UNIVERSIDADE FEDERAL DE MINAS GERAIS Instituto de Ciências Biológicas Programa de Pós-graduação em Neurociências

Sara Edith Souza de Assis Leão

MEMÓRIA DE TRABALHO E DESTREZA MANUAL DE CRIANÇAS E ADOLESCENTES COM DISLEXIA: revisão sistemática e metanálise

Belo Horizonte 2021 Sara Edith Souza de Assis Leão

MEMÓRIA DE TRABALHO E DESTREZA MANUAL DE CRIANÇAS E ADOLESCENTES COM DISLEXIA: revisão sistemática e metanálise

Dissertação apresentada ao Programa de Pós-Graduação em Neurociências do Instituto de Ciências Biológicas da Universidade Federal de Minas Gerais, como requisito parcial para obtenção do título de Mestre em Neurociências.

Orientadora: Dra. Ângela Maria Vieira Pinheiro Coorientador: Dr. Guilherme Menezes Lage

Belo Horizonte 2021

043 Leão, Sara Edith Souza de Assis. Memória de trabalho e destreza manual de crianças e adolescentes com dislexia: revisão sistemática e metanálise [manuscrito] / Sara Edith Souza de Assis Leão. - 2021. 89 f. : il. ; 29,5 cm.

> Orientadora: Profa. Dra. Ângela Maria Vieira Pinheiro Alijah. Coorientador: Prof. Dr. Guilherme Menezes Lage.

> Dissertação (mestrado) - Universidade Federal de Minas Gerais, Instituto de Ciências Biológicas. Programa de Pós-Graduação em Neurociências.

 Neurociências. 2. Memória de Curto Prazo. 3. Capacidade Motora. 4. Caligrafia. 5. Destreza Motora. 6. Dislexia. 7. Metanálise. I. Alijah, Ângela Maria Vieira Pinheiro. II. Lage, Guilherme Menezes. III. Universidade Federal de Minas Gerais. Instituto de Ciências Biológicas. IV. Título.

CDU: 612.8

Ficha catalográfica elaborada pela bibliotecária Rosilene Moreira Coelho de Sá - CRB 6 - 2726

21/09/2021 15:33

SEI/UFMG - 0920283 - Folha de Aprovação



UNIVERSIDADE FEDERAL DE MINAS GERAIS INSTITUTO DE CIÊNCIAS BIOLÓGICAS PROGRAMA DE PÓS-GRADUAÇÃO EM NEUROCIÊNCIAS

FOLHA DE APROVAÇÃO

MEMÓRIA DE TRABALHO E DESTREZA MANUAL DE CRIANÇAS E ADOLESCENTES COM DISLEXIA: revisão sistemática e metanálise

SARA EDITH SOUZA DE ASSIS LEÃO

Dissertação submetida à Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação em NEUROCIÊNCIAS, como requisito para obtenção do grau de Mestre em NEUROCIÊNCIAS, área de concentração NEUROCIÊNCIAS CLÍNICAS.

Aprovada em 31 de agosto de 2021, pela banca constituída pelos membros:

Prof(a). Tércio Apolinário de Souza Instituto Izabela Hendrix

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Belo Horizonte, 31 de agosto de 2021.

seil assinatura eletrônica	Documento assinado eletronicamente por Tércio Apolinário de Souza, Usuário Externo , em 31/08/2021, às 11:04, conforme horário oficial de Brasília, com fundamento no art. 5º do <u>Decreto nº 10.543, de 13 de novembro de 2020</u> .
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Dedico este trabalho ao meu amado San, por sempre segurar a minha mão e por ser o meu companheiro de todas as horas.

AGRADECIMENTOS

Agradeço primeiramente a Deus por guiar os meus passos e por me permitir concluir este trabalho. Sem Ele, nada disso seria possível!

À minha querida orientadora, Professora Dra. Ângela Pinheiro, a quem tenho imensa admiração e respeito. Agradeço por me dar a oportunidade de ser sua aluna, pela paciência e generosidade nas orientações, apoio e incentivo que tornaram possível a conclusão deste trabalho e, principalmente, por ter acreditado no meu trabalho. Profa. Ângela, muito mais que minha orientadora, a senhora foi uma mãezona acadêmica. Muitíssimo obrigada por tanto!!

Ao meu querido coorientador, Professor Dr. Guilherme Lage, por fazer parte da minha trajetória acadêmica e por compartilhar seu conhecimento, proporcionando grande aprendizado e crescimento profissional. Minha imensa gratidão por toda contribuição no desenvolvimento deste trabalho e por ser esse exemplo de pesquisador que nos inspira muito! Obrigada por tudo!

Ao querido Professor Renan Pedra por todo auxílio e disposição em me ajudar com a metanálise deste estudo, sempre com muita boa vontade e gentileza.

Aos queridos Professores Stela Maris, Tércio Apolinário e Luciana Alves que se dispuseram a fazer parte da minha banca e a contribuir com as melhorias deste trabalho.

Aos meus amigos do Neurofamily pela rica troca de experiência. Vocês contribuíram muito para o meu aprendizado! Agradeço em especial às minhas queridas amigas, Nathy, Bárbara e Joana pela parceria, por tamanha paciência e por compartilharem momentos de descontração e alegria como também de companheirismo e incentivo nos momentos mais difíceis. Com vocês, aprendi o que não é ensinado nos livros. Minha eterna gratidão!

Às minhas queridas colegas do LabCog, Ana Paula e Camila Peixoto por todo auxílio e apoio no desenvolvimento deste trabalho. Muito obrigada!

À Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), pelo apoio financeiro que permitiu minha dedicação integral aos estudos e à pesquisa, podendo concretizar esta etapa em minha vida acadêmica.

Às minhas amigas Michelle, Cheila, Soninha e Ferdinanda, obrigada pelo carinho, paciência e compreensão de minhas ausências, afinal, a amizade é o amor que nunca morre.

A toda minha família, em especial aos meus irmãos, Hebinho, Tiago e ao meu caçula Filipe (para sempre em meu coração), pelo amor incondicional e por me incentivarem em todos os momentos. Amo muito vocês!

Aos meus sobrinhos Tiago Junior e Lucas por alegrarem os meus dias, trazendo mais leveza e mais vida aos meus dias mesmo nos momentos mais delicados. Agradeço também à família que a vida me presenteou, Tarzan, Ana e Jó, por todo apoio e auxílio, sempre com muita generosidade. Sou muito grata por tê-los em minha vida!

Ao meu marido Sandino pela compreensão, carinho e disposição a me ajudar sempre que preciso e, principalmente, por se dispor a caminharmos juntos até nos caminhos mais difíceis. Sem essa cumplicidade muito pouco teria sido possível. Amo muito você!!

A todos que contribuíram para a realização deste trabalho, expresso aqui minha gratidão. Com todos vocês aprendi a acreditar em sonhos, pois eles são realizáveis.

"De tudo, ficaram três coisas: a certeza de que ele estava sempre começando, a certeza de que era preciso continuar e a certeza de que seria interrompido antes de terminar. Fazer da interrupção um caminho novo. Fazer da queda um passo de dança, do medo uma escada, do sono uma ponte, da procura um encontro".

Fernando Sabino – O Encontro Marcado (1967).

RESUMO

Introdução: As crianças disléxicas geralmente apresentam comprometimentos em uma série de habilidades, como consciência fonológica, codificação fonológica, déficit ortográfico, memória de trabalho, sequenciamento, equilíbrio deficiente e atrasos nos marcos motores, na velocidade, precisão e automação, além de dificuldades na motricidade fina e em tarefas de escrita. Diversas hipóteses tentam explicar os problemas cognitivos e motores relacionados à dislexia, porém, ainda existe uma lacuna nessa área que não deixa claro quais são os fatores subjacentes a esse transtorno. Contudo, estudos têm mostrado que quando o desenvolvimento cognitivo apresenta déficits, como na memória de trabalho, o desenvolvimento motor é frequentemente afetado, especialmente a destreza manual, o que permite inferir a possibilidade de que ambas as áreas interfiram no funcionamento adequado uma da outra. Objetivo: Realizar uma revisão sistemática e metanálise para averiguar as habilidades de memória de trabalho e destreza manual e a existência de uma relação entre alterações nessas duas habilidades em crianças e adolescentes disléxicos. Métodos: A elaboração e o protocolo desta revisão foram realizados de acordo com os critérios estabelecidos pelo Preferred Reporting for Systematic Reviews and Meta-analysis (PRISMA). Seis bancos de dados de literatura foram pesquisados para buscar estudos publicados entre 2000 e 2020: EMBASE, ERIC, ISI Web of Science, PubMed, PsycINFO e Scopus. Os critérios de elegibilidade e a qualidade metodológica foram avaliados de forma independente por dois revisores. A metanálise foi realizada usando a função "rma.mv" do pacote Metafor na versão R 4.1.0. Resultados: Foram encontrados 167 estudos, sendo que apenas 21 deles se enquadravam nos critérios de inclusão estabelecidos. Os resultados consistiram dos dados extraídos desses 21 estudos que incluíram um total de 3.129 participantes nos quais o tamanho da amostra variou de 24 a 893 e a média de idade foi de 10.69 anos, desvio padrão 1.53. Os resultados são apresentados em gráficos forest plots em que a diferença entre os grupos em cada estudo é representada por um diamante. Conclusões: Os resultados sugerem que crianças disléxicas apresentam memória de trabalho visuoespacial e verbal significativamente mais pobres, e ainda com mais comprometimentos na alça fonológica. Nas tarefas motoras, embora o grupo com crianças disléxicas tenha apresentado pior desempenho nas habilidades de controle motor fino, caligrafia e velocidade motora manual, essas diferenças não foram significativas entre os grupos. Foram observados correlatos neurais entre a memória de trabalho e a destreza manual, indicando que crianças disléxicas exibiram disfunção na conectividade entre áreas do cérebro para processos cognitivos e motores durante o processo de escrita.

Palavras-chave: Memória de trabalho. Destreza manual. Caligrafia. Habilidades motoras finas. Dislexia. Metanálise.

ABSTRACT

Introduction: Dyslexic children usually have impairments in a range of skills, such as phonological awareness, phonological coding, spelling deficits, working memory, sequencing, poor balance and delays in motor milestones, speed, accuracy and automation, in addition to difficulties in fine motor tasks and writing skills. Several hypotheses try to explain the cognitive and motor problems related to dyslexia, however, there is still a gap in this area that does not make it clear which the subjacent factors are for this disorder. However, studies have shown that when cognitive development is disturbed, as in working memory, motor development is often adversely affected, especially the manual dexterity, which allows us to infer the possibility that both areas interfering with each other's proper functioning. Objective: To perform a systematic review and meta-analysis to investigate working memory skills and manual dexterity and the existence of a relationship between alterations in these two skills in dyslexic children and adolescents. Methods: The elaboration and protocol of this review were carried out according to the criteria established by Preferred Reporting for Systematic Reviews and Metaanalyzes (PRISMA). Six literature databases were searched to locate studies published between 2000 and 2020: EMBASE, ERIC, ISI Web of Science, PubMed, PsycINFO and Scopus databases. Eligibility criteria and methodological quality were independently assessed by two reviewers. The meta-analysis was performed using the "rma.mv" function of the Metafor package in R version 4.1.0. Results: A total of 167 studies were found, 21 of them fit the inclusion criteria. The results were obtained from the data of these 21 studies that included a total of 3129 participants in which sample sizes ranged from 24 to 893 and the mean age was 10.69 years of age, standard deviation 1.53. The results are presented in forest plots in which the difference between groups in each study is represented by a square. Conclusions: The results suggest that dyslexic children have significantly poorer visuospatial and verbal working memory, with more impairments in the phonological loop. Although differences were observed in fine motor control skills, handwriting and manual motor speed, these differences were not significant between groups. Neural correlates between working memory and manual dexterity were observed, indicating that dyslexic children exhibited dysfunction in the connectivity between brain areas to cognitive and motor processes during the writing process.

Keywords: Working memory. Manual Dexterity. Handwriting. Fine Motor Skills. Dyslexia. Meta-analyzes.

LISTA DE FIGURAS E TABELAS

FIGURAS

Figura 1 – Os circuitos neurais envolvidos na leitura.

Figura 2 – Os circuitos neurais envolvidos nos componentes da memória de trabalho e no comportamento motor.

Figura 3 – Funcionamento do cérebro disléxico.

Figura 4 – Fluoxograma das etapas adotadas na revisão sistemática dos artigos e metanálise.

Figura 5 – Análise dos estudos que avaliaram a memória de trabalho visuoespacial.

Figura 6 – Análise dos estudos que avaliaram a memória de trabalho verbal.

Figura 7 – Análise dos estudos que avaliaram as habilidades motoras finas.

Figura 8 – Análise dos estudos que avaliaram as habilidades de escrita à mão.

Figura 9 – Análise dos estudos que avaliaram a velocidade motora manual.

TABELAS

Tabela 1 – Informações sobre o país e as revistas científicas em que os estudos foram publicados.

Tabela 2 – Qualidade metodológica dos estudos revisados usando a Lista de verificação de avaliação crítica do Joanna Briggs Institute for Analytical Cross Sectional Studies.

Tabela 3 – Dados sobre autores, título e objetivo dos artigos analisados.

Tabela 4 – Dados demográficos e clínicos, instrumentos de avaliação e resultados dos participantes nos estudos analisados.

Tabela a – Ferramentas utilizadas para avaliar a memória de trabalho e a destreza manual.

Tabela b – Descrição das ferramentas utilizadas para avaliar a memória de trabalho e a destreza manual.

