acquisition | | | | b-Value (s/mm ²) | N. of Diffusion Gradients | Time | Software | Corrections | DTI Processing | | Atlas | ROIs/ TRACTS | Tracts Difference between Groups | DTI Outcomes | |
|-------------------------------|--------------|----------|------------|-----------------|----------------------|---------------|------------------|------------------------------|---------------------------|-------------------------------|---|------------------|----------------|--------------------------------------|---|------------------------------------|----------------------------------|---|--|
| | | | | Slice Number | Slice Thickness (mm) | FOV (mm) | Type of Analyses | | | | | | DTI Metrics | Clinical Correlations | | | | | |
| Borghesani V, et al. [33] | Siemens 3T | DKI | 8200/86 | 60 | 2.2 | 220x220 | 0; 700; 20,000 | 30 and 64 | 15 min | FSL (NODDI model), FS-TRACULA | AP-PA, EC, and HM | Voxel-based; ROI | NDI ODI | FSL, Desikan–Killiany Atlas and MNI | I-VOT | ↑ODI in DYS at the I-VOT | | NR | |
| Vander Stappen C, et al. [34] | Philips 3T | DTI | 6422/83 | 70 | 2 | 224x224 | 800 | 55 | NR | BrainVoyager | EC, HM | ROI | FA | Talairach space | AF, IFOF, and ILF | NR | | RAN Gains negative correlated with FA in the I-long aAF, and the r-pAF, a reduction in naming times was linked to an increase in FA in those tracts at DYX | |
| El-Sady S, et al. [35] | Philips 1.5T | DTI | NR | 70 | 2 | 230x230 | NR | 32 | NR | NR | EC, HM | ROI | FA ADC | NR | SLF, AF, CR, PLIC of CS | NR | | Negative correlation between r-AF FA and at-risk quotient, l-sCR ADC with writing, and r-SLF ADC with bDS and positive with VF. Positive correlation between l-SLF-aCR FA and RAN, spelling, and VF, as r-PLIC ADC with writhing, and l-aCR ADC with bDS | |
| Wang HLS, et al. [36] | Siemens 3T | DTI | 6700/97 | NR | 2.7 | NR | 5000 | 128 | NR | DSI Studio | NR | Whole brain | NR | MNI, AAL atlas | IFOF, CC, cerebellar, and Tha-pontine tracts | NR | | I-IFOF, cerebellar, and Tha-pontine tracts had positive correlated with chinese character recognition; pCC association with auditory FM processing in DD | |
| Vanderauwera J, et al. [37] | Phillips 3T | DTI | 8872/2.5 | 55 | 2.5 | 240x240x137.5 | 1000 | 60 | 13:52 min | ExploreDTI, Trackvis | HM (>1.5 mm) and EC | ROI | FA | Native Space | AF, IFOF, UF, and ILF | NR | | Word reading had positive correlation with l-long-AF FA and negative with l-long-AF RD and UF RD. Paternal educational level had positive correlation with l-long AF FA, and UF FA; after covariate by HM, only the l-UF remained significant | |
| Lou C, et al. [38] | Siemens 3T | DTI | 14,000/91 | 70 | 1.7 | 218 | 0; 1400 | 60 | 18 min (3x6 min) | ExploreDTI, FSL (FLIRT) | EC, HM | Whole brain | FA | AAL atlas; MNI; Harvard-Oxford atlas | Left of MTG-MOG, MOG-TPOsup, TPOsup-HG, HG-ROL, Ins-ROL, STG-Ins, and Ins-SMG | ↓mean FA in DYX for all ROIs | | Literacy skills had positive correlation with clustering coefficient, local efficiency, transitivity, and global efficiency, in DYX | |
| Lebel C, et al. [39] | Siemens 1.5T | SE EPI | 9000/85 | 28 | 5 | 240x240 | 1000 | NR | 7:24 min | FSL | Motion artifacts (signal drop out, venetian blind artifact, and mechanical vibration artifact, >10), EC | ROI | FA MD AD RD | MNI; JHU ICBM-DTI-81 atlas | sCC, ALIC of CS, aCR, pCR, SS (includes the ILF and IFOF), UF, and SLF | ↓MD in r-CR, and l-UF in DYX | | Age had a positive correlation with pCR, r-SLF FA, negative with pCR, l-UF MD. Sight words and VF were positively correlated with l-SLF FA and MD, respectively, as well as with l-pCR MD. Phonological decoding had a negative correlation with r-pCR MD and mean MD and positive with mean FA | |
| Bañfí C, et al. [40] | Siemens 3T | DTI | 3400/105 | 48 | 2.5 | 240 | 0; 2000 | 64 | NR | MRTrix, FSL, and AFQ | AP-PA, EC, HM, and susceptibility-induced distortion | Whole brain | FA | NR | ThR, FMj, FMn, IFOF, ILF, SLF, and AF, UF, CS, and CG | ↑FA in ILF, r-SLF, and r-CG in DYX | | Negative correlation between r-ILF FA and reading measures, controlling for spelling. | |

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| Ref | MRI Field | Sequence | TR/TE (ms) | DTI Acquisition | | | b-Value (s/mm ²) | N. of Diffusion Gradients | Time | Software | Corrections | DTI Processing | | Atlas | ROIs/ TRACTS | Tracts Difference between Groups | DTI Outcomes | |
|---------------------------------|------------|----------|--|-----------------|----------------------|-------------|------------------------------|---------------------------|---------------------|---------------------------------------|---|-----------------------|----------------------------|-------------------------------|---|--|--|--|
| | | | | Slice Number | Slice Thickness (mm) | FOV (mm) | | | | | | Type of Analyses | DTI Metrics | | | | Clinical Correlations | |
| Žarić G, et al. [41] | Siemens 3T | DTI | 10,800/84(protocol1) 11,000/85(protocol2) | 85 | 1.8 | NR | 0; 1000 | 72 | 15 min | VISTALab (mrDiffusion), SPM, AFQ | EC, HM and phase-encoding direction corrections | Whole brain; ROI | FA | NR | AF, SLF, ILF, IFOF, UF, ICS, antThR, FMn, and FMj | ↑FA in the AF, r-SLF, and aThR in DYX | r-SLF showed age effects that differed between groups. Age effect in ILF FA, and CC (FMj and FMn). L-aThR positive correlation with age appropriate reading accuracy scores | |
| Su M, Zhao J, et al. [43] | Siemens 3T | DTI | 8000/89 | NR | 2.2 | 282x282 | 0; 1000 | 30 | NR (repeated twice) | ExploreDTI, Trackvis, and FSL | EC and HM | Whole brain; ROI | FA RD AD | MNI152; native space | AF, IFOF, and ILF | ↓FA and AD in the l-AF and l-ILF in DYX | AF and ILF FA positive correlation with character recognition, digit recall, phoneme deletion (only AF), and morphological production (only ILF). ILF FA negative correlation with RAN | |
| Yagle K, et al. [42] | NR | DTI | 8593/78 | NR | 2 | 220x220x128 | 0; 1000 | 32 | 9:35 min | FSL | NR | ROI | FA RA AD RD MD | NR | OR, CS, ILF, SLF, and CG | ↓FA in l-OR in DYX | NR | |
| Christodoulou JA, et al. [44] | Siemens 3T | DTI | 9300/84 | 74 | 2 | 256 | 0; 700 | 30 | NR | FS-TRACULA, DTIprep, and FSL (FLIRT) | EC, HM | Tract-based | FA AD RD | MNI152 | SLF, AF | ↓FA in the l-AF in RDs | Positive correlation of l-AF FA and negative DA with real-word reading | |
| Zhao JT, et al. [45] | Siemens 3T | DTI | 14,000/91 | 70 | 1.7 | 218 | 0; 1400 | 60 | 18 min | ExploreDTI, FSL, and Trackvis | Motion corrections | Whole brain; HMOA ROI | HMOA FA | MNI152 | IFOF, ILF, SLF, and AF | ↓FA of r-IFOF and l-SLF in DYX | r-IFOF FA negative correlation with reading and spelling accuracy | |
| Koerte IK, et al. [46] | Siemens 3T | NR | 9600/110 | 65 | 2 | 208 | 0; 1000 | 30 | NR | 3DSlicer, FSL (FLIRT), and FSL (TBSS) | EC, HM | Tract-based | FA AD RD trace | MNI152 | NR | No group difference | Positive correlation arithmetic test with FA and AD and negative with RD (Temporo-parietal) | |
| Garcia-Zapirain BC, et al. [47] | Philips 3T | DTI | 6819/81 | 60 | 2 | 224x224 | 800 | 15 | 7min | FSL (BET), FSL (FDT), and FSL (TBSS) | NR | Whole-brain; ROI | FA MD AD RD | MNI; Atlas JHU White-matter | CC, SLF, ILF, lower FOF, l-AE, IFOF | ↓FA in l-AF in DYX | NR | |
| Fernandez VG, et al. [48] | Philips 3T | DTI | 6100/84 | 44 | 3 | 240x240 | 0; 1000 | 21 | NR | FSL (DTIFIT) | EC, HM | ROI | FA AD RD | Desikan and Destrieux atlases | LAC/RAC to bilateral TP, OT, and IFG | ↑FA of cerebellar to TP and IFG; ↓RD in TP in DYX | FA of AC-OT had interaction between age and group, younger DYX have ↓FA in this region. | |
| De Moura LM, et al. [49] | GE 1.5T | DTI | 11,600/99 | 47 | 3 | 240x240 | 0; 800 | 15 | NR | FSL, FSL(TBSS) | EC correction and non brain voxels removed | Voxel-based | FA RD MD AD | MNI152 | aThR, CG, CS, IFOF, ILF, UF, FMj, FMn, and CGH | ↓FA left of aThR, CG, CS, FMj, FMn, UF, right of IFOF, ILF TRD in the left of CG, CS, and SLF in DYX | NR | |
| Richards TL, et al. [50] | Philips 3T | DTI | 8593/78 | NR | 2.0 | 220x220x128 | 0; 1000 | 32 | 9 min 35 s | DTIPre (GTRAC), FSL (TBSS), and FSL | NR | ROI | FA AD RD RA MD | FSL white matter atlas (FHU) | aThR, FMn, CS, SLF, ILF, IFOF, UF, and CG | ↓RA in aThR, IFOF, SLF, UF, and l-CG, and FMn; ↓AD in CS, r-ThR, CG, IFOF, SLF, and UF in DYX | NR | |