LISTA DE ABREVIAÇÕES E SIGLAS

- ADHD = Attention-Deficit Hyperactivity Disorder;
- ADHD-I = DHD-Predominantly Inattentive Type;
- ADHD-C = ADHD-Combined Type;
- ADHD-DCD = ADHD-Developmental Coordination Disorder;
- ADHD-RD = ADHD Reading Disorder/Disorder of Written Expression;

BA = Brodmann area;

- BAS = British Abilities Scales–II;
- BDT = Bangor Dyslexia Test;
- LTT = Leonard Tapping Task;
- BHK = Concise evaluation scale for children handwriting;
- BOT-2 = Bruininks–Oseretsky Test of Motor Proficiency–2nd edition;
- CA = Chronological Age-Matched Controls;
- CD = Comorbid Diagnosis;
- CG = Control Group;
- CG2 to CG6 = Typical Students from the 2^{nd} to the 6^{th} grade;
- CHAT = Chinese Handwriting Assessment Tool;
- CMS = Control students of Middle School;
- CPS = Control students of Primary School;
- CTOPP = Comprehensive Test of Phonological Processing;
- DASH = Detailed Assessment of Speed of Handwriting;
- DC = Different Comorbidities;
- DCD = Developmental Coordination Disorder;
- DD = Developmental Dyslexia;
- DD2 to DD6 = Students Diagnosed with Developmental Dyslexia from the 2^{nd} to the 6^{th} grade;

DD-DCD = Combined Diagnosis Developmental Dyslexia and Developmental Coordination Disorder;

- DG = Dysgraphia Group;
- D-KEFS = Delis Kaplan Executive Functions;
- DMS = Dyslexic students of Middle School;
- DPS = Dyslexic students of Primary School;
- DLPFC = Dorsolateral Prefrontal Cortex;
- DST = Dyslexia Screening Test;

EG = Experimental Group;

fMRI = Functional Magnetic Resonance Imaging;

IIV = Intraindividual variability;

LOMDS = Lincoln-Orseretsky Motor Development Scale;

MABC-2 = Movement Assessment Battery for Children, second edition;

MeSH = Medical Subject Headings;

OWL = Oral and Written Language Learning Disability;

PAL = Process Assessment of the Learner;

PRISMA = Preferred Reporting for Systematic Reviews and Meta-analyzes;

RA = Reading Age-Matched Controls;

RAN = Rapid Automatic Letter Naming;

RAS = Rapid Automatic Switching;

SA = Spelling-ability Matched Control;

SEN = Special Education Needs;

SRT = Simple Reaction Time Task;

TD = Typical Development Control Group;

TOSWRF = Test of Silent Word Reading Fluency;

UN = Unclear;

VA-SDL = Verbally Average Students with Specific Learning Disabilities – Written Language;

VAW-SDL = Verbally Average Students Without Specific Learning Disabilities – Written Language;

VG-SDL = Verbally Gifted Students with Specific Learning Disabilities – Written Language;

VGW-SDL = Verbally Gifted Students Without Specific Learning Disabilities – Written Language;

WISC – III = Wechsler Intelligence Scale for Children – 4th edition;

WISC-IV = Wechsler Intelligence Scale for Children -4^{th} edition;

WMTB-C = Working Memory Test Battery for Children;

WNV = Echelle non verbale d'intelligence de Wechsler.

SUMÁRI	0
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1 CONSIDERAÇÕES INICIAIS
1.1 Memória de trabalho 16
1.2 Destreza manual
2 OBJETIVOS
2.1 Objetivo geral
2.2 Objetivos específicos
2.3 Hipóteses
Referências
3 ARTIGO
ABSTRACT
INTRODUCTION
METHODS
RESULTS
DISCUSSION
CONCLUSIONS
APPENDIX
REFERENCES
SUPPLEMENTARY MATERIAL 82
4 CONSIDERAÇÕES FINAIS

1. CONSIDERAÇÕES INICIAIS

A dislexia é um transtorno específico da aprendizagem, descrito pelo Manual Diagnóstico e Estatístico de Transtornos Mentais em sua quinta edição (DSM-5, 2014), como sendo um transtorno do neurodesenvolvimento, com origem biológica, caracterizado pela dificuldade na aprendizagem da leitura, com problemas na precisão ou fluência para reconhecer palavras, nas habilidades de decodificação e de ortografia, dada inteligência adequada e oportunidades educacionais, principalmente associado a um déficit de processamento fonológico. Este transtorno tem início dos sintomas durante os anos iniciais de escolarização formal e são caracterizados por dificuldades inesperadas, persistentes e prejudiciais às habilidades básicas acadêmicas. Dentro dos transtornos específicos de aprendizagem há uma subdivisão em três domínios que especificam quais as habilidades acadêmicas estão prejudicadas, sendo elas: o prejuízo na leitura (condição também chamada de dislexia), na expressão escrita e na matemática. De acordo com o manual, para que ocorra o diagnóstico de prejuízos nestas habilidades, é necessário que seja verificada a presença de ao menos um dos sintomas a seguir que tenha persistido por no mínimo seis meses, mesmo após provisão de intervenções dirigidas a essas dificuldades:

- esforço significativo para ler, leitura lenta ou imprecisa de palavras com dificuldade de soletrá-las;
- dificuldade para compreender o sentido do que é lido, ainda que haja precisão na leitura;
- dificuldades para escrever ortograficamente, adicionando, omitindo ou substituindo as letras;
- dificuldades de clareza na expressão escrita, com erros gramaticais ou na pontuação de frases, organização inadequada de parágrafos;
- dificuldades no domínio do senso numérico, fatos ou calculos;
- dificuldades no raciocínio para aplicação de operações matemáticas e solução de problemas quantitativos.

Após a identificação do especificador do comprometimento, a sua gravidade deve ser determinada, podendo ser leve, moderada ou grave, de acordo com o nível de dificuldade no aprendizado da habilidade, do número de domínios afetados e da capacidade de compensação mediante os serviços de apoio recebidos. Outras características das condições incluídas no transtorno, além de sua origem biológica, as habilidades acadêmicas afetadas estão substancialmente abaixo do esperado para a idade cronológica do indivíduo, impactando significativamente no desempenho acadêmico ou nas atividades cotidianas. Além disso, os transtornos do neurodesenvolvimento são condições crônicas que persistem até a idade adulta, ocorrem independentemente da cultura, gênero ou classe social e podem se manifestar de forma diferente em diferentes condições de desenvolvimento (DSM-5, 2014).

A dislexia é um transtorno que afeta entre 5% a 15% da população mundial (DSM-5, 2014), desconsiderando cultura, classe social ou gênero e tem uma carga genética importante como fator de risco, sendo que até 50% de crianças com dislexia apresentam pais também com o transtorno e as estimativas de herdabilidade variam de 44% a 75% (MENG et al., 2005). Diversas teorias tentam explicar as causas da dislexia e dentre elas, uma teoria amplamente estudada e a mais adotada entre os pesquisadores é a do déficit fonológico, a qual considera que os problemas da leitura são decorrentes de dificuldades no processamento fonológico (MEDINA; SOUZA; GUIMARÃES, 2018). Contudo, diversos estudos tem mostrado que os prejuízos observados em indivíduos com dislexia vão além dos déficits no processamento fonológico e compromentem outras habilidades além da alfabetização, como memória de trabalho (SMITH-SPARK et al., 2003; SMITH-SPARK; FISK, 2007; CAMPEN; SEGERS; VERHOEVEN, 2018; HABID, 2021), sequenciamento (STEIN; WALSH, 1997; PETER et al., 2017; HEBERT et al., 2018), problemas com a postura, equilíbrio, velocidade, precisão, automatização, marcos motores atrasados (NICOLSON; FAWCETT, 1995; NICOLSON; FAWCETT; DEAN, 1995, 2001; NICOLSON; FAWCETT, 2011), além de dificuldades em tarefas motoras finas e habilidades de escrita à mão (PREIS; SCHITTLER; LENARD, 1997; CHENG-LAI et al., 2013; SUÁREZ-COALLA et al., 2020; YANG et al., 2021). O comprometimento destas habilidades pode ocasionar prejuízos no processo de alfabetização, que é um processo complexo por si só, pois, envolve a superposição de habilidades cognitivas, linguísticas e motoras, contudo, é um momento crucial para que ocorra o aprendizado da leitura e escrita (OKUDA et al., 2011). Problemas nestas habilidades podem influenciar o desempenho escolar, bem como intensificar a dificuldade na aprendizagem da leitura e da escrita, especialmente nos disléxicos.

Focando nas habilidades cognitivas, especialmente a memória, Medina, Minetto e Guimarães (2017) realizaram uma revisão sistemática da literatura para analisar as produções científicas sobre o funcionamento das funções executivas na dislexia. Os resultados encontrados em suas buscas indicam que indivíduos com dislexia apresentam déficits na memória de trabalho quando avaliada como componente integral, no entanto, quando avaliados os seus subcomponentes isoladamente, os estudos não tiveram consonância, visto que, alguns estudos indicaram prejuízos na alça fonológica e no executivo central, porém, não identificaram

déficits no esboço visuoespacial. Contudo, de acordo com os autores, ainda assim, seria possível afirmar que a qualidade da leitura depende da performance da memória de trabalho, uma vez que, a memória de trabalho é necessária para manter detalhes de uma história na mente, para construir uma representação coerente que dê sentido ao texto, incluindo detalhes descobertos durante o processo de leitura.

A memória de trabalho também é necessária na realização do ato motor da escrita, uma vez que envolve o planejamento, a manipulação e correção das palavras, fazendo uma ligação entre a forma das palavras com a escrita à mão (BERNINGER *et al.*, 2008). Capellini, Coppede e Valle (2010) investigaram a função motora fina de 20 crianças com dislexia e identificaram uma maior porcentagem de crianças com disfunção motora leve e moderada quando comparados ao grupo controle de desenvolvimento típico. Também foi observada uma maior frequência de disgrafia no grupo disléxico, evidenciando que as alterações motoras finas, sensoriais e perceptivas mostraram-se prejudicadas neste grupo. Estes achados corroboram os resultados de Okuda *et al.* (2011) que investigaram o desempenho da coordenação motora fina em 11 crianças com dislexia e identificou uma diferença estatisticamente significativa entre o grupo disléxico e o grupo controle, revelando que o grupo disléxico apresentou desempenho nas habilidades motoras finas muito inferiores à idade cronológica, com dificuldades em tarefas de preensão e pressão de objetos e coordenação visuoespacial, o que pode ser justificado pela idade motora fina aquém do esperado para idade e escolaridade.

As características neuropsicológicas de crianças disléxicas foi objeto de estudo de Cruz-Rodrigues *et al.* (2014), que contou com uma amostra de 39 crianças disléxicas, comparadas a um grupo controle formado por 34 crianças com desenvolvimento típico. Foram encontradas diferenças significativas entre os grupos, em que o grupo formado por crianças disléxicas apresentou pior performance nas tarefas envolvendo as funções executivas, memória de trabalho fonológica, memória semântica e discriminação direita-esquerda. Estes resultados corroboram os achados de Lukasova, Barbosa e Macedo (2009) que identificaram uma perda mais rápida da informação fonológica na memória de trabalho de crianças disléxicas e de Ramus, Pidgeon e Frith (2003) que verificaram que aproximadamente 77% dos disléxicos apresentaram mais de um desvio padrão abaixo do grupo controle em habilidade fonológica. Ramus, Pidgeon e Frith (2003) investigaram a relação entre habilidades fonológicas e controle motor em crianças com dislexia. O estudo contou com a participação de 22 crianças com idades entre 8 e 12 anos, recrutadas de uma escola especial para crianças disléxicas e revelou que crianças com dislexia apresentaram um índice significativamente abaixo em todas as tarefas comparadas ao grupo controle, sendo que 59% das crianças disléxicas apresentaram comprometimento nas habilidades motoras. Estes achados indicam que a aprendizagem e o desenvolvimento de habilidades envolvendo leitura e escrita em crianças estão relacionadas com o desenvolvimento de funções neuropsicológicas, biológicas e fatores maturacionais (CRUZ-RODRIGUES *et al.*, 2014).

De acordo com Diamond (2000), o desenvolvimento e amadurecimento das habilidades cognitivas e motoras ocorrem de forma concomitantemente, sendo que o desenvolvimento cognitivo e o desenvolvimento motor parecem estar fundamentalmente interligados. Ainda segundo a autora, o controle motor fino, a coordenação bimanual e as habilidades visuomotoras não são totalmente desenvolvidos até a adolescência, assim como as funções cognitivas mais complexas, como o controle inibitório, flexibilidade cognitiva e memória de trabalho. Smith-Spark e Fisk (2007) analisaram a memória de trabalho de 22 estudantes adultos com dislexia, e observaram que o grupo disléxico apresentou desempenho mais baixo do que os controles em todas as tarefas verbais, simples e complexas, indicando que as dificuldades da memória de trabalho na dislexia se estendem até a idade adulta, podendo afetar o desempenho na área fonológica e visuoespacial, implicando uma disfunção executiva central, além de causar problemas com o armazenamento.

1.1 Memória de trabalho

A memória é a capacidade de utilizar processos cognitivos complexos que permitem que os indivíduos realizem a codificação da informação, armazenamento e consolidação para que posteriormente também seja possível recuperar essas informações (GAZZZANIGA, 2018). Essa capacidade possibilita que os indivíduos levem informações de experiências e armazenemnas para posterior recuperação. O bom funcionamento da memória é fundamental para a aquisição e consolidação do aprendizado, sendo que, do ponto de vista funcional, a memória de trabalho é crucial no momento da aquisição e da evocação de toda e qualquer outra memória, sendo esta declarativa ou não (LENT, 2008). A memória de trabalho diz respeito à habilidade de manter e manipular as informações na mente durante um curto período de tempo (BADDELEY; HITCH, 1974), permitindo o raciocínio, a aprendizagem, a compreensão e a resolução de problemas (DIAMOND, 2013). Embora o termo "memória de trabalho" tenha sido utilizado pela primeira vez por Miller, Galanter e Pribam (1960), sua definição e melhor compreensão se deu a partir dos estudos conduzidos por Alan Baddeley (MECCA; DIAS; ABREU, 2019). Em 1974, Baddeley e Hitch propuseram o modelo multicomponente da memória de trabalho, no qual haviam três componentes, distintos em sua função e hierarquia, sendo o executivo central e dois sistemas escravos: a alça fonológica e o esboço visuoespacial. A alça fonológica é supostamente especializada na gravação de sequências acústicas ou itens baseados na fala, enquanto que o esboço visuoespacial exerce uma função semelhante em itens codificados visual e/ou espacialmente (BADDELEY, 2011). Este modelo pressupõe que a alça fonológica tenha dois subcomponentes, um armazenador de curta duração e um processo de treino articulatório. Baddeley (2011) explica que este armazenador é responsável pela estocagem de uma quantidade limitada de informações que duram poucos segundos, porém, estas informações podem ser reavivadas por treino subvocal, dizendo-se os itens para si mesmo, o que depende de um processo articulatório vocal ou subvocal a partir de uma reverberação articulatória. Analogamente à alça fonológica, o esboço visuoespacial também se constitui por dois subocomponentes: o armazenador visual e o mecanismo espacial (MECCA; DIAS; ABREU, 2019). O armazenador visual é responsável por manter as informações acerca das características físicas dos objetos de acordo com a percepção da imagem visual, enquanto que, o mecanismo espacial está relacionado ao planejamento dos movimentos e reativação das informações visuoespaciais previamente armazenadas (BADDELEY, 2011).