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|-----------------------------|--------------|----------|------------|-----------------|----------------------|----------|------------------------------|---------------------------|------------|---|---|--------------------------|-----------------------------|---|--|--|--|-----------------------|
| | | | | Slice Number | Slice Thickness (mm) | FOV (mm) | | | | | | Type of Analyses | DTI Metrics | | | | | |
| Marino C, et al. [51] | Philips 3T | DTI | 9775/58 | NR | 2.3 | NR | 0; 1000 | 35 | NR | BrainVoyager (Brainvisa), SPM | EC, smooth 6 mm | Voxel-based | FA | White matter atlases of FSL | ILF, IFOF, AE, SLF, CC, and OR | NR | DYX with DCDC2d gene x without found ↓FA in ILF and I-CC | |
| Fan Q, et al. [52] | Philips 3T | DTI | 6237/75 | 60 | 2.2 | 212x212 | 0; 700 | 32 | 3 min 32 s | FSL (FDT), FS-TRACULA | EC, HM | ROI | FA | Desikan–Killiany Atlas | Thalamus to OFC, MPFC, LPFC, SMC, PC, MTC, LTC, OCC, and Ins | ↑FA of LPFC and SMC to ThR in DYX | Th-SMC showed negative correlation with basic reading score | |
| Fan Q, et al. [53] | Philips 3T | DTI | 6237/75 | 60 | 2.2 | 212x212 | 700 | 32 | 3 min 38s | FSL | EC, HM | ROI | NR | MNI152 | 5 ROIs of I-OT/E, MTG, ITG, LOCC, PaHipp, and ILF | Left Mid, Inf and sup-TG, lingual, fusiform, Sup and Inf PG in DYX | NR | |
| Hasan KM, et al. [54] | Philips 3T | DTI | 6100/84 | 44 | 3 | NR | 1000 | 21 | 7 min | NR | NR | ROI | FA MD AD RD Dav | NR | CC | ↑mFA of CC in DYX | MD and AD correlation with age (CC2); MD positive correlated with Letter-Word ID test in CC5 | |
| Gebauer D, et al. [55] | Siemens 3T | DTI | 6700/95 | 35 | 2.5 | 250 | NR | NR | NR | FSL (TBSS, FDT, DTIFIT, and BET) | EC | Voxel-based | FA | JHU ICBM-DTI-81 White-Matter Labels | aCR, CC | ↓FA in the l-aCR and aCC | NR | |
| Hoefl F, et al. [56] | GE 3T | DTI | 11600/64.5 | 23 | 4 | 240 | 800 | 13 | NR | SPM, DTIStudio, and ROQS | EC, HM | Whole-brain | FA | NR | SLF | NR | Positive correlation between r-SLF FA and single-word reading | |
| Sihvonen AJ, et al. [57] | Siemens 3T | DTI | 9000/80 | 70 | 2.5 | 240x240 | 0; 1000 | 64 | NR | MRTrix, DSI Studio | Thermal noise with MP-PCA, Gibbs ringing correction | Whole brain | QA | MNI using (QSDR) | NR | ↓QA in VOF, SLF, AE, CC, CSI-UF, and ThR; ↑QA in l-SLF, VOF, and CS in DYX | Reading skill positive association with l-CG and right fornix, and frontal cortico-pontine tracts and cerebellum | |
| Tschentscher N, et al. [58] | Siemens 3T | DTI | 12900/100 | 88 | 1.7 | 220x220 | 0; 1000 | 60 | 16 min | FSL (FDT), FSL (PROBTRACKX), and FSL (BEDPOSTX) | Head motion corrections | Voxel-based; ROI | FA | MNI; Juelich histological; Harvard-Oxford atlases | A1, l-mPT, and MGB, IC | ↓connectivity between l-mPT-MGB in DYX | Negative correlation of l-mPT-MGB with reading skills in TR | |
| Moreau D, et al. [59] | Siemens 1.5T | DTI | 6601/101 | NR | 3 | 230 | 0; 1000 | 30 | NR | FSL (DTIFIT), FSL (FLIRT), and FSL (TBSS) | EC and motion corrections | Whole brain; Voxel-based | FA | MNI152 | Bilateral CR and AF | No group difference | NR | |
| Müller-Axt C, et al. [60] | Siemens 3T | DTI | 12900/100 | 88 | 1.7 | 220x220 | 0; 1000 | 60 | 16 min | FSL | Motion correction | ROI | FA | Talairach; MNI; Juelich Histological atlas | LGN, l-V1, V5/MT | ↓LGN FA and between l-V5/MT-LGA in DYX | DYX showed negative correlation between l-V5/MT-LGN and name letters and numbers aloud time | |
| Vandermosten M, et al. [61] | Philips 3T | DTI | 11043/55 | 68 | 2.2 | 220x220 | 0; 800 | 45 | 21 min 8 s | Explore DTI, FSL (CATNAP) | EC and motion-induced artifacts | Whole-brain; ROI | FA | Harvard-Oxford atlas in MNI space | Post STG, AE, sCC | NR | Positive correlation between coherence 20 Hz and FA of the STGp Lat and sCC in DYX and a negative in HC, without outliers | |
| Lebel C, et al. [62] | Siemens 1.5T | DTI | 9000/85 | 28 | 5 | 240x240 | 0; 1000 | 6 | 7 min 24 s | SPM | Smooth of 4 mm kernel | Voxel-based | FA MD | ICBM template | ALIC, sCC, ThR, CR, ILF, IFOF, anf aCR | NR | GORT fluency positive correlated with FA of aCC, sCC, right: aLimb, SLF, MCP, aCR, ILF, sCC, Th, IFOF; Word attack with FA of aCC, SLF, aLimb; l-Th, SLF, and r-IFOF | |

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|------------------------------|------------|----------|------------|-----------------|----------------------|----------|------------------|------------------------------|---------------------------|---------------------------|---|-------------|-----------------------|--------------|------------------------------|---------------------|--|--------------|-----------------------|
| | | | | Slice Number | Slice Thickness (mm) | FOV (mm) | Type of Analyses | | | | | | DTI Metrics | | | | | | |
| Vanderm-osten M, et al. [63] | Philips 3T | DTI | 11043/55 | 68 | 2.2 | 220x220 | 0; 800 | 45 | 21 min 8 s | Explore DTI, FSL (CATNAP) | EC, motion-induced artifacts correction | ROI | FA RD AD | Native space | AF, IFOF | ↓FA of l-AF in DYX | Direct and l-AF FA positive correlated with phoneme awareness, and speech perception, respectively, and l-IFOF with orthography | | |
| Frye RE, et al. [64] | Philips 3T | DTI | 6100/84 | 44 | 3 | 240x240 | 1000 | NR | 7 min | SPM | Distortion correction, masking, and isotropic voxel interpolation | Whole-brain | FA AD RD Dav | ICBM | FTP, SLF, SFOF, IFOF, and CR | No group difference | Negative correlated: FA—word attack in SLF, SFOF, aCR, and pCR; Dav—word attack in SLF; and positive correlation: Dav and AD—word attack in SFOF | | |