De acordo com este modelo, os sistemas da alça fonológica e do esboço visuoespacial são controlados pelo executivo central, um sistema gerenciador com um controle atencional, em um lugar de um sistema de memória (BADDELEY, 2011). Esse componente é responsável pela manipulação e pela atualização das informações durante a realização de tarefas e sua principal função está ligada a dois modos de controle: um automático, baseado em hábitos existentes e outro dependente de um executivo atencional limitado, que entra em ação com estratégias alternativas para soluções de problemas quando o sistema automático se depara com uma situação nova (NORMAN; SHALLICE, 1986). Enquanto os sistemas da alça fonológica e do esboço visuoespacial são responsáveis por estocar uma quantidade limitada de informações (Span), o executivo central é demandado em tarefas que apresentam maior complexidade e maior demanda cognitiva, como na manipulação de informações da ordem inversa do Span de Dígitos e Cubos de Corsi (MECCA; DIAS; ABREU, 2019). Esses limites acerca da capacidade de processamento de informações foram investigados por George Miller, professor da Universidade de Harvard, que propôs em 1956, aspectos que influenciariam a quantidade de elementos mantidos na memória de curto prazo durante a realização de uma tarefa, atribuindo esta quantidade de elementos ao conceito de Span (MECCA; DIAS; ABREU, 2019). O Span é a capacidade de extensão e alcance acerca da quantidade de elementos que podem ser mantidos durante a execução de uma tarefa (MILLER, 1956).

Por fim, Baddeley (2000) propôs um quarto componente a este modelo de memória de trabalho: o *buffer* episódico ou retentor episódico, que permite a integração das informações dos sistemas de armazenamento temporário e de longo prazo, resgatando memórias de longo prazo para que possam ser manipuladas durante o processamento da memória de curto prazo (CRUZ-RODRIGUES; LIMA, 2015). Isto significa manter essas informações por um curto período de tempo, podendo manipulá-las e atualizá-las, além de poder fazer relações com informações prévias já consolidadas na memória de longo prazo (MECCA; DIAS; ABREU, 2019). De acordo com Baddeley (2011), qualquer sistema de memória, seja físico, eletrônico ou humano, requer três qualidades: a capacidade de codificar ou introduzir a informação no sistema, de armazenar para posteriormente encontrar e evocar essa informação. Lent (2008), explica que a fase de aquisição é coloquialmente chamada de "aprendizagem", enquanto a evocação recebe também as denominações: expressão, recuperação e lembrança. Embora esses três estágios atendam a diferentes funções, Baddeley (2011) ressalta a interação que ocorre, uma vez que o método de registro da codificação determina o que e como a informação é armazenada, o que, por sua vez, limitará o que pode ser evocado posteriormente.

Na dislexia, um déficit envolvendo o armazenamento temporário de informações verbais e visuais pressupõe que haja disponibilidade reduzida de recursos no processamento do componente executivo central do sistema de memória de trabalho (MENGHINI *et al.*, 2011). Como o executivo central coordena os sistemas escravos, integrando sua capacidade de armazenamento e disponibilizando recursos de atenção para o processamento online das informações recebidas (BADDELEY, 2011), uma falha do executivo central em supervisionar a atividade de ambos os sistemas, tanto da alça fonológica quanto do esboço visuoespacial, ou seja, podem ser responsáveis pelos déficits em tarefas de extensão verbal e visuoespacial (MENGHINI *et al.*, 2011). Prejuízos nesses processos terão impacto negativo não só no desempenho e na aprendizagem acadêmica, mas também no controle e na aprendizagem motora (SEIDLER; BO; ANGUERA, 2012).

1.2 Destreza manual

O comportamento motor é um sistema complexo, constituído de inúmeros subsistemas com fortes interações (MANOEL, 1999) que envolve múltiplas estruturas cerebrais, corticais e subcorticais para o ato de planejar, gerar e controlar o comportamento motor (TANJI, 2001). A ativação de respostas motoras envolve diversas variáveis, tais como a relação do indivíduo com o contexto em que a atividade ocorre e a ação conjunta de processos mentais como a atenção,

memória, tomada de decisões, controle sobre respostas prepotentes (LAGE, 2010). De acordo com Diamond (2000) o córtex pré-frontal dorsolateral, área relacionada às funções cognitivas complexas, apresenta extensivas conexões com as áreas envolvidas em funções motoras, como o córtex pré-motor e a área motora suplementar e, parece também contribuir para o desempenho motor. Esta interconexão entre as áreas pode influenciar tanto no desenvolvimento da motricidade, como da cognição, especialmente durante processos complexos, como o ato de escrita, que envolve muitas habilidades linguísticas e não linguísticas.

Durante o período de alfabetização ocorre a superposição de habilidades para a ocorrência da aprendizagem da leitura e escrita, envolvendo as habilidades cognitivas, linguísticas e motoras, principalmente de destreza manual (OKUDA et al., 2011). Essa última habilidade exige dos escolares o uso dos componentes sensório-motores e perceptivos para que ocorra a ação motora com uma preensão e pressão adequados para a execução do ato motor da escrita. Sendo assim, a criança é estimulada a treinar o ato motor para que desenvolva um bom controle motor, que diz respeito à capacidade de regular ou orientar os mecanismos essenciais para a execução do movimento (SHUMWAY-COOK; WOOLLACOTT, 2003). Esse processo propicia também que ocorra a aprendizagem motora que acontece com auxílio de uma prática sistemática a partir de informações externas sobre a habilidade e sobre a própria execução e é um processo que ocorre em minutos, horas, dias ou semanas (MANOEL, 1999). Contudo, embora uma criança aos seis anos de idade, no início da sua vida escolar, já apresente uma reprodução gráfica com traços bem definidos e integrados, sua habilidade gráfica continuará a ser modificada ao longo dos anos, uma vez que a aquisição de habilidades motoras é um processo contínuo no qual ordem e desordem se complementam (MANOEL, 1999). Um déficit, ou provavelmente a presença de múltiplos déficits, nestas habilidades, pode acarretar em diversos prejuízos durante o processo de alfabetização.

Déficits no sistema sensório-motor de crianças e adolescentes com dislexia refletem em um menor desempenho em tarefas manuais como o *tapping* (tarefa de toques repetidos dos dedos com exigência de precisão temporal), *peg moving* (tarefa de posicionamento que envolve velocidade e precisão espacial) e tarefas de tempo de reação (FAWCETT; NICOLSON, 1995; PREIS; SCHITLLER; LENARD, 1997; STEIN; STOODLEY, 2006). Ainda que se tenha estudos bem documentados acerca da memória de trabalho e destreza manual de crianças e adolescentes com dislexia, é escassa a literatura científica correlacionando as duas habilidades. Como o controle motor depende da memória de trabalho (SEIDLER; BO; ANGUERA, 2012) e ambos estão afetados em crianças disléxicas, é possível haver uma relação entre déficits na função de memória de trabalho impactando nos déficits motores. Dessa forma, o presente estudo tem como objetivo realizar uma revisão sistemática da literatura, comparar os resultados com metanálise e verificar se há uma associação entre as habilidades de memória de trabalho e destreza manual de crianças e adolescentes disléxicos.

2. OBJETIVOS

2.1 Objetivo Geral

Realizar uma revisão sistemática da literatura acerca dos estudos que avaliaram as habilidades de memória de trabalho e/ou destreza manual em crianças e adolescentes disléxicos e comparar os resultados com o emprego de uma metanálise.

2.2 Objetivos Específicos

- Realizar metanálise comparando os resultados encontrados para o grupo disléxico e para o grupo controle nos estudos que investigaram as habilidades de memória de trabalho e/ou destreza manual de crianças e adolescentes disléxicos.
- Realizar uma revisão sistemática da literatura com o emprego de metanálise para verificar se há uma associação entre as habilidades de memória de trabalho e destreza manual em crianças e adolescentes disléxicos.

2.3 Hipóteses

- Crianças e adolescentes com dislexia apresentariam pior desempenho nas tarefas de memória de trabalho e/ou destreza manual quando comparados à um grupo controle com desenvolvimento típico.
- As habilidades de memória de trabalho e destreza manual apresentariam algum nível de associação entre si.

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3. ARTIGO

WORKING MEMORY AND MANUAL DEXTERITY IN CHILDREN AND ADOLESCENTS WITH DYSLEXIA: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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ABSTRACT

Dyslexic children usually have impairments in a range of skills, among them, deficits in working memory and manual dexterity. Several hypotheses try to explain the cognitive and motor problems related to dyslexia, and some studies have shown a strong interconnection between both domains, and the possibility of interference with each other's proper functioning. Therefore, the aim of this study was to perform a systematic review and meta-analysis to analyze working memory and manual dexterity in dyslexic children. The elaboration and protocol were carried out according to the criteria established by PRISMA. Six literature databases were searched to locate studies published between 2000 and 2020: EMBASE, ERIC, ISI Web of Science, PubMed, PsycINFO and Scopus. The meta-analysis was performed using the meta package in R version 4.1.0. A total of 164 studies were found, 21 met the inclusion criteria. The findings suggest that dyslexic children have significantly poorer visuospatial and verbal working memory with more impairments in the phonological loop. No significant differences were found in manual dexterity.

Keywords: Working memory. Manual Dexterity. Handwriting. Fine Motor Skills. Dyslexia.

1. INTRODUCTION

Although there are many studies in the literature reporting on the deficit in phonological processing as one of the main factors involved in developmental dyslexia (Stanovich & Siegel, 1994; Snowling et al., 1997; Swan & Goswami, 1997; Snowling & Melby-Lervåg, 2016; Campen et al., 2018), this deficit does not explain the countless other problems that dyslexic children suffer from. There is still a gap in the area that does not make it clear which the subjacent factors are for dyslexia, as well as whether the extent of these difficulties in phonological processing can affect other areas, resulting in other deficits that can also impair reading learning. Studies have shown that dyslexic children usually have impairments in a range of skills such as phonological awareness, phonological coding, spelling, working memory (Swanson & Ashbaker, 2000; Smith-Spark et al., 2003; Smith-Spark & Fisk, 2007; Campen et al., 2018; Habid, 2021), sequencing (Stein & Walsh, 1997; Peter et al., 2017; Hebert et al., 2018), balance, speed, accuracy, automatization, and delayed motor milestones (Nicolson et al., 1995, 2001; Nicolson & Fawcett, 1995, 2011), in addition to difficulties in fine motor tasks and handwriting skills (Preis et al., 1997; Cheng-Lai et al., 2013; Suárez-Coalla et al., 2020; Yang et al., 2021). Several hypotheses try to explain the cognitive and motor problems related to dyslexia. An explanation widely studied in the literature focuses on an abnormality of the magnocellular system, which is specialized in processing fast temporal information, and these alterations in this system would lead to impairments in the perception of auditory and visual information (Stein & Walsh, 1997; Vidyasagar & Pammer, 1999; Gori et al., 2015). Galaburda et al. (1994) examined magnocellular pathway neurons in five post mortem dyslexic brains and compared them with seven typical controls, the authors identified that dyslexics had disordered lateral geniculate nucleus magnocellular layers and that the magnocells themselves were about 20% smaller than in controls. These alterations in the magnocellular pathways lead dyslexics to have problems processing fast sensory information adequately in any domain (Stein & Walsh, 1997), which could further compromise their process of learning to read and write.

Another theory widely studied in the literature suggests a hypothesis of a cerebellar deficit in dyslexic individuals that could lead to learning impairment (Nicolson & Fawcett, 1995; Nicolson et al., 1995, 1999, 2001). In addition to participating in the learning stages, the cerebellum has been reported in the literature as being important not only for motor functions but also for cognitive functions, especially when there are tasks that require activation of the dorsolateral prefrontal cortex (DLPFC) (Diamond, 2000; Stoodley, 2012; Marvel et al., 2019). According to Diamond (2000), a cognitive task increases activation in the DLPFC and

concomitantly also leads to an increase in activation of the contralateral cerebellum, and the opposite also happens when there is a decrease in activation of the DLPFC a decrease in cerebellar activation is also observed. The activation of these two areas can be observed in the study of Raichle et al. (1994) in which they utilized positron emission tomography (PET) to analyze the brain mechanisms associated with performance improvement. There was a simple answer selection task and individuals were asked to repeat the nouns presented visually. It was found that the areas of the brain most active during the task the were cortices anterior cingulate, left prefrontal and left posterior temporal, and the right cerebellar hemisphere. Berman et al. (1995) also utilized PET to analyze the neural circuit activated during a cognitive task that used the Wisconsin Card Sorting Test (WCST). They encountered that the brain areas activated during WCST performance involve the frontal cortex, the inferior parietal lobe, and inferior temporal cortices, as well as portions of the cerebellum. These findings indicate the participation of the cerebellum in the learning process and establish that during the early stages of learning, the cerebellum is more active while learning fixation and skill automation require less cerebellar activation (Nicolson et al., 1995, 1999, 2001).

Hertrich et al. (2021) performed a literature review to analyze the DLPFC for speech and neural correlates, and their findings demonstrated that the lateral parts of the cerebellum seem to be involved in evolution, concurrently with the prefrontal cortex, and damage to the cerebellum during child development may result in cerebellar-induced hypo-development of the DLPFC. One possible explanation is that both the prefrontal cortex and the neocerebellum have a prolonged maturation period, and development damage may affect the maturation of the neural structures leading to profound consequences for prefrontal and cerebellar development (Diamond, 2000). These two areas are interconnected throughout the maturation and aging of the brain, and a decrease in cerebellar volume was observed in older individuals, which may be associated with cognitive and motor decline, and a correlation between the volume in the cerebellar hemisphere and verbal performance and non-verbal working memory tasks were also identified (Bernard & Seidler, 2014). These findings in the literature show that activation of the DLPFC and the cerebellum may be fundamentally correlated and closely coupled (Diamond, 2000).

Anatomical, electrophysiological, and functional neuroimaging studies have contributed to elucidate the organization and functioning of these areas in dyslexic brains. Stoodley (2014) conducted a literature study and meta-analysis with anatomical probability estimation in voxel-based morphometry studies to analyze the gray matter of the cerebellum in individuals with dyslexia, comparing with a group of individuals with autism spectrum

disorder, a group with a disorder attention deficit hyperactivity and with age-matched typical developmental controls. The results of the study by Stoodley (2014) indicated that different regions of the cerebellum showed reduced gray matter in all three groups with a neurodevelopmental disorder. Although, the author emphasizes that some regions were overlapped in the different disorders groups, making it unclear whether it was really the disorder or possible comorbidity, which is very common in these neurodevelopmental disorders. In the group with dyslexia, a significant difference was found in the bilaterally lobule VI, however, the right lobule VI and right Cruss II showed a significant decrease in the gray matter of the cerebellum. The right lobule VI is involved in language and working memory processing while left lobule VI is involved in visuospatial attention (Stoodley, 2014), and reduced gray matter in the left area could influence the difficulties in learning to read and write in dyslexia. Furthermore, it was shown that during reading tasks, an overactivation in the left VI cerebellar lobule in dyslexic individuals was observed, indicating an increase in effort or activation of compensatory strategies for performing the tasks. These findings corroborate the discovered in the literature that show the cerebellum is involved in the processing of cognitive and motor functions (Nicolson & Fawcett, 1994, 1995; Fawcett & Nicolson, 1999; Stoodley & Stein, 2013; Marien & Beaton, 2014; Ashida et al., 2019; Ashburn, 2019).

Several studies have shown impairment of cerebellar functions in individuals with dyslexia (Nicolson & Fawcett, 1995; Nicolson et al., 1995; Fawcett et al., 1996; Fawcett & Nicolson, 1995; Nicolson et al., 2001; Nicolson & Fawcett, 2011; Stoodley & Stein, 2013; Mariën & Beaton, 2014) and problems in tasks involving DLPFC functions, such as planning, decision making and working memory tasks in dyslexic individuals (Swanson, 2000; Swanson & Ashbaker, 2000; Smith-Spark et al., 2003; Cowan et al., 2017; Habib, 2021). Thus, these neural alterations may intensify the difficulty in the learning process of dyslexic children, since literacy is a complex period that involves the overlap of several concomitant skills. Literacy completely changes neural structures and improves initial visual processing and reorganizes the ventral occipitotemporal pathway that is responsible for responses to written characters (Dehaene et al., 2015), as can be seen in Figure 1, which shows the brain areas involved in reading. However, learning to read is a complex process that could be influenced by a range of cognitive factors, from low-level sensory processes to higher-order cognitive processes such as working memory (Beneventi et al., 2010).



Figure 1. (A) The brain areas involved in reading: Brodmann areas (BA). (B) The neural circuits involved in reading: The information captured by the eyes is sent to the primary occipital area for a first screening (A) which is sent to the fusiform gyrus (B) where the invariant traces that form the letters are stored. After word recognition, lexical access and the meaning of the word occur (C) in the inferior frontal, anterior temporal, anterior fusiform, and angular gyrus areas. Access to speech pronunciation and articulation takes place in the areas of the anterior insula, precentral areas, superior temporal regions, and in the supramarginal region (D) and occurs regardless of whether the reading is silent or aloud (Dehaene, 2012; Pinheiro and Scliar-Cabral, 2017). The dorsolateral cerebral cortex (E) is also involved in the reading process along with the right lobe VI of the cerebellum which is involved in language processing (Stoodley, 2014).

Working memory is a memory system of limited capacity that allows the temporary storage, processing, and manipulation of information necessary for complex tasks such as comprehension, learning, and reasoning (Baddeley, 1986). It is defined as a multi-component system whose information processing is based on four distinct components in its function and hierarchy, comprising the central executive and two slave systems of specific modalities: the phonological loop and the visuospatial sketchpad (Baddeley, 2000). The central executive is a management system, which works as an attentional control system, responsible for handling and updating information during tasks responsible for controlling the supervisory activation system (Baddeley et al., 2011). The phonological loop and the visuospatial sketchpad are the components responsible for short-term storage, working in parallel, the phonological loop being responsible for the temporary storage of spoken information and the visuospatial sketchpad for storing visuospatial information (Baddeley, 2003). Finally, the last component to be inserted in the model was the episodic buffer or retainer, which allows the integration of information from temporary storage systems (Baddeley et al., 2017). Although the components of working memory are in spread across different regions of the brain (Baddeley, 2003; Paulesu et al., 1993), they remain in constant communication, including the cerebellum, which seem to be involved in neural systems important for cognitive and motor functions (Figure 2) (Diamond, 2000).



Figure 2. The neural circuits involved in working memory components and motor behavior. (**A**) The visuospatial working memory involves activation primarily of the right hemisphere with activation of the central executive, and activation of areas responsible for visual storage (BA 19 and 37), and for spatial rehearsal (47 and 7), and the locus of the storage component of the loop (BA 40) along with the rehearsal component (BA 6), are also activated (Baddeley, 2003). (**B**) The central executive is also involved in verbal working memory, including the dorsolateral prefrontal cortex and inferior frontal gyrus areas (BA 46, 9 and 47), the articulatory rehearsal (BA 44), the phonological store (BA 40), the passive perception of phonemes (BA 42 and 22) activated bilaterally, and visual processing of letters area in the left (BA 18), in addition, cerebral areas thought to be devoted to motor aspects of speech planning and execution (BA 6), and cerebellum and primary sensorimotor areas of mouth and larynx (BA 4, 3, 2, 1) were activated even though there was no overt speech (Paulesu et al., 1993). (**C**) During activation of the dorsolateral prefrontal cortex (46 and 9) in working memory, there is an activation of the contralateral neocerebellum (Diamond, 2000), and also from the right lobe VI of the cerebellum (Stoodley, 2014). The same happens when demand is a motor task, there is activation of the cerebellum and dorsolateral prefrontal cortex (Diamond, 2000).

Deficits in working memory could lead to various impairments in learning, making it difficult to acquire reading and writing skills, since the acquisition of these skills depends on the proper functioning of working memory, where the words read can be processed and mentally manipulated by enough time for the meaning and form of writing to be extracted (Van Galen, 1991; Baddeley et al., 1998). In relation to writing, for example, the findings by Berninger et al. (2008) show that the planning of handwriting was significantly correlated with the word form factor, indicating that the orthographic loop of working memory can link spelling word forms with the hand, just as the phonological loop links the phonological word forms with the writing is not just a motor skill (Berninger et al., 2008). Regardless of the path taken to access the orthographic representation, this representation must be kept in working memory storage, in which the abstract graphemic units are kept for later use, assigning the letter name in oral

spelling or the letter format in handwriting (Afonso et al., 2019). Thus, as seen above, dyslexic children have deficits in working memory skills and manual dexterity (handwriting skills), so there is a possibility that both compromised functions are interfering with each other's proper functioning, as can be seen in Figure 3.



Figure 3. The functioning of the dyslexic brain: There are cortical under-thicknesses and numerous ectopias concentrated in the left hemisphere (Galaburda et al., 1985). The temporal lobe anatomy is disorganized, its connectivity is altered and there is hypoactivation in this region (\clubsuit) (Dehaene, 2012). There is a partial disconnection of the left temporal region with the rest of the brain, particularly in the frontal regions, resulting in impairment of working memory (\clubsuit). There is a significant decrease in gray matter in the right lobe VI and Cruss II of the cerebellum (\clubsuit) (Stoodley, 2014).

As for DLPFC subserves cognitive functions, allowing us to keep information in mind so we can remember what to do, organize it, resist distraction and stay on task, and inhibit inappropriate action. All of these cognitive functions are clearly important for qualified motor performance (Diamond, 2000). The development of handwriting skills is complex and involves several components, such as fine motor control, precision, proprioception, in addition to visual perception skills (Van Galen, 1991; Feder & Majnemer, 2007). Learning the motor act of writing takes place from a process in which the child learns to integrate all these skills through development, progression and maturation, therefore, handwriting skills usually become more mature as the child grows (Lam et al., 2011). Failures in the proper development of writing speed or in the ability to make adjustments imply more time needed to perform writing tasks, which makes schoolwork even more difficult (Borella et al., 2011). Studies have shown that dyslexic children have difficulties with handwriting and, during writing, are slower and produce more and longer pauses than typically developing children (Stoodley & Stein, 2006; Sumner et al., 2013, 2014; Hebert et al., 2018; Suárez-Coalla et al., 2020). However, not only readability and speed are important when writing, but also automaticity so that there is a quick and effortless recovery in the production of readable letters (Berninger et al., 2008). The present study aimed to perform a systematic review of the literature, comparing the results with metaanalysis of working memory and manual dexterity skills between the dyslexic group and the control group of the studies analyzed and verified whether there is an association between these two skills in dyslexic children and adolescents.

2. METHODS

The methodology of this review was previously registered in the PROSPERO database, the international prospective register of systematic reviews by Leão et al. (2021), under the registration number: CRD 42021238901. The preparation and reporting of this review were undertaken according to the guidelines established by Preferred Reporting for Systematic Reviews and Meta-analyzes - PRISMA statement (Moher et al., 2009). A literature search was performed for articles published in each database from 2000 until December 31th 2020. The organization of the studies found as well as the initial screening of abstracts and titles of each study was carried out using the Rayyan tool for systematic reviews (Ouzzani et al., 2016).

2.1 Search strategy and studies found

The bibliographic search was performed in EMBASE, ERIC, ISI Web of Science, PubMed, PsycINFO, and Scopus databases, using the advanced search terms following combinations of terms (1 AND 2 AND 3):

- Dyslexia ("dyslexia"[MeSH Terms] OR "dyslexi*"[All Fields] OR "reading disabilit*"[All Fields] OR "reading disorder*"[All Fields] OR "reading difficult*"[All Fields] OR "reading deficit*"[All Fields] OR "reading impairment*"[All Fields] OR "developmental dyslexia"[All Fields] OR "specific reading disorder"[All Fields] OR "developmental reading disorder"[All Fields] OR "developmental language deficit"[All Fields]).
- Working memory ("working memory"[MeSH Terms] OR "working memor*"[All Fields] OR "short term memor*"[All Fields] OR "short-term memor*"[All Fields] OR "shortterm memor*"[All Fields] OR "immediate memor*"[All Fields] OR "immediate recall"[All Fields]).
- Manual dexterity ("manual dexterity"[All Fields] OR "handwriting"[All Fields] OR "fine motor skills"[All Fields] OR "motor control"[All Fields] OR "motor skills deficit"[All Fields] OR "motor difficult"[All Fields] OR "motor performance"[All Fields] OR "motor impairment"[All Fields]).
The keywords used during the research were consulted in the Medical Subject Headings (MeSH), in addition, there were used terms in articles already published but which were not in MeSH. A total of 167 articles were identified in the initial search on the six databases: EMBASE (n = 57), ERIC (n = 4), ISI Web of Science (n = 42), PubMed (n = 17), PsycINFO (n = 13) and Scopus (n = 34). Subsequently, the snowballing technique was used for a search based on the references that were listed in the studies found.

2.2 Eligibility criteria

The inclusion criteria of the studies were: a) articles that investigated the working memory skills and/or manual dexterity of dyslexic children; b) focus on children aged 6-16 years old; c) individuals diagnosed with developmental dyslexia; d) period of publication between 2000 and 2020; e) articles published in the English language; f) original articles. The children's age range was chosen because it covers the period of literacy and schooling, a period in which learning difficulties and possible diagnoses occur. A limited range of literature was selected between 2000 and 2020, because it gives an overview of the most recent literature on the relationship between working memory and manual dexterity in dyslexic children. The studies with their special populations (e.g., brain injuries, children born preterm), review articles, case studies and opinions that did not provide detailed descriptions of their procedures were excluded.

Two review authors (SESAL and AMVP) examined the articles found in the database searches and excluded the irrelevant studies based on the eligibility criteria. The titles and abstracts of all articles were read. In cases where the reading of the title and the abstract were not sufficient to meet the inclusion criteria, the full text was examined. A search for eligibility of studies was carried out, the authors discussed the coherence of the data and, individually, analyzed each study for the final selection. Any disagreements that arose between the authors were resolved through discussion, or with a third reviewer. If the inclusion of a study was unclear due to missing information, the reviewers tried to contact the authors for further details. After a consensus between the same two reviewers' authors, the total of twenty-one articles was considered eligible and, therefore, included in the present study.



Figure 4. Flow diagram of stages adopted in the systematic review of articles and meta-analysis.

2.3 Study quality

The methodological quality of the included studies was evaluated using the tool Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies (Appendix 1). This tool consists of eight items that assess whether the studies showed the criteria as the following assessment for each item: "yes", "no", "unclear" or "not applicable". To further reduce bias, all items were evaluated by two evaluators. The two authors independently assessed the quality of each article, any disagreements between them were resolved through discussion until a consensus was reached, or with a third reviewer.

2.4 Data extraction

The studies were evaluated according to their methodological structure, following main categories: study purpose, study design, sample, outcomes, results, conclusions and if containing necessary information about the experiment and the type of evaluation that was carried out, as well as if the comparison was made intrasubject or if there was a control group which could be compared and synthesized. Information about the country and the scientific journals in which the studies were published can be seen in Table 1. The Table 2 shows detailed information on the methodological quality of the reviewed studies. Data on the type of study, the authors, title, and purpose are presented in Table 3. The samples of the studies were composed of participants male and female with the clinical diagnosis of dyslexia. Table 4 provides a summary of the demographic and clinical data of the sample, the information from each study on the assessment, assessment tools, including the results section.