Abbreviations: Ref.: Reference; MRI: magnetic resonance imaging; N: number; DTI: diffusion tensor image; DKI: diffusion kurtosis imaging; NR: Not reported; TR: Time of repetition; TE: time of echo; FOV: field of view; b: diffusion weighting; l: left; r: right; UF: Uncinate fasciculus; FAT: frontal aslant tract; EC: Eddy Current; ICBM: International Consortium for Brain Mapping; SLF: Superior longitudinal fasciculus; SFOF: superior frontal–occipital fasciculus.; IFOF: inferior frontal–occipital fasciculus; ROQS: Reproducible Objective Quantification Scheme; CC: corpus callosum; CC5: posterior midbody of CC; CC2: genu of CC; sCC: splenium of CC; aCC: anterior CC; VOT: ventral occipitotemporal cortex; OT/F: occipitotemporal/fusiform; SMC: supramarginal cortex; IFG: inferior frontal gyrus; FTP: frontal-temporo-parietal regions; TP: temporo-parietal regions; FMj: forceps major; FMn: forceps minor; ThR: thalamic radiations; aThR: anterior ThR; CG: cingulum; CS: corticospinal tract; AF: arcuate fasciculus; aAF: anterior AF; pAF: posterior AF; ILF: inferior longitudinal fasciculus; HMOA: Hindrance-modulated oriented anisotropy; VAS: Visual Attention Span; AFQ: Automated Fiber Quantification software; SCP: superior cerebellar peduncle; ICP: inferior cerebellar peduncle; MCP: middle cerebellar peduncle; FA: fractional anisotropy, gFA: global white matter fractional anisotropy; AAL: automated anatomical labeling; MNI: Montreal Neurological Institute; SOG: superior occipital gyrus; MTG: middle temporal gyrus; ORBsupmed: medial orbital superior frontal gyrus; TR: typical readers; RD: reading disorder; QSDR: q-space diffeomorphic reconstruction; QA: quantitative anisotropy; FDT: FMRIB's Diffusion Toolbox; MD: mean diffusivity; STG: superior temporal gyrus; ITG: inferior temporal gyrus; SMG: supramarginal gyrus; DYX: dyslexia; AnG: angular gyrus; IPL: inferior parietal lobe; IOG: inferior occipital gyrus; PreCG: precentral gyrus; ROL: Rolandic operculum; FFG: fusiform gyrus; QUAD: Quality Assessment of dmRI; DTIfit: diffusion tensor modeling tool; MDLF: middle longitudinal fasciculus; VOF: ventral occipital fasciculus; CBD: dorsal cingulum; FX: fornix; AWF: axonal water fraction; Da: intra-axonal diffusivity; MDe: extra-axonal mean diffusivity; NDI: neurite density index; ODI: orientation dispersion index; FHD+: positive familial risk to develop dyslexia; FHD−: negative familial risk to develop dyslexia; CR: corona radiata; aCR: anterior CR; pCR: posterior CR; PLIC: posterior limb of internal capsule; FM: frequency modulation; A1: primary auditory cortex; mPT: planum temporale; MGB: medial geniculate body; IC: inferior colliculus; BEDPOSTX: Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques; MOG: middle occipital gyrus; -TPOsup: temporal pole; HG: Heschl's gyrus; AD: axial diffusivity; RD: radial diffusivity; ALIC: anterior limb of the internal capsule; SD: spelling disorder; TBSS: Tract-based spatial statistics; FLIRT: FMRIB linear image registration tool; RA: relative anisotropy; SLD: specific learning disability; WM: white matter; TP: temporoparietal; LGN: lateral geniculate nucleus; V1: primary visual cortex; V5/MT: middle temporal area; TRACULA: TRActs Constrained by UnderLying Anatomy; TP-AF: temporo-paietal portion of the AF; ASD: autism spectrum disorder; SOS/TOS: superior and transversal occipital sulci; BET: Brain Extraction Tool; LAC: left anterior cerebellum; RAC: right anterior cerebellum; HC: health control; JHU: Johns Hopkins School; OFC: orbitofrontal cortex; MPFC: medial prefrontal cortex; LPFC: lateral prefrontal cortex; PC: parietal cortex; MTC: medial temporal cortex; LTC: lateral temporal cortex; OCC: occipital cortex; Ins: insular cortex; LOCC: lateral OCC; PaHipp: parahippocampal regions; GORT: Gray Oral Reading Test; aLimb: anterior limb; SS: sagittal stratum; IC: inferior colliculus; OR: Opptic radiation; IFoG: pars opercularis of inferior frontal gyrus; IFtG: pars triangularis of IFG; IFobG: pars orbitalis of IFG; bDS: backward digit span; and VF: verbal fluency.

Most of the selected studies (91.8%) used the sequence DTI for the diffusion analysis, and only 6.1% used diffusion kurtosis imaging (DKI) protocols [25,32,33] that require at least 3 b-values (as compared to 2 b-values for DTI) and at least 30 independent diffusion gradient directions (as compared to 6 for DTI), in which these 3 b-values were used: 0, 700 or 800 or 1000, and 2000 s/mm² with 30 or 32, and 64 noncollinear diffusion directions. In two studies, the DTI sequence also was reported with 3 b-values (0, 700, or 1000, and 1000 or 2000 for b-values with 64 diffusion directions), 50% of DTI studies used 2 b-values (0 and 700 or 800 or 1000 or 1400) and 37% studies only one b-value (700 or 800 or 1000 or 1300 or 1400 or 5000). Regarding the number of noncollinear diffusion gradient directions in the studies that acquired DTI sequence, 41.3% reported more than 60 directions (28.3% was 60 and 2.2% was 128 directions), 34.8% used between 30 to 56 directions, 13% of studies used less than 30 directions (the smaller number of directions was 6), and 10.9% did not report this parameter [46] (Table 2).

The basic pulse sequence repetition time (TR) and echo time (TE) parameters ranged from 3000 to 14,000 ms and from 55 to 110 ms, respectively; the slice image ranged from 23 slices with 5 mm of thickness to 160 slices with around 1.7 mm to cover the entire brain, and the field of view (FOV) ranged from 208 to 282 mm.

The DTI analysis was performed in the selected studies by different softwares, and usually (82%) used more than one software to conduct all of the analysis. Most of the studies (63%) used the FSL software [18,19,23–26,28,30–33,38–40,42–50,52,53,55,58–61,63] and its different tools (Neurite orientation dispersion and the density imaging (NODDI) model, Tract-Based Spatial Statistics (TBSS), FDT, DTIFIT, PR00BTRACKX, and BEDPOSTX, among others) associated or not with other software; 18% of studies [16–18,21,22,27,32,40,41] used the VistaLab developed at Stanford University that comprises different tools such as MrDiffusion and Automated Fiber Quantification (AFQ); 20% used ExploreDTI [20,23,24,29,37,38,43,45,61,63]; 16% used the Track-Vis [18,20,23,24,26,37,43,45]; 12% DTIprep [16–18,22,44,50], 10% MRTrix [19,25,32,40,57]; 10% SPM [41,51,56,62,64]; 6% TRActs Constrained by UnderLying Anatomy (TRACULA) [33,44,52]; 4% DSI Studio [36,57]; and 2% BrainVoyager [34,51], the only commercial software; and few studies used PANDA, DIPY, Reproducible Objective Quantification Scheme (ROQS), TORTOISE, and TractSeg.