2.5 Data Analyses

The meta-analysis was performed using the "metacont" function of the meta package in R version 4.1.0 (Viechtbauer, 2010; Assink & Wibbelink, 2016). We present both fixed-and random-effect models. It has been suggested to use random-effects model when heterogeneity was at least moderately high (> 40%), a small number of studies were obtained, or different experimental designs were observed across studies (Higgins et al., 2003). Means, standard deviations and sample size during the post-test were extracted from each study to determine the overall effect size (Hedges' g). By convention, an effect size of 0.2, 0.5, and 0.8 was considered small, medium, and large, respectively (Durlak, 2009). The heterogeneity among the studies was assessed using the Inconsistency (I²) statistic. According to Bryan et al., (2021), most

treatment effects are heterogeneous, therefore, variation in effect characteristics between replication studies is expected; in addition, heterogeneity can help dispel the confusion and uncertainty caused by unexplained inconsistency in research results, and knowing how to identify the moderators of experimental effects can be a powerful tool to identify causal mechanisms. The results are presented in forest plots in which the difference between groups in each study is represented by a square. Publication bias was assessed using the Egger (Egger et al., 1997) and Begg (Begg & Mazumdar, 1994) tests when the number of studies was greater than ten primary studies.

3. RESULTS

3.1 Included studies

Twenty-one articles comprised the sample were published between 2000 and 2020 in the following scientific journals can be seen in Table 1. Five studies were carried out in the United States of America, four in the United Kingdom, two in Canada, China, France and Italy, one in Belgium, Greece, Norway, and Spain. A total of 3.129 participants were included across twenty-one studies. Sample sizes ranged from 24 to 893. The mean [M] age of participants was 10.69 years, standard deviation [SD] = 1.53, with 62.90% boys (M = 54.25, SD = 77.73) and 37.10% girls (M = 32, SD = 54.93). The study by Mati-Zissi and Zafiropoulou (2003) was not included in this pooled analysis, as it did not present the necessary data. From a total of twentyone studies, eleven included the assessment of both skills working memory and manual dexterity (Mati-Zissi & Zafiropoulou, 2003; Ramus et al., 2003; Jeffries & Everatt, 2004; Berninger et al., 2005; Savage & Frederickson, 2006; Chaix et al., 2007; Berninger et al., 2015; Lyman et al., 2017; Sanders et al., 2017; Marchand-Krynski et al., 2018; Afonso et al., 2019), five assessed only working memory (Toplak et al., 2003; Beneventi et al., 2010; Menghini et al., 2011; Parke et al., 2015; Maziero et al., 2020), and five assessed only manual dexterity (Borella et al., 2011; Lam et al., 2011; Cheng-Lai et al., 2013; Sumner & Barnett, 2014; Gosse & Reybroeck, 2020).

	Fable 1. In	formation	about the o	country a	and the	scientific	journals	s in	which	the stu	idies v	were j	published	1.
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Authors (Year)	Country	Journal
Afonso et al. (2019)	Spain	Journal of Learning Disabilities
Beneventi et al. (2010)	Norway	Scandinavian Journal of Psychology
Berninger et al. (2008)	United States	Journal of School Psychology
Berninger et al. (2015)	United States	Reading and Writing
Borella et al. (2011)	Italy	Brain and Cognition
Chaix et al. (2007)	France	European Paediatric Neurology
Cheng-Lai et al. (2013)	China	Research in Developmental Disabilities
Gosse and Reybroeck (2020)	Belgium	Research in Developmental Disabilities
Jeffries and Everatt (2004)	United Kingdom	Dyslexia
Lam et al. (2011)	China	Research in Developmental Disabilities
Lyman et al. (2017)	United States	Journal of Behavioral and Brain Science
Marchand-Krynski et al. (2018)	Canada	Developmental Neuropsychology
Mati-Zissi and Zafiropoulou (2003)	Greece	Perceptual and Motor Skills
Maziero et al. (2020)	France	Journal of Clinical and Experimental
		Neuropsychology
Menghini et al. (2011)	Italy	Developmental Neuropsychology
Parke et al. (2015)	United States	Journal of Attention Disorders
Ramus et al. (2003)	United Kingdom	Journal of Child Psychology and Psychiatry
Sanders et al. (2017)	United States	Journal of Learning Disabilities
Savage and Frederickson (2006)	United Kingdom	Journal of Learning Disabilities
Sumner and Barnett (2014)	United Kingdom	Journal of Experimental Psychology:
		Learning, Memory, and Cognition
Toplak et al. (2003)	Canada	Journal of Child Psychology and Psychiatry

3.2 Quality assessment

The methodological quality of the reviewed studies was analyzed using the Critical Appraisal Checklist for Analytical Cross-Sectional Studies by Joanna Briggs Institute. The checklist is in accordance with the types of study selected and was considered the most appropriate study quality tool to be used. This checklist does not provide an arbitrary classification to indicate for low-quality studies versus high-quality studies, however a total summated score of each article is provided in Table 2. The methodological quality score of the included studies ranged from 3 to 8, with a mean of 5.86 (SD = 1.31).

Authors (Year)	1	2	3	4	5	6	7	8	Total
Afonso et al. (2019)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Beneventi et al. (2010)	Yes	8							
Berninger et al. (2008)	Un.	Un.	Yes	Yes	Yes	Un.	Yes	Yes	5
Berninger et al. (2015)	Yes	Un.	Yes	Yes	No	No	Yes	Yes	5
Borella et al. (2011)	Yes	Yes	Yes	Yes	Un.	Un.	Yes	Yes	6
Chaix et al. (2007)	Un.	Yes	Yes	Yes	Yes	Un.	Yes	Yes	6
Cheng-Lai et al. (2013)	Yes	Yes	Yes	Yes	Un.	Un.	Yes	Yes	6
Gosse and Reybroeck (2020)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Jeffries and Everatt (2004)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Lam et al. (2011)	Yes	Yes	Yes	Yes	Un.	Un.	Yes	Yes	6
Lyman et al. (2017)	Un.	No	Yes	Yes	No	No	Yes	Yes	4
Marchand-Krynski et al. (2018)	Yes	8							
Mati-Zissi and Zafiropoulou (2003)	No	Un.	Yes	Yes	No	No	Yes	Un.	3
Maziero et al. (2020)	Yes	8							
Menghini et al. (2011)	Yes	8							
Parke et al. (2015)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Ramus et al. (2003)	Yes	Yes	Yes	Yes	Un.	Un.	Yes	Yes	6
Sanders et al. (2017)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Savage and Frederickson (2006)	No	Yes	Yes	Yes	No	No	Yes	Yes	5
Sumner and Barnett (2014)	Un.	Yes	Yes	Yes	No	No	Yes	Yes	5
Toplak et al. (2003)	Yes	Yes	Yes	Yes	Un.	Un.	Yes	Yes	6
Total (Yes/No and Un.)	13/8	18/3	21/0	21/0	6/15	4/17	21/0	20/1	

Table 2. Methodological quality of the reviewed studies using the Joanna Briggs Institute Critical Appraisal

 Checklist for Analytical Cross Sectional Studies.

Abbreviations: Un. = unclear. Questions: (1) Were the criteria for inclusion in the sample clearly defined? (2) Were the study subjects and the setting described in detail? (3) Was the exposure measured in a valid and reliable way? (4) Were objective, standard criteria used for measurement of the condition? (5) Were confounding factors identified? (6) Were strategies to deal with confounding factors stated? (7) Were the outcomes measured in a valid and reliable way? (8) Was appropriate statistical analysis used?

Table 3. Data on the authors, title, and objective of the analyzed articles.

Authors (Year)	Title	Goal
Afonso et al. (2019)	Writing impairments in Spanish children with developmental dyslexia	To evaluate which components of the writing production process are impaired in Spanish children with developmental dyslexia.
Beneventi et al. (2010)	Executive working memory processes in dyslexia: Behavioral and fMRI evidence	To investigate cortical activation related to verbal Working Memory in dyslexic and normal readers, controlling for phonological awareness processing.
Berninger et al. (2008)	Writing problems in developmental dyslexia: Under- recognized and under-treated	To evaluate whether individuals with dyslexia show the same pattern of relationships between transcription and composition as the typically developing writers.
Berninger et al. (2015)	Differential diagnosis of dysgraphia, dyslexia, and OWL LD: behavioral and neuroimaging evidence	To evaluate the working memory components supporting language learning across the three diagnostic groups – dysgraphia, dyslexia, and oral and written language learning disability compared to control typical learners and also in fMRI functional connectivity during the same word-specific spelling task.
Borella et al. (2011)	Increased intraindividual variability is a marker of ADHD but also of dyslexia: A study on handwriting	To investigate the role of intraindividual variability in children with ADHD and with dyslexia, by comparing them in a handwriting task and in a simple response time task.
Chaix et al. (2007)	Motor impairment in dyslexia: the influence of attention disorders	To determine the frequency of motor impairments in a population of children with phonological dyslexia and specify possible links with attention deficit.
Cheng-Lai et al. (2013)	Writing to dictation and handwriting performance among Chinese children with dyslexia: Relationships with orthographic knowledge and perceptual-motor skills	To investigate the relationships between writing to dictation, handwriting, orthographic, and perceptual-motor skills among Chinese children with dyslexia.
Gosse and Reybroeck (2020)	Do children with dyslexia present a handwriting deficit? Impact of word orthographic and graphic complexity on handwriting and spelling performance	To evaluate the hypothesis of the presence of handwriting difficulties in dyslexia, through the investigation of the impact of graphic and orthographic complexity of words on writing.
Jeffries and Everatt (2004)	Working Memory: Its role in dyslexia and other specific learning difficulties	To compare the executive functioning and motor coordination of dyslexic children against a control group of children without special educational needs and a group with varied.
Lam et al. (2011)	Chinese handwriting performance of primary school children with dyslexia	To investigate the Chinese handwriting performance of typical children and children with dyslexia, and to examine whether speed and accuracy of handwriting could reliably discriminate these two groups of children.
Lyman et al. (2017)	Translating interdisciplinary research on language learning into identifying specific learning disabilities in verbally gifted and average children and youth	To investigate the cognitive ability and multiple-working memory endophenotypes in students with and without specific learning disabilities in written language.
Marchand-Krynski et al. (2018)	Cognitive predictors of sequential motor impairments in children with dyslexia and/or attention deficit/hyperactivity disorder	To examine cognitive predictors of sequential motor skills in children with dyslexia and/or attention deficit/hyperactivity disorder.

Mati-Zissi and Zafiropoulou (2003)	Visuomotor coordination and visuospatial working memory of children with specific reading disabilities: A study using the Rey-Osterrieth Complex Figure	To examine the visuospatial perception, short-term working memory, and motor skills of children with special reading difficulties.
Maziero et al. (2020)	Influence of comorbidity on working memory profile in dyslexia and developmental coordination disorder	To compare working memory performance in children with developmental dyslexia and developmental coordination disorder.
Menghini et al. (2011)	Working memory impairment in children with developmental dyslexia: is it just a phonological deficit?	To ascertain whether the working memory deficit in developmental dyslexia is confined to verbal material or whether it also involves visual-object and visual-spatial information.
Parke et al. (2015)	Intellectual profiles in children with ADHD and comorbid learning and motor disorders	To examine Wechsler Intelligence Scale for Children–Fourth Edition profiles of children with attention-deficit/hyperactivity disorder alone and with comorbid neurodevelopmental disorders.
Ramus et al. (2003)	The relationship between motor control and phonology in dyslexic children	To investigate the automaticity cerebellar theory of dyslexia.
Sanders et al. (2017)	Sequential prediction of literacy achievement for specific learning disabilities contrasting in impaired levels of language in grades 4 to 9	To evaluate whether the finding that cognitive-linguistic translation explains unique variance in typical children's reading and writing outcomes can be replicated in students who have language-related specific learning disorders.
Savage and Frederickson (2006)	Beyond phonology: what else is needed to describe the problems of below-average readers and spellers?	To explore questions concerning the cognitive and motor difficulties of below- average readers.
Sumner and Barnett	The influence of spelling ability on handwriting production:	To examine execution speed and temporal characteristics of handwriting and to
(2014)	children with and without dyslexia	determine the predictive value of spelling, pausing, and motor skill on handwriting production in children with dyslexia.
Toplak et al. (2003)	Time perception deficits in attention-deficit/ hyperactivity disorder and comorbid reading difficulties in child and adolescent samples	To investigate time perception in attention-deficit/hyperactivity disorder with and without comorbid reading difficulties in child and adolescent participants.

Authors	Sample	Sex (M/F)	Average	Measure(s) of	Assessments tools of	Measure(s) of	Assessments tools of	Results
(Year)	size		age M	working	working memory	manual	manual dexterity	
<u>A.C.</u>			(SD)	memory		dexterity		
Atonso et al. (2010)	EG = 20 CA = 20	EG = 13/7 CA = 13/7	EG = 9.35	Copy and recall	Copying task and a spalling to distation	Handwriting:	Copying task and a spalling to distation	uritten latencies than CA more errors
(2019)	CA = 20 RA = 20	CA = 13/7 RA = 13/7	(1.33) CA = 9.7		Task: thirty-two common	latencies	Task: thirty-two common	than CA and RA and writing
	101 - 20	$\mathbf{R} \mathbf{I} = \mathbf{I} \mathbf{S} \mathbf{I} \mathbf{I}$	(1.34)		Spanish nouns	writing	Spanish nouns	durations similar to CA.
			RA = 8.17		1	durations and	Intuos 5 graphic tablet	The EG and RA groups produced
			(0.71)			errors	connected to the	longer written latencies in the copying
							computer and an Intuos	than in the spelling-to-dictation task,
							Inking Pen	while the CA group was not affected
								by the task.
Beneventi et	EG = 11	EG = 6/5	EG = 13.2	Recall	N-Back task			The EG group performed slowed and
al. (2010)	CG = 13	CG = 6/7	(0.4)		fMRI			worse than the CG in all conditions.
			CG = 13.5					Compared with the EG group, CG
			(0.5)			_	_	showed increased IMRI activation in the left superior parietal lobule and the
								right inferior prefrontal gyrus.
								Unlike CG, the EG group did not
								show a significant increase in
								activation in WM areas with increased
								memory load.
Berninger et	EG = 122	EG =	EG =	Copy and recall;	PAL: the receptive coding,	Handwriting	Alphabet task;	The EG group was impaired in
al. (2008)		80/42	11.52	Phonological	the expressive coding and	legibility and	PAL: timed finger	handwriting.
			(1.72)	loop;	the word choice subtest	automaticity;	succession subtest	The CG group markers were less
				loop:	KAN; RAS	Graphomotor planning		In the EG group graphomotor
				Switching		plaining		planning was significantly correlated
				attention				with working memory component
								word form.
Berninger et	EG = 88	59/29	EG = 12.3	Phonological,	CTOPP;	Handwriting	Alphabet task;	All three groups: DD, DG, and OWL
al. (2015)	DD = 38 DG = 26		CG = 13.5	orthographic	TOSWRF;	quality and	DASH	showed poor handwriting quality and
	OWL = 13		(0.5)	and	Comes from;	speed		worse performance in working
	CG = 11			morphological	KAIN,			memory tasks when compared to the