Artifacts in DWI acquisitions lead to errors in tensor estimation, and Eddy Current (EC) distortions and Head Motion (HM) are the two primary intrinsic DTI acquisition abnormalities that may obliterate the voxel-wise correlation across all the DWIs. Most of the selected studies (73%) reported in the pre-processing step comprise the EC and HM (with a cutoff from 1.5 mm to 6 mm) corrections. Other studies (10%) reported corrections to the image (EPI) distortions, 4% for the Gibbs artifact (truncation or ringing artifact) or Marchenko–Pastur Principal Component Analysis (MP-PCA), and only 14% did not report any correction in the preprocessing image step.

Some FSL tools were used for these corrections such as CATNAP (Coregistration, Adjustment, and Tensor-solving a Nicely Automated Program), which is a data processing pipeline for Philips PAR/REC Magnetic Resonance data files, performing motion correction for both diffusion and structural images using FSL FLIRT; it adjusts the diffusion gradient directions for scanner settings (i.e., slice angulation, slice orientation, etc.) and motion correction (i.e., the rotational component of the applied transformation) and computes tensor and derived quantities (FA, MD, colormaps, eigenvalues, etc). Also, the TOPUP tool of FSL is used to correct images of the susceptibility-induced distortions (fix EPI distortions), and QUAD (Quality Assessment for DMRI) for automatically performing image quality control (QC) at the single subject.

The tracking of DTI group analysis was normally reported as whole brain, tract, or ROI-based, from voxel-based, and 34.7% of studies reported as ROI-based methods [17,18,20–22,34,35,37,39,42,48,50,52–54,60,63], 26.5% as whole brain and ROI-based methods [16,19,23,27–31,33,41,43,45,47], 22.4% only whole brain or fiber tract-based analysis [24–26,32,36,38,40,44,46,57,64], and 12.2% as voxel-based analysis [49,51,55,58,59,62].

Regarding DTI quantitative analysis, 92% measured FA; of these, 29% also reported AD or RD [18,22,31,39,42–50,54,61], and 22% MD. In a few studies, other anisotropy metrics were used such as 4% relative anisotropy (RA) [42,50], 2% QA [57], or hindrance-modulated orientation anisotropy (HMOA) [45]. The MD measure was also described by directionally averaged mean diffusivity (Dav) [54,64] and extra-axonal mean diffusivity (MDe) [32], in 4% and 2% of studies, respectively. The ADC [35] or exponential apparent diffusion coefficient (eADC) metrics were reported in 2% of studies. Some White Matter Tract Integrity (WMTI) metrics from DKI were reported in 2% of studies, such as axonal water fraction (AWF) [32], intra-axonal diffusivity (Da) [32], or MDe [32], and NODDI metrics such as Neurite density index (NDI) and Orientation dispersion index (ODI) were reported in 4% of studies each [31,33].

Different types of atlas were reported in the selected studies to segment the cortical and white matter region; 54% used one of FSL atlas such as Julich-Brain Cytoarchitectonic Atlas, MNI (Montreal Neurological Institute) Structural Atlas, JHU (Johns Hopkins University) ICBM-DTI-81 White-Matter Tractography Atlas, and Harvard-Oxford atlas; 19% used one of three FS's atlas (Desikan–Killiany, Destrieux, and Desikan–Killiany–Tourville cortical atlas); 9% used native space; 7% used the automated anatomical atlas (AAL), the template for SPM, AFQ, ExploreDTI, and PANDA software; 3% used Talairach atlas; and 9% did not report this information.

Most of the studies (90%) specified the tracts/ROI used to explore the group comparison or association between structural data and demographic or neuropsychological data, the main tracts were AF (49%) [16–23,25,27,32,34,35,37,40,41,43–45,47,51,59,61,63], inferior longitudinal fasciculus (ILF) (41%) [17,22,25,27,32,34,37,39–44,46,48–51,53,62], inferior frontal-occipital fasciculus (IFOF) (39%) [20,23,25,32,34,36,37,39–41,43,45,47,49–51,62–64], superior longitudinal fasciculus (SLF) (37%) [16,17,22,25,27,31,32,35,39–42,44,45,47,50,51,56], 24% for corpus callosum (CC) [17,25,36,39,47,51–55,61,62], 18% for corticospinal (CS) tract [18,32,35,39–42,49,50], 12% for CR (including anterior and posterior parts - aCR and pCR) [35,39,55,59,62,64], 20% for uncinate fasciculus (UF) [24,25,32,37,39–41,43,49,50], and 16% for thalamic radiation (ThR) (including anterior and posterior parts- aThR and pThR) [32,36,40,41,49,50,52,62]. Forceps minor (FMn) and major were reported in 10% of studies [32,40,41,49,50], as well as the cingulum (CG) [31,40,42,49,50]; less frequently was also reported in 4% optical radiation (OR) [42,51], as well as cerebellar peduncles [36], internal capsule [62], temporal and temporo-occipital regions [19], frontal aslant tract (FAT) [24], primary auditory cortex, lateral geniculate nucleus (LGN) [60], and inferior colliculus (2% each). 6% of studies reported only the atlas used [26,29,30], did not specify the tracts or ROIs, and 4% did not report this information [46,57].

Regarding the results of the structural analysis of the brain, 89% of the studies described this finding, with the predominance of a decrease in FA in the left hemisphere, when comparing the dyslexia group with the control group, and 10% of the studies did not show a significant difference between the groups [19,25,46,59,64], occurring mainly in the group of adults (25%) [59,64].