Table 4. Demographic and clinical data, assessment tools and results of the participants in the analyzed studies.

				word storage and processing; Working memory loops for integrating internal and output codes; Switching and supervisory attention	D-KEFS; RAS; fMRI			CG group. However, some components of impaired working memory varied between diagnostic groups. The results provided based on behavioral and brain evidence for DD, DG, and OWL, appear to be unique specific learning disabilities, even though they share some commonalities.
Borella et al. (2011)	EG = 30 ADHD = 15 DD = 15 CG = 15	EG = 21/9 ADHD = 12/3 DD = 9/6 CG = 12/3	EG = 9.3 (1.4) $ADHD = 9.3$ (1.4) $DD = 9.3$ (1.4) $CG = 9.4$ (1.4)	-	-	Reaction time; Handwriting	SRT task; Batteria per la valutazione delle competenze ortografiche nella scuola dell'obbligo	The EG group showed a greater IIV and more variable in their slowest responses as compared to the CG in both tasks. The results did not show any significant effect between EG and CG groups on response latencies. The pattern of the relationship between IIV in SRT and handwriting was different in ADHD and DD: the IIV in the handwriting task was found to depend on IIV in the SRT task only in DD.
Chaix et al. (2007)	EG = 58	EG = 42/16	EG = 11.57 (2.08)	Verbal and visuospatial working memory	RAN Digit span Block design	Fine motor mobility; Manual coordination	Purdue Pegboard Test; LOMDS	An important sub-group of EG (40– 57% depending on the severity of motor difficulties) presented a motor impairment affecting coordination, balance, and manual dexterity.
Cheng-Lai et al. (2013)	EG = 45	EG = 32/13	EG = 9.14 (0.43)	-	-	Fine motor skills: fine manual control and manual coordination;	BOT-2; CHAT	The EG group showed significantly lower performance than children with typical development in multiple domains, in handwriting speed, fine manual control, fine manual coordination, and RAN. The EG group performances in writing to dictation were positively

						Handwriting process, speed and product		associated with average handwriting speed. A negative association was found between the average handwriting speed and the pause time to on-paper time ratio, variability of character size, and RAN. Both the mean writing pressures and variability of writing pressures were negatively associated with visual- perceptual skills and fine manual control.
Gosse and Reybroeck (2020)	EG = 23 CA = 23 SA = 23	EG = 10/13 CA = 10/13 RA = 12/11	EG = 9.09 (0.61) CA = 9.20 (0.58) RA = 7.65 (0.47)	-	-	Handwriting quality and speed	BHK test	The two variables of handwriting products were highly correlated. The EG group wrote as fast as the CA group and they had the same handwriting quality as the SA group. However, the EG group showed more impact by graphic complexity of words than both the CA and SA groups.
Jeffries and Everatt (2004)	$\begin{array}{l} EG=47\\ DD=21\\ SEN=26\\ CG=40 \end{array}$	EG = 42/5 DD = 18/3 SEN = 24/2 CG = 35/5	EG = 10.68 (2.13) $DD = 10.8$ (2.39) $SEN = 10.57$ (1.87) $CG = 11.08$ (2.30)	Phonological loop; Visuospatial sketchpad; Central executive	WMTB-C: forward digit recall and non-word list recall subtests; Block recall and maze memory; Listening recall and backward digit recall	Fine motor coordination	DST: the bead-threading task; BDT: the pointing task	The DD and SEN groups performed worse than CG on working memory phonological loop measures. The DD group performed as well as CG on working memory visuo-spatial scratchpad. The SEN group showed more deficits in the visuo-spatial/motor coordination tasks than the DD and CG groups. However, the DD group performed worse than SEN and CG
Lam et al. (2011)	EG = 137 DD2 = 24 DD3 = 34 DD4 = 30 DD5 = 31	EG = 97/40 DD2 = 13/11 DD3 = 25/9	EG = 9.64 (0.40) DD2 = 7.71 (0.34)			Handwriting	СНАТ	groups on the pointing task. Significant differences were found in the process of handwriting in measures of the writing pressure,

DD6 = 18	DD4 = 25/5	DD3 = 8.68
CG = 756	DD5 =	(0.37)
CG2 = 147	20/11	DD4 = 9.64
CG3 = 153	DD6 = 14/4	(0.42)
CG4 = 156	CG =	DD5 =
CG5 = 159	444/312	10.55 (0.43)
CG6 = 141	$CG^{2} =$	DD6 =
	84/63	11.63 (0.46)
	CG3 -	CG = 9.90
	89/64	(0.51)
	CG4 =	$CG^2 = 7.81$
	90/66	(0.59)
	CG5 =	CG3 = 8.93
	99/60	(0.45)
	CG6 =	CG4 = 9.91
	82/59	(0.39)
		CG5 =
		10.97 (0.58)
		CG6 =
		11.89 (0.53)

Lyman et al.	EG = 49	EG =		Phonological	CTOPP;	Handwriting	DASH	The VGW-SDL group scored higher
(2017)	VG-SDL =	33/16		loop;	TOSWRF;	quality and		than the VG-SDL group on six
	27 VA SDI -	VGSDL =		Orthographic	Comes from;	speed		language skills (oral sentence
	$\sqrt{A-SDL} = 22$	18/9 VASDI —		Loop;	RAN;			construction, best and fastest
		VASDL = 15/7		Focused	Alphabet writing 15 task;			handwriting in copying single real
	CG = 20			attention;	D-KEFS;			word oral reading accuracy, oral
	VGW-SDL	CG = 12/8		Switching	RAS			pseudoword reading accuracy and
	= 14 VAW SDI	VGWSDL =		attention				rate) and on four endophenotypes
	= 6	9/5 VAWSDI –	Not					(orthographic and morphological
		3/3	reported.					coding, orthographic loop, and
								switching attention).

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speed, average size of characters, and accuracy across the grades. The EG group exhibited significantly slower speed, the greater average size of characters, greater SD of the size of characters, lower accuracy, the greater total number of stroke errors, a greater number of missing stroke errors, and a greater number of concatenated stroke errors when compared to the CG group.

The VAW-SLD group scored higher than the VA-SLD group on four language skills (best and fastest handwriting in copying, accuracy, and rate of oral reading of real words and

endophenotypes (orthographic coding

and

two

pseudowords)

and orthographic loop).

Marchand- Krynski et al. (2018)	EG = 215 DD = 67 ADHD = 66 CD = 82	EG = 138/77 DD = 32/35 ADHD = 48/18 CD = 58/24	EG = 13.08 (2.59) DD = 13.61 (2.51) ADHD = 12.82 (2.60) CD = 12.80 (2.67)	Visuospatial working memory	Visual working memory task	Range of sequential hand/arm motor skills	LTT: unimanual sequential tapping, bimanual in- phase/balanced tapping, bimanual out-of-phase/ unbalanced tapping and rapid tapping	There were no differences in the measurement of visual working memory between groups regarding the number of correct responses. The motor performance measures LTT showed no differences between groups observed on the rapid tapping and the unimanual sequential tapping condition, but a main effect of group was observed on the bimanual in- phase/balanced tapping coordination conditions.
Mati-Zissi and Zafiropoulou (2003)	EG = 204 DD = 102 OWL = 102 CG = 102	Not reported	Not reported	Visuospatial working memory	The Rey-Osterrieth Complex Figure: drawing it from memory	Visuomotor coordination	The Rey-Osterrieth Complex Figure: copying the shape	The DD group showed significant differences against both OWL and CG groups not only in copying but also in drawing from memory.
Maziero et al. (2020)	EG = 96 DD = 47 DCD = 22 DD-DCD = 27 CG = 42	EG = 59/37 DD = 26/21 DCD = 15/7 DD-DCD = 18/9 CG = 22/20	EG = 9.98 (1.26) $DD = 10.03$ (1.14) $DCD = 9,84$ (1.29) $DD-DCD = 10.07 (1.36)$ $CG = 9.99$ (1.14)	Verbal working memory; Visuospatial working memory; Visuospatial central executive	Forward digit span; Backward digit span; WNV: forward and backward block-tapping test	-	-	The DD group showed poorer performance than the CG group for the Forward Digit Span. For the Backward Digit Span, the DD group performed worse than for both the CG and DCD groups. The DD group showed a deficit in verbal working memory including a specific deficit in the phonological loop. The DCD group showed a deficit on visuospatial working memory. The DD-DCD showed poorer performance on verbal and visuospatial working memory.
Menghini et al. (2011)	EG = 54 $DPS = 28$ $DMS = 26$ $CG = 46$ $CPS = 22$ $CMS = 24$	EG = 32/22 DPS = 14/14 DMS = 18/8 CG = 26/20	EG = 11.1 (0.8) DPS = 9.8 (0.7) DMS = 12.4 (0.9)	Verbal, visuospatial and visual-object span	Prove di Memoria e Apprendimento per l'Età Evolutiva by Vicari's battery of tasks			Significant differences were found between the groups. The CG group showed higher scores than the EG group on all verbal, visuospatial, and visual-object.

		CPS = 12/10 CMS = 14/10	CG = 11.35 (0.95) CPS = 10.1 (1.0) CMS = 12.6 (0.9)			-	-	Although the CG group performed higher scores than the EG group on all three-span tasks, the group difference was significantly higher on the visual object than on the verbal task and on the visuospatial than on the verbal task.
Parke et al. (2015)	EG = 296 ADHD-I = 100 ADHD-C = 78 ADHD-RD/DWE = 76 ADHD-DCD = 42	EG = 204/92	EG = 10.4 (2.8)	Verbal and visuospatial working memory	WISC-IV	-	-	Significant differences were found in all groups, indicating that the working memory and processing speed were significantly poor. All groups tended to perform worse on Block Design and Coding, which both include a strong motor component. The ADHD-RD/DWE group demonstrated weaker processing speed and working memory relative to perceptual and verbal indexes when compared with ADHD.
Ramus et al. (2003)	EG = 22 CG = 20	EG = 16/6 CG = 10/10	EG = 9.8 (1.3) CG = 9.9 (1.2)	Verbal and visuospatial working memory	WISC – III: freedom from distractibility, digit span, coding and picture span subtests	Manual dexterity	Finger to thumb; DST: bead-threading task; Time estimation	The EG group showed significantly poorer results than the CG group on the working memory index and on all motor control tasks but time estimation. Three dyslexic subjects from the EG group were unable to perform the finger to thumb task.
Sanders et al. (2017)	EG = 103 DD = 60 DG = 25 OWL = 18	EG = 66/37 DD = 34/26 DG = 20/5 OWL = 12/6	EG = 11.85 (1.34)	Phonological loop; Supervisory attention	CTOPP; Comes from; TOSWRF; RAN; Alphabet 15; D-KEFS; RAS	Handwriting quality and speed	DASH	The DG group showed a significantly higher working memory result than the DD group. All three groups were below the mean on handwriting, but only the DD and OWL groups were below the mean on spelling measures.

Savage and Frederickson (2006)	EG = 34 CG = 33	EG = 22/12 CG = 24/9	EG = 10.49 (1.81) CG = 10.83 (1.74)	Recall, phonological loop and executive processing	BAS – II: recall of digits forward and backward subtests; RAN	Motor functioning; Proficiency in writing speed; Handedness and cerebral dominance	DST: bead-threading task; Timed letter formation Task; Annett's pegboard task	The EG group showed poor proficiency in the rapid automatic naming of digits when compared with the CG group. The EG group did not show other independent problems in a range of memory, motor, speed, and handedness tasks compared to the CG group.
Sumner and Barnett (2014)	EG = 31 CA = 31 SA = 31	EG = 15/16 CA = 15/16 SA = 15/16	EG = 9.44 (0.90) CA = 9.41 (0.84) SA = 6.63 (0.78)	-	-	Fine motor control; Speed of handwriting	MABC-2; DASH	The EG group was significantly slower than the CA group at a copying task in terms of words copied per minute. The EG group paused more and for longer within words than the CA group. The EG group also made at least one spelling error in the copying tasks, whereas none of the members of the CA group misspelled the words.
Toplak et al. (2003)	Study 1 EG = 50 ADHD/RD = 19 ADHD = 31 CG = 50 Study 2 EG = 59 ADHD/RD = 24 ADHD = 35 CG = 39	Study 1 EG = 39/11 CG = 30/20 Study 2 EG = 35/24 CG = 30/20	Study 1 EG = 8.9 (1.3) ADHD/RD = 8.9 (1.3) ADHD = 8.9 (1.3) CG = 8.9 (1.3) Study 2 EG = 15.0 (1.4) ADHD/RD = 14.9 (1.4) ADHD = 15.2 (1.4)	Verbal and visuospatial working memory	WISC – III: digit span and block design subtests	-	-	Study 1 - The ADHD/RD group exhibited significantly longer reproductions of the 400ms interval than the CG group, but significantly shorter intervals for the 6000ms interval compared to both the ADHD and CG groups, who did not differ. The ADHD/RD group also displayed significantly more variability at the 400ms interval level than both ADHD and CG groups. Study 2 - The ADHD/RD were less able to discriminate among durations in the 400ms range and less precise in their reproduction, compared to both ADHD and CG groups.

The	ADH	ID/RD	grou	p had
signifi	icantly	lower	working	memory
tasks t	than the	ADH	D and CC	groups.