The tractography analyses of the pre-reader group reported by the selected studies were based on the FA changes according to the risk of familial history of dyslexia (FHD); 13% reported higher FA of right SLF [16] or CC [17] compared to the children with positive FHD than TR negative FHD, and 50% showed lower FA of the left AF (as also long portion) [18,21–23] and 13% in IFOF [20], as shown in Figure 2, highlighting the frequency in green color. Almost all of these regions also showed a positive correlation with age and some language tests and predicted decoding skills or reading impairment.

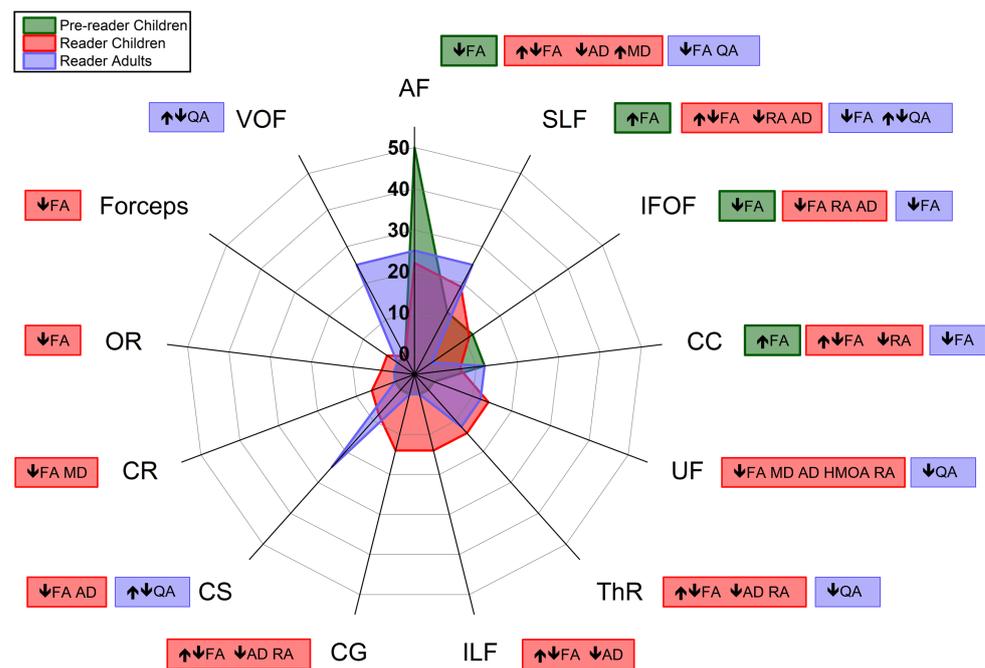


Figure 2. Spider graphic of the diffusion tensor image (DTI) outcomes percentage distributed by the main tracts reported in the systematic review and their DTI metrics behavior found according to tract and age group of dyslexia participants (pre-reader children in green, reader children in red, and reader adults in purple). The arrows indicate the increase or decrease in DTI metrics in the dyslexia group in comparison to the control group. Abbreviations: AF: arcuate fasciculus; SLF: superior longitudinal fasciculus; IFOF: inferior fronto-occipital fasciculus; CC: corpus callosum; UF: uncinate fasciculus; ThR: thalamic radiations; ILF: inferior longitudinal fasciculus; CG: cingulate cortex; CS: corticospinal fasciculus; CR: corona radiata; OR: optic radiation; Forceps: forceps major and minor; VOF: ventral occipital fasciculus; FA: fractional anisotropy; AD: axial diffusivity; MD: mean diffusivity; QA: quantitative anisotropy; RA: relative anisotropy; and HMOA: hindrance-modulated oriented anisotropy.

In the reading children, 42% of these studies reported a significant change in FA values (27% lower [27,38,42–45,47,49,55] and 15% higher values [40,41,48,52,54] in dyslexic children than the TR group), decreasing mainly in the left tracts such as AF, SLF, ILF, CR, and IFOF and increasing in the right SLF, aThR, cingulum, and CC. These studies also showed 6% of AD [43,50] decreased in dyslexic children in IFOF, SLF, UF, FMn, CG, and the right ThR [50], as well as in the left AF and ILF [43], and 12% of MD [28,32,39] changes between groups (6% higher [28,32] and 6% lower values in dyslexic children [32,39]). Only 3% of these studies reported higher values of ODI in the left ventral optical tract [33] of DYX and lower values of RD and HMOA (in UF of DYX males) [24], as shown in Figure 2, highlighting the frequency in red color. No group differences were reported in 6% of these studies [25,46], and 30% did not report brain changes [26,29–31,34–37,51,56].

In the selected studies with adult participants, 50% showed group differences, in which the DYX had low FA in lateral geniculate nucleus, TOC, and left-AF [60,63], and another DTI metric was the QA with high values for DYX group in left-UF, CS, CC, ThR, FMj, and parietal tracts and low in left SLF, CS, and OF in comparison to TR group [57], as shown in Figure 2, highlighting the frequency in purple color. In total, 25% of these studies did not find a group difference [59,64] or report this information [61,62].

The outcomes were also reported by the correlation analysis between clinical, demographic, and neuropsychological data, with white matter changes in 83.6% of studies, in which 60.9% showed a positive correlation between FA/MD changes and age (12%) [18,25,39,41,48,54]; gender (4%) [25,29], mainly in children; and neuropsychological tests (phonological awareness, word/no-word identification skill, VAS, working memory, verbal fluency, digit span, and Chinese character

recognition) (44.9%) [20,22,24,25,27,29–32,35–39,43,44,46,54,56,57,61,63] in all ages; 32.6% reported a negative correlation between FA/MD/RD changes and neuropsychological performance [28, 30,32,34,35,37,39,40,43–46,52,57,60,61]; 5% of studies reported [19,21,23] changes between white matter and DYX diagnoses or neuropsychological outcomes/skills; and 16.4% did not find or report correlation results [33,42,47,49,50,53,55,59].