Abbreviations: ADHD = Attention-Deficit Hyperactivity Disorder; ADHD-I = DHD-Predominantly Inattentive Type; ADHD-C = ADHD-Combined Type; ADHD-DCD = ADHD-Developmental Coordination Disorder; ADHD-RD = ADHD Reading Disorder/Disorder of Written Expression; BAS = British Abilities Scales-II; BDT = Bangor Dyslexia Test; LTT = Leonard Tapping Task; BHK = Concise evaluation scale for children handwriting; BOT-2 = Bruininks-Oseretsky Test of Motor Proficiency-2nd edition; CA = Chronological Age-Matched Controls; CD = Comorbid Diagnosis; CG = Control Group; CG2 to CG6 = Typical Students from the 2nd to the 6th grade; CHAT = Chinese Handwriting Assessment Tool; CMS = Control students of Middle School; CPS = Control students of Primary School; CTOPP = Comprehensive Test of Phonological Processing; DASH = Detailed Assessment of Speed of Handwriting; DCD = Developmental Coordination Disorder; DD = Developmental Dyslexia; DD2 to DD6 = Students Diagnosed with Developmental Dyslexia from the 2nd to the 6th grade; DD-DCD = Combined Diagnosis Developmental Dyslexia and Developmental Coordination Disorder; DG = Dysgraphia Group; D-KEFS = Delis Kaplan Executive Functions; DMS = Dyslexic students of Middle School; DPS = Dyslexic students of Primary School; DST = Dyslexia Screening Test; EG = Experimental Group; fMRI = Functional Magnetic Resonance Imaging; IIV = Intraindividual variability; LOMDS = Lincoln-Orseretsky Motor Development Scale; MABC-2 = Movement Assessment Battery for Children, second edition; OWL = Oral and Written Language Learning Disability; PAL = Process Assessment of the Learner; RA = Reading Age-Matched Controls; RAN = Rapid Automatic Letter Naming; RAS = Rapid Automatic Switching; SA = Spelling-ability Matched Control; SEN = Special Education Needs; SRT = Simple Reaction Time Task; TOSWRF = Test of Silent Word Reading Fluency; VA-SDL = Verbally Average Students with Specific Learning Disabilities – Written Language; VAW-SDL = Verbally Average Students Without Specific Learning Disabilities – Written Language; VG-SDL = Verbally Gifted Students with Specific Learning Disabilities – Written Language; VGW-SDL = Verbally Gifted Students Without Specific Learning Disabilities – Written Language; WISC – III = Wechsler Intelligence Scale for Children – 4th edition; WISC-IV = Wechsler Intelligence Scale for Children – 4th edition; WMTB-C = Working Memory Test Battery for Children; WNV = Echelle non verbale d'intelligence de Wechsler.

CG = 15.0 (1.2)

3.3 Meta-analytic estimates

Sixteen studies were included in five meta-analyses and were divided based on the measures evaluated in the studies: visuospatial working memory, verbal working memory, fine motor skills, handwriting, and manual motor speed. For the visuospatial working memory and verbal working memory assessment, most studies used the Block-tapping and the Digit span task, respectively. For measures related to fine motor skills, most studies applied the Dyslexia Screening Test and for the handwriting and manual motor speed assessment, most studies used the copying best and copying fast subtests from Detailed Assessment of Speed of Handwriting. For the studies that did not use the same assessment tools, we selected the results provided by equivalent instruments that are also widely used in the literature. The calculation of the effect size was based on the mean and the standard deviations of scores from the samples with dyslexia and the control groups during the assessment. The interpretation of Hedge's is according to the criteria formulated by Cohen (1988), stating that 0.2 is a small effect, 0.5 is a medium effect, and 0.8 is a large effect.

3.3.1 Visuospatial working memory

Seven studies with a total sample of 994 participants were included in the visuospatial working memory meta-analysis comparing the Developmental Dyslexia group (DD) with the Typical Developmental control group (TD) (Figure 5A) and seven with a sample of 1.103 participants comparing the DD and the control group with Different Comorbidities (DC) (Figure 5B). The estimate of the global difference between the groups was negative, indicating a worse performance in visuospatial working memory skills in the DD group when compared with the TD group. The hypothesis of homogeneity between studies was rejected (p-value <0.01) and the I² value = 71% indicates that 71% of the observed variation is due to heterogeneity between studies. The full effect size was moderate (-0.61, 95% CI [-0.87; -0.35]) in the comparison between the DD and the TD group, and a small effect when compared to the DD with the DC (-0.16, 95% CI [-0.53; 0.20]).

3.3.2 Verbal working memory

Seven studies with a total sample of 449 participants were included in the verbal working memory meta-analysis comparing the DD with the TD group (Figure 6A) and six with

a sample of 491 participants comparing the DD and the DC group (Figure 6B). The estimate of the global difference between the groups was negative, indicating a worse performance in verbal working memory skills in the DD group. The hypothesis of homogeneity between studies was not rejected (p-value = 0.67) and the I² value = 0% indicates there is homogeneity between studies. The full effect size was large (-0.83, 95% CI [-1.03; -0.63]) in the comparison between the DD and the TD group and a small effect when compared to the DD with the DC group (-0.38, 95% CI [-0.66; -0.10]).

3.3.3 Fine motor skills

Four studies with a total sample of 232 participants were included in the fine motor skills meta-analysis comparing the DD with the TD group (Figure 7A) and only one with a sample of 61 participants comparing the DD and the DC group (Figure 7B). The estimate of the global difference between the groups was positive, indicating that the DD group had more errors during tasks that assessed fine motor skills. The hypothesis of homogeneity between studies was rejected (p-value = 0.01) and the I² value = 73% indicates that 73% of the observed variation is due to heterogeneity between studies. The full effect size was small (0.02, 95% CI [-0.50; 0.53]) in the comparison between the DD and the TD group.

3.3.4 Handwriting

Eight studies with a total sample of 947 participants were included in the handwriting meta-analysis comparing the DD with the TD group (Figure 8A) and four with a sample of 776 participants comparing the DD and the DC group (Figure 8B). The estimate of the global difference between the groups was negative, indicating a worse performance in handwriting in the DD when compared to the TD group. The hypothesis of homogeneity between studies was rejected (p-value <0.01) and the I² value = 79% indicates that 79% of the observed variation is due to heterogeneity between studies. The full effect size was small (-0.22, 95% CI [-0.53; 0.09]) in the comparison between the DD and the TD group and small effect when compared to the DD with the DC group (0.31, 95% CI [-0.13; 0.74]). No publication bias was observed using linear regression test of funnel plot asymmetry (Egger's test t = -0.28, df = 8, p-value = 0.7831) and Begg's rank correlation test of funnel plot asymmetry (z = -0.18, p-value = 0.8580 - with continuity correction).

3.3.5 Manual motor speed

Eight studies with a total sample of 1.123 participants were included in the manual motor speed meta-analysis comparing the DD with the TD group (Figure 9A) and two with a sample of 79 participants comparing the DD and the DC group (Figure 9B). The estimate of the global difference between the groups was positive, indicating that the DD group spent more time during the manual motor speed task. The hypothesis of homogeneity between studies was rejected (p-value <0.01) and the I² value = 92% indicates that 92% of the observed variation is due to heterogeneity between studies. The full effect size was small (0.17, 95% CI [-0.28; 0.63]) in the comparison between the DD and the TD group and medium effect when compared to the DD with the DC group (0.59, 95% CI [-0.30; 1.48]). No publication bias was observed using linear regression test of funnel plot asymmetry (Egger's test t = -1.32, df = 12, p-value = 0.2117) and Begg's rank correlation test of funnel plot asymmetry (z = -1.20, p-value = 0.2284 - with continuity correction).

		Expe	rimental			Control	Standardised Mean			Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
Berninger et al. (2015)	38	96.38	11.6100	11	114.00	13.9100		-1.43	[-2.16; -0.70]	3.1%	7.0%
Jeffries and Everatt (2004)	21	4.05	0.6700	40	4.25	0.7400		-0.28	[-0.81; 0.26]	5.9%	9.5%
Lyman et al. (2017)	27	98.80	11.2000	14	109.00	11.2000		-0.89	[-1.57; -0.22]	3.6%	7.6%
Mati-Zissi and Zafiropoulou (2003) - Age 7*	102	9.03	57.8300	102	21.53	34.5900		-0.26	[-0.54; 0.01]	21.7%	13.3%
Mati-Zissi and Zafiropoulou (2003) - Age 8*	102	8.87	58.0000	102	23.61	46.2600		-0.28	[-0.56; 0.00]	21.7%	13.3%
Mati-Zissi and Zafiropoulou (2003) - Age 9*	102	12.30	69.4500	102	22.63	46.5200	· · ·	-0.17	[-0.45; 0.10]	21.8%	13.3%
Maziero et al. (2020)	47	51.77	8.9800	42	56.40	8.5500	- <u>iel</u>	-0.52	[-0.95; -0.10]	9.2%	11.1%
Menghini et al. (2011) - Primary School*	28	9.20	2.9000	22	14.70	6.2000		-1.17	[-1.77; -0.56]	4.5%	8.4%
Menghini et al. (2011) - Middle School*	26	9.70	2.4000	24	15.70	5.5000		-1.41	[-2.04; -0.79]	4.2%	8.2%
Ramus et al. (2003)	22	95.41	14.9800	20	103.85	11.8900		-0.61	[-1.23; 0.01]	4.3%	8.3%
Fixed effect model	515			479			\$	-0.43	[-0.56; -0.31]	100.0%	
Random effects model							<u></u>	0.61	[-0.87; -0.35]		100.0%
Heterogeneity: $I^2 = 71\%$, $\tau^2 = 0.1117$, $p < 0.01$								I			
							-2 -1 0 1	2			

в

		Expe	rimental			Control	Standardised Mean			Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
Berninger et al. (2015)	38	96.38	11.6100	26	110.31	9.3100		-1.28	[-1.83; -0.73]	4.9%	10.2%
Jeffries and Everatt (2004)	21	4.05	0.6700	26	3.69	0.6800	i 	0.52	[-0.06; 1.11]	4.3%	9.9%
Mati-Zissi and Zafiropoulou (2003) - Age 7*	102	9.03	57.8300	102	15.85	44.1400		-0.13	[-0.41; 0.14]	19.7%	12.3%
Mati-Zissi and Zafiropoulou (2003) - Age 8*	102	8.87	58.0000	102	21.97	25.4600		-0.29	[-0.57; -0.02]	19.5%	12.3%
Mati-Zissi and Zafiropoulou (2003) - Age 9*	102	12.30	69.4500	102	19.36	39.4100		-0.12	[-0.40; 0.15]	19.7%	12.3%
Maziero et al. (2020)	47	51.77	8.9800	22	40.59	9.2300		1.22	[0.67; 1.77]	4.9%	10.2%
Parke et al. (2015)	76	9.20	2.9000	100	10.00	2.7000		-0.29	[-0.59; 0.01]	16.5%	12.2%
Sanders et al. (2017)	60	95.98	11.8500	25	109.56	9.8800		-1.19	[-1.69; -0.69]	5.9%	10.6%
Toplak et al. (2003)	19	11.50	3.7000	31	10.70	3.9000		0.21	[-0.37; 0.78]	4.5%	10.0%
Fixed effect model	567			536			÷=	-0.20	[-0.32; -0.07]	100.0%	
Random effects model Heterogeneity: $l^2 = 88\%$, $\tau^2 = 0.2594$, $p < 0.01$								-0.16	[-0.53; 0.20]		100.0%
							-1.5 -1 -0.5 0 0.5 1 1.5				

Figure 5. Analysis of studies that assessed visuospatial working memory skills in the experimental (dyslexic children) and control groups: A - typical development; B - different comorbidities.

Α			Expe	rimental			Control	Standardised Mean			Weight	Weight
	Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
	Berninger et al. (2015)	38	97.88	13.1100	11	113.82	10.4600		-1.25	[-1.96; -0.53]	7.7%	7.7%
	Jeffries and Everatt (2004)	21	4.24	0.4400	40	5.03	0.9700		-0.94	[-1.50; -0.38]	12.8%	12.8%
	Lyman et al. (2017)	27	98.60	14.7000	14	107.80	12.0000		-0.65	[-1.31; 0.01]	9.0%	9.0%
	Maziero et al. (2020)	47	8.23	2.6200	42	10.52	2.6900		-0.86	[-1.29; -0.42]	20.9%	20.9%
	Menghini et al. (2011) - Primary School*	28	5.70	1.6000	22	7.30	1.1000		-1.12	[-1.73; -0.52]	10.9%	10.9%
	Menghini et al. (2011) - Middle School*	26	6.50	1.4000	24	7.80	1.5000	<u> </u>	-0.88	[-1.47; -0.30]	11.7%	11.7%
	Ramus et al. (2003)	22	96.18	13.8500	20	105.15	13.8100		-0.64	[-1.26; -0.01]	10.2%	10.2%
	Savage and Frederickson (2006)	34	45.71	11.7000	33	50.82	8.7600		-0.49	[-0.97; 0.00]	16.8%	16.8%
	Fixed effect model	243			206				-0.83	[-1.03; -0.63]	100.0%	
	Random effects model Heterogeneity: $I^2 = 0\% r^2 = 0.p = 0.67$								-0.83	[-1.03; -0.63]		100.0%
	1000000000000000000000000000000000000							-1 0 1				

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		Expe	rimental			Control	Standardised Mean			Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
Berninger et al. (2015)	38	97.88	13.1100	26	108.31	11.7100		-0.82	[-1.34; -0.30]	12.7%	15.5%
Jeffries and Everatt (2004)	21	4.24	0.4400	26	4.19	0.6900		0.08	[-0.49; 0.66]	10.4%	13.9%
Maziero et al. (2020)	47	8.23	2.6200	22	9.18	2.2800		-0.37	[-0.88; 0.14]	13.2%	15.8%
Parke et al. (2015)	76	95.90	12.1000	100	99.10	12.4000		-0.26	[-0.56; 0.04]	38.4%	24.1%
Sanders et al. (2017)	60	96.78	13.7500	25	107.76	12.3300		-0.81	[-1.30; -0.33]	14.7%	16.7%
Toplak et al. (2003)	19	8.90	2.5000	31	9.00	3.1000	- <u>i</u>	-0.03	[-0.61; 0.54]	10.6%	14.0%
Fixed effect model	261			230				-0.37	[-0.55; -0.18]	100.0%	
Random effects model								-0.38	[-0.66; -0.10]		100.0%
Heterogeneity: $I^2 = 52\%$, $\tau^2 =$	0.0620	p = 0.0)7								
							-1 -0.5 0 0.5 1				

Figure 6. Analysis of studies that assessed verbal working memory skills in the experimental (dyslexic children) and control groups: A – typical development; B – different comorbidities.