4. Discussion

This systematic review provided an overview of the main structural brain changes findings by the DTI technique in developmental dyslexia in different age groups, including early at-risk children due to a family history of the disorder, as well as children and adults with reading disorders who have been diagnosed with dyslexia. By comparing the results of several studies, we describe converging evidence on structural abnormalities of the brain and the associations between imaging results and changes in this population's characteristics. This systematic review observed that the assessment of different cognitive functions by the neuropsychological instruments of the selected studies varied according to age, country, and language; however, the lack of standardized procedures among age and language groups drastically reduces the possibility of comparing the behavioral outcomes and its relation to the structural brain changes. While some aspects of reading, mainly word decoding and recognition, are the most assessed skills in all the age groups, others such as language, attention, and working memory are reported exceptionally. The intelligence measure showed an expected outcome in terms of experimental and control group matching, with more studies reporting lower performance of children with dyslexia on verbal but not on non-verbal tests of intelligence. The intelligence assessment has generated a long-time debate in the field of learning, and while in typically developing children intelligence performance generally correlates with the achievement level, in reading impairment the intellectual disability is inconsistent with a diagnosis of dyslexia [65].

The importance of matching groups on intelligence measures is also supported by a growing body of evidence linking the brain white matter organization to intelligence level and processing efficiency. A recent study showed stronger integration of white matter structures within a local community (ex. frontal region) and especially with external brain networks (ex. frontal to parietal regions) in adults scoring high on non-verbal tests compared to average performers [66].

The structural brain changes shown by the DTI measurements were examined or extracted using the atlases, and nearly all studies (92%) examined the fractional anisotropy, which represents the directionality and organization of tissue microstructure; other studies examined some of its variants, including RA, QA, and HMOA, providing additional information to FA. The studies also examined the following measures: the AD measure, which can show changes in the density or integrity of axons within white matter pathways; the RD measure, whose increase frequently denotes disruptions in the microstructure of white matter, such as demyelination or axonal damage; and the MD measure, which, along with some variations like Dav and MDe, typically shows higher values that indicate decreased tissue integrity and increased diffusion.

In children before reading acquisition who had a positive family history of dyslexia, the structural changes analyzed by DTI metrics were shown mainly by the FA alterations. The decrease in FA was predominant in the left of the AF, as well as for IFOF, a result also reported in a recent study with dyslexic children with this profile [21], and a pattern of increased FA occurred in few studies, and only in the right hemisphere of the SLF and sCC, which may suggest possible early neural compensatory mechanisms in the right hemisphere [17]. This pattern was also similar in reading children, with low FA values mainly in the left hemisphere involving the AF, but also high FA values in the right hemisphere of AF, showing more neuroplasticity signals than the other young group. In addition, in these reader groups the structural changes covered more areas, still with a predominance of the left hemisphere, and were identified in other DTI metrics, such as low AD values in AF, SLF, IFOF, UF, ThR, ILF, CG, and CS, as well as a high MD values in

AF, and low in UF and CR. Children submitted to reading intervention show an increase in MD values in AF and other reading brain circuitry such as the left ILF and posterior CC [67]. Variations of anisotropy, such as RA and HMOA, also showed low values in brain structural changes reported in the articles with reader children, but only FA showed high values in the following tracts AF, SLF, CC, ThR, ILF, and CG.

In dyslexic adults, the percentage of structural changes reported was much lower than those reported in children. It seems that with brain development, in adulthood, the structural differences of dyslexia become less evident due to neuroadaptation. However, the pattern of decreased FA measurements in dyslexic adults remained the same, with predominance in the left hemisphere of AF and the region that comprises the AF (lateral geniculate nucleus, and temporo-occipital cortex), as well as bilaterally SLF, CC, CS, and the left of UF and ThR by the QA measurements. This anisotropy variation, the QA measure, also showed an increase in the left side of SLF, VOF, and CS, which may represent neuroplasticity in adulthood. Nonetheless, due to literature scarcity on dyslexia in adults it is difficult to compare these results found in the review with other studies.

Another form of result widely explored between studies was the analysis of association, be it through correlation or the prediction of structural data with demographic or neuropsychological data, and this occurred with a greater incidence of significant findings between studies than the actual comparison of structural changes. These association analyses are normally applied to assist in the interpretation of results, mainly in studies with adults when there were no structural difference between the groups, but measures mainly of FA were positively or negatively correlated with the results of neuropsychological tests. In children, the structural changes helped predict some performance in neuropsychological tests, especially in children with a family risk of dyslexia.

In addition to the structural results found in participants with dyslexia and controls, this review considered how DTI data were acquired, processed, and extracted as an analysis. In general, all studies included in this review took good care to ensure good image and data quality, reducing bias in the interpretation of results.

The DTI acquired in high magnetic field equipment, such as 3 Tesla, can increase the capacity to acquire higher resolution scans more quickly, with higher b-values and thinner slices, as well as to increase tissue contrast and reduce background noise (thereby increasing the signal-to-noise ratio and contrast-to-noise ratio) [68]; this magnetic field was used in 88% of the studies (49% Siemens, 35% Philips, and 4% GE), in the acquisition of both DKI and DTI sequences to study tractography. The latter sequence is the more traditional sequence and was used in most of the selected articles in our systematic review. The difference between the two is that DKI significantly reduces the error of dODF orientation estimates compared to DTI and makes it possible to detect crossing fibers, which leads to a noticeable improvement in tractography across regions with complex fiber bundle geometries [69,70]. DKI-based tractography has potential benefits, especially in clinical contexts when time is of the essence [71].

The acquisition parameters of the DTI is important because they affect values of white matter (WM) scalar metrics, including FA, MD, Signal Noise Ratio (SNR), and even entire brain tractography investigations. These acquisition parameters include the diffusion sensitivity coefficient (*b*-value), which is a factor that reflects the strength and timing of those gradients used to generate DWI, as well as the reliability of DTI results concerning image and data quality; diffusion directions, in which there are more directions the longer the acquisition time; and voxel size (the smaller the size, the higher the quality [72,73]).

The adequate b-value for diffusion imaging quality evaluation in dyslexia was unclear and varied according to the equipment's magnetic field. In a healthy brain, a greater b-value usually results in a poorer SNR and image quality because increased signal attenuation owing to diffusion as well as increased TE (and therefore additional signal loss due to T2 decay), would lead to the decrease of MD, AD, and RD when the gradient directions and voxel resolution remained constant [73,74]. In the literature, this is more evident at the low field strength of the MR scanner as 1.5 T [75], and only 10% of the selected studies

of this review used this field, less evident in high field strength (3 T and 7 T) due to their relatively high SNR, in which the increase in b value has little influence on the decrease in SNR, showing the best image and data quality with the respective b-values, 200 and 900 s/mm² [73]. The selected studies included in this review reported normally more than one b-value and the MRI of 1.5T used b-values ranging from 800 to 1000 s/mm² and the 3 T from 700 to 5000 s/mm² [73,74].

The increased number of diffusion-encoding gradient directions can also improve DTI quality by averaging and strengthening the tensor estimation, and the opposite can reduce all DTI scalar values' accuracy and precision; a minimum of 18 diffusion directions is advised to produce trustworthy DTI scalar results using the TBSS toolbox of FSL software [76]. In our study, just a small number of the selected studies (11.8%) used fewer than 30 directions, and of these, 7.8% used less than 18 directions, whereas the majority (78.4%) used 30 directions or more (41.3% used more than 60 directions).

Considering the impact of MRI acquisition parameters on the values of DTI measures, changes in the number of gradients and voxel resolution have the greatest impact on the FA, but variations in the b-value have a special effect on MD [72]. Another study also showed that the number of gradient directions was more relevant than the spatial resolution in some quantitative measures of DTI, such as tract volume, median fiber density, and mean FA, but this did not occur for all tracts evaluated in the same way, only for SLF and IFOF [77].

One of the most defining and defiant components of building a tracking algorithm is determining the underlying model that connects the raw dMRI images to the local fiber orientations, and presently, there is a wide range of software packages that incorporate higher-order fiber-tracking techniques that can calculate the relative contributions and orientations of several fiber populations within each voxel, which are easily applied to clinically relevant data sets [78].

A wide range of processing functions are offered by these software packages, such as tensor calculations, fiber tracking, visualization, statistical analysis, quantitative measure extraction from DTI datasets, and integration with additional neuroimaging tools. They vary, though, when it comes to the tractography algorithms that are applied, such as probabilistic, which produces a vast collection or distribution of potential trajectories from each seed point, and deterministic, which assumes a unique fiber orientation estimate in each voxel [79]; as well as the local approach, which is a fast and widely used method, it follows the local orientations of previously extracted fibers independently of each other, but the sum of small errors in these local orientations can significantly affect the final result, making it a very weak predictor of data with little quantitative significance or biological [78]. On the other hand, the global methods offer improved stability concerning noise and imaging artifacts and a greater agreement with the real dMRI data that was recorded; however, they rely on stochastic optimization approaches and hence do not guarantee convergence to a globally optimal solution [80].

The choice of software to analyze the DTI normally depends on the specific analysis requirements, familiarity with the software, and preference for user interface and workflow, and the studies normally used more than one software to employ specific tools to conduct the entire analysis.

Several image adjustments are usually conducted before DTI analysis to enhance the data quality and reduce common artifacts that may occur during data acquisition, allowing for appropriate interpretation and trustworthy outcomes. Most of the adjustments reported by the studies were Eddy current correction (74%) which aligns the DWI to a reference image acquired without diffusion weighting [81], and motion correction (74%); few explore structural analyses but they realign the image to compensate for subject motion, ensuring that the diffusion measurements are accurate and consistent across the dataset [82]. However, in low frequency the Gibbs ringing correction (4%) of the discontinuities in the k-space data caused by undersampling during image acquisition was also reported, resulting in obscure anatomical structures and affecting diffusion measurements, as well as EPI distortion correction (10%), considering the spatial variations in the strength and direction

of the magnetic field gradients used for diffusion encoding. Unhappily, 14% of the studies did not report any adjustment before DTI analyses.

Regarding the type of quantitative DTI analyses reported by the studies, most (69.2%) used voxel-wise, which analyzes each voxel to identify differences in diffusion properties between groups or conditions, providing more detailed spatial information about diffusion metrics at a voxel-level; this is present in some of the software such as FSL, SPM, MRITrix, and ExploreDTI. Interestingly, a lot of articles reported this analysis as the whole brain since voxel-based analysis includes all the cerebro voxels. Also, ROI-based analysis used in 61.5% of studies is frequently conducted after voxel-based, making it challenging to determine which method was used in each study.

The outcome description of the studies was based on anatomical regions of interest or specific tracts outlined by a well-established atlas that facilitates the interpretation of imaging data by providing standardized anatomical labeling and spatial coordinates. While the atlases share the goal of delineating brain structures and regions, they differ in several aspects, including their origins, resolutions, and intended applications.

The study's limitations stem mainly from the differences in how dyslexia was defined across studies. The use of the terms dyslexia, developmental dyslexia, reading disorders, or never reading difficulties point to the lack of a common terminology and diagnosis criteria. The impact of the findings of this study could be that the results may be possibly drawn from a very heterogeneous sample. However, the cognitive testing of participants may ameliorate this and emerge as a potential tool mainly in internationally normed tests.

Another limitation of the study was the influence of language on dyslexia's reading acquisition history. It is a well-known fact that readers in irregular language systems have longer reading acquisition and struggling readers may develop different compensation strategies.

Studies on neuroimaging may be limited by variations in image acquisition parameterization; however, despite this wide range, all studies used optimal acquisition and analysis parameters that did not affect the comparability of results, even in cases where certain fundamental information was not stated. In terms of results, a certain study focused on describing the anatomical regions examined rather than the tract as most studies did, taking into account the tracts involved in the regions described.

5. Conclusions

This systematic review of structural alterations in the brain associated with dyslexia revealed that over the past ten years studies on children have outnumbered those on adults, primarily focusing on boys and the English language. The studies also showed that brain changes concentrated in FA reduction in the fasciculus arcuate of the left hemisphere at all ages, and in the left superior longitudinal fascicle for reading in children and adults, as well as an increase in the right hemisphere, which may indicate signs of neuroadaptation. A better understanding of structural brain changes of dyslexia and neuroadaptations can be a guide for future interventions.

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