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		Experiment	al		Control	S	Standardised Mean			n		
Study	Total	Mean S	D Tota	al Mear	n SD		Dif	feren	ice		SMD	95%-CI
Jeffries and Everatt (2004)	21	9.29 2.120	04	0 7.54	1.6800	.∟ -1	-0.5	0	0.5	1	0.94	[0.38; 1.49]

Figure 7. Analysis of studies that assessed fine motor skills in the experimental (dyslexic children) and control groups: A – typical development; B – different comorbidities.



Figure 8. Analysis of studies that assessed handwriting skills in the experimental (dyslexic children) and control groups: A – typical development; B – different comorbidities.

Α			Exp	erimental			Control	Standar	dised Mean			Weight	Weight
	Study	Total	Mean	SD	Total	Mean	SD	Diff	ference	SMD	95%-CI	(fixed)	(random)
	Afonso et al. (2019)	20	2.02	725.0000	20	1.45	390.0000		++++	0.00	[-0.62; 0.62]	3.5%	7.5%
	Berninger et al. (2015)	38	6.93	3.3200	11	11.09	1.8700	.		-1.33	[-2.06; -0.61]	2.6%	7.1%
	Borella et al. (2011)	15	456.68	34.8000	15	423.83	23.4100			1.08	[0.30; 1.85]	2.2%	6.9%
	Gosse and Reybroeck (2020)	23	187.09	43.6500	23	219.61	49.2100		-	-0.69	[-1.28; -0.09]	3.8%	7.5%
	Lam et al. (2011) - Age 7.81*	24	727.01	291.2800	147	673.21	408.6400	2		0.14	[-0.30; 0.57]	7.2%	8.0%
	Lam et al. (2011) - Age 8.93*	34	682.82	260.8500	153	482.52	119.4300			1.29	[0.90; 1.69]	8.6%	8.1%
	Lam et al. (2011) - Age 9.91*	30	523.48	138.0600	156	413.31	105.3400			0.99	[0.58; 1.39]	8.2%	8.1%
	Lam et al. (2011) - Age 10.97*	31	430.57	130.1400	159	349.99	89.9800			0.82	[0.43; 1.22]	8.7%	8.1%
	Lam et al. (2011) - Age 11.89*	18	420.83	118.3700	141	318.04	77.6300			1.23	[0.72; 1.74]	5.2%	7.8%
	Lam et al. (2011) - Total *	137	564.17	236.1400	756	446.77	236.2100			0.50	[0.31; 0.68]	39.9%	8.5%
	Lyman et al. (2017)	27	8.40	2.6000	14	12.70	3.5000			-1.44	[-2.16; -0.71]	2.6%	7.1%
	Ramus et al. (2003)	22	13.50	8.4000	20	8.00	3.1000			0.84	[0.20; 1.47]	3.3%	7.4%
	Sumner and Barnett (2014)	31	13.16	4.9300	31	19.73	3.2700			-1.55	[-2.12; -0.98]	4.1%	7.6%
	Fixed effect model	450			1646				\diamond	0.43	[0.31; 0.54]	100.0%	
	Random effects model								$\langle \rangle$	0.17	[-0.28; 0.63]		100.0%
	Heterogeneity: $I^2 = 92\%$, $\tau^2 = 0.62$	239, p •	< 0.01					1 1	1 1 1				
								-2 -1	0 1 2				

В

	Experimental						Standardised Mean			Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
Berninger et al. (2015) Borella et al. (2011)	38 15	6.93 456.68	3.3200 34.8000	11 15	6.41 426.26	2.9000 18.0100		0.16 1.07	[-0.51; 0.83] [0.30; 1.84]	56.9% 43.1%	52.3% 47.7%
Fixed effect model Random effects model Heterogeneity: $l^2 = 67\%$ r	53 ² = 0.27	78 n = (1.08	26				0.55 0.59	[0.04; 1.06] [-0.30; 1.48]	100.0% 	 100.0%
	0.21	ι υ , μ					-1.5 -1 -0.5 0 0.5 1 1.5				

Figure 9. Analysis of studies that assessed manual motor speed in the experimental (dyslexic children) and control groups: A – typical development; B – different comorbidities.

4. DISCUSSION

The present study aimed to review and synthesize data found in the literature on working memory and manual dexterity in children and adolescents with dyslexia, as well as checking if there is a possible association between working memory and manual dexterity skills and, if one skill may be interfering with the other. Two meta-analyses were performed to compare working memory between dyslexic children and control groups, and three meta-analyses were performed to compare manual dexterity between groups of dyslexics and controls. In addition, an analysis was carried out to verify a possible association between working memory and manual dexterity skills in dyslexic children and adolescents. The discussion of the present study will be divided into sections based on the results found. Regarding the comparison of working memory data, most studies show that the dyslexic group had significantly lower rates when compared to the group of children with typical development. Concerning manual dexterity skills, although no significant differences were found between the groups, the dyslexic group showed poorer performance in manual dexterity tasks, longer latency time, less precision and spent more time on fine manual control when compared to the group of typically developing children.

4.1 Working memory and dyslexia

The results found in the meta-analysis of visuospatial working memory showed a moderate effect size between the Developmental Dyslexia group (DD) and the Typical Development control group (TD) (-0.59, 95% CI [-0.83; -0.36]), and a small effect when compared to the DD with the Different Comorbidities group (DC) group (-0.16, 95% CI [-0.53; -0.20]), and in verbal working memory was found a large effect size between the DD and the TD group (-0.83, 95% CI [-1.03; -0.63]), and a small effect when compared to the DD with the DC group (-0.38, 95% CI [-1.03; -0.63]), and a small effect when compared to the DD with the DC group (-0.38, 95% CI [-0.66; -0.10]). These findings corroborate the findings in the literature (Smith-Spark & Fisk, 2007; Cowan et al., 2017; Campen et al., 2018; Habid, 2021) which show that dyslexic children present impairments in tasks that demand working memory, both in the visuospatial sketchpad and in the phonological loop, however, the results show that these differences are even greater in the phonological loop. The greatest difference between groups was found in the study by Berninger et al. (2015) with a negative large effect size in all measures, the DD showed worse performance both in visuospatial and verbal working memory tasks when compared to both control groups: TD (-1.43, 95% CI [-2.16; -0.70]; -1.25, 95% CI

[-1.96; -0.53]), and DC (-1.28, 95% CI [-1.83; -0.73]; -0.82, 95% CI [-1.34; -0.30]), respectively. However, the TD control group sample size was much smaller with only 11 participants, while the DD group had 38 participants. This difference in sample size may have contributed to a greater discrepancy between group's results. Significant differences were also found between the DD and TD groups on visuospatial working memory, with a negative large effect size: (-0.89, 95% CI [-1.57; -0.22], Lyman et al., 2017), in primary school and middle school respectively (-1.17, 95% CI [-1.77; -0.56]; -1.41, 95% CI [-2.04; -0.79], Menghini et al., 2011), and a negative medium effect size (-0.52, 95% CI [-0.95; -0.10], Maziero et al., 2020). On verbal working memory, significant differences were also found between the DD and TD groups, with a negative large effect size: (-0.94, 95% CI [-1.50; -0.38], Jeffries & Everatt, 2004), (-0.86, 95% CI [-1.29; -0.42], Maziero et al., 2020), and in primary school and middle school respectively (-1.12, 95% CI [-1.73; -0.52]; -0.88, 95% CI [-1.47; -0.30], Menghini et al., 2011). These findings corroborate the study by Sanders et al. (2017) which showed that the dyslexic had a significantly lower working memory score than the control group and also with the findings by Afonso et al. (2019) that characterized the spelling difficulties often experienced by children with dyslexia in a copy and spelling dictation task, and their results showed that the dyslexic produced longer recording latencies than the typical development group. This pattern suggests that the dyslexic group had a particularly slow processing speed, indicating some difficulty in recognizing words quickly, including short words. In addition, the dyslexic group made more mistakes than the typical development group. In the study by Parke et al. (2015) differences were also found between the groups, however, the comparison was made between the DD and DC groups. It showed that the DD had a weaker processing speed and working memory in relation to perceptual and verbal indices compared to the DC group. In addition, intraindividual variability is a factor that can influence the performance of these skills, as shown in the study by Borella et al. (2011) that found significant differences between the dyslexic and the typical development group, in which the dyslexic showed greater intraindividual variability and more variable in their slower responses in simple response time task when compared with the control group. Thus, slower processing speed indicates that more mental effort is required to perform simple tasks, with fewer resources available for higher levels of learning and cognitive processing, such as reading comprehension and perceptual skills (Parke et al., 2015).

The study by Maziero et al. (2020) evaluated the working memory of children with dyslexia compared to the developmental coordination disorder group (DCD), and to a group control. The clinical groups showed worse performance in working memory tasks compared to the control group. It is noteworthy that the DD did not differ from the DCD group, indicating

that both groups did not have more or less of a deficit than the other, which presupposes the absence of an additive effect for the comorbidity. The authors highlight the presence of heterogeneity in the functioning of working memory and that, although the diagnosis of ADHD as a comorbidity of dyslexia is very common, the study took care to verify the absence of comorbidity with ADHD in the sample, assuming that a deficit in working memory is not a consequence of ADHD. However, they also emphasize that another explanation for the heterogeneity of the study results may be the presence of comorbidities between dyslexia and DCD. In that regard, the study by Jeffries and Everatt (2004) also showed that the differences between the DD and the DC group were less evident, whereas these two clinical groups had significantly worse differences than the control in measures of the phonological loop of working memory. Moreover, the DD performed worse than the DC and TD groups in the pointing task, which may suggest evidence of poor visuospatial/motor coordination, besides working memory deficits, since the pointing task requires them to be following certain sequences of verbal commands, working memory deficits can impair performance in sequencing and pointing tasks. These findings corroborate the study by Parke et al. (2015) which found differences between DD and TD groups, indicating that working memory and processing speed were significantly poor in both groups and they tended to perform worse on block design and coding tasks, which include a strong motor component.

Furthermore, the results by Jeffries and Everatt (2004) showed that dyslexics had more problems with reverse amplitude in the younger years and more interference from correct digit names in the older cohort. According to the authors, these data show that the differences between primary and secondary school children need to be considered in more detail, as this difference may indicate deficits that become more evident, or less apparent with age development or with the use of compensation strategies. On the other hand, the study by Menghini et al. (2011) showed that the DD obtained lower scores than the TD group, not only on a verbal extension task, but also on extension tasks that assess the retention of working memory sequences of abstract figures and spatial positions, and the authors point out that these data did not vary depending on the age of the children, as the study obtained substantially the same results when the data analysis was confined to participants in the last three years of primary school or in the first three years of high school from school.

Another confounding factor for the diagnosis of dyslexia can be twice-exceptional, that is, with giftedness and with reading learning disability children as shown in the Lyman et al. (2017) findings that investigated the reading problems in this population. The results found show that gifted children with reading learning deficits had a worse performance in language skills, accuracy, and visuospatial working memory tasks than the group of gifted children with no reading deficits. In addition, the gifted group with reading deficits also had problems in orthographic and morphological coding, spelling loop, and shift in attention when compared to the control group. These findings provide evidence that giftedness can mask learning difficulties. Furthermore, some components of impaired working memory varied between diagnostic groups. For example, impairments in verbal working memory, including a specific deficit in the phonological loop were frequently observed in dyslexia, but never in dysgraphia alone (Berninger et al., 2015) and in the DCD group (Maziero et al., 2020).

In contrast, although all studies have shown a worse performance of the DD group on visuospatial working memory, some studies did not find significant differences between the TD group: (-0.28, 95% CI [-0.81; 0.26], Jeffries & Everatt, 2004), with children aged 7, 8 and 9 years, respectively (-0.26, 95% CI [-0.54; 0.01]; -0.28, 95% CI [-0.56; 0.00]; -0.17, 95% CI [-0.45; 0.10], Mati-Zissi & Zafiropoulou, 2003), and (-0.61, 95% CI [-1.23; 0.01] Ramus et al., 2003). While in the studies by Berninger et al. (2015), Lyman et al. (2017), Maziero et al. (2020), and Menghini et al. (2011), showed that the greatest difference in performance between the DD and the TD group was in the visuospatial span which the task that the dyslexic sample obtained the highest score in the study by Menghini et al. (2011). Curiously, the study by Jeffries and Everatt (2004) showed that the DD group had the same level of performance as the TD group, which was corroborated by the study by Smith-Spark et al. (2003), in which the dyslexic group had a similar performance to the control group in this type of task and a significant difference emerged only when the memory task's update load was increased, thus taxing the resources of the central executive system. According to Menghini et al. (2011) it can be hypothesized that dyslexic individuals are not particularly impaired in working memory of spatial positions, but show deficits in encoding and/or short-term retention of temporal sequences of events and the more the task demands memory of order sequential, as was the case in their study, the worse is the performance of these individuals. Instead, when less emphasis is placed on serial-order memory and the task primarily requires remembering space or other features of the item, then these individuals may perform at average levels or close to the average (Menghini et al., 2011). Furthermore, these results provide convergent behavioral evidence, for dyslexia and other neurodevelopmental comorbidities, being different, specific diagnosable learning difficulties for persistent written language problems during middle childhood and early adolescence, but also some variations within diagnostic groups, consistent with individual differences and genetic heterogeneity (Berninger et al., 2015). Therefore, dyslexic children may fall further and further behind in their learning because of diminished cognitive resource reserves and diminished academic fluency skills and, these underlying weaknesses in speed processing can aggravate reading, writing, and perceptual difficulties already present in the disorder.

4.2 Manual dexterity and dyslexia

The results found in the meta-analysis of fine motor skills showed no significant difference between the DD and the TD group (0.02, 95% CI [-0.50; 0.53]), and although some studies have shown that the dyslexic children had poorer performance in fine motor skills compared to the typically developing children (Preis et al., 1997; Feder & Majnemer, 2007), no significant differences were found in these studies: (0.13, 95% CI [-0.40; 0.66], Jeffries & Everatt, 2004), (-0.37, 95% CI [-0.85; 0.11], Savage & Frederickson, 2006), and (-0.41, 95% CI [-0.91; 0.09], Sumner & Barnett, 2014). Only one study showed a significant difference between the groups (0.82, 95% CI [0.18; 1.45], Ramus et al., 2003), which the DD group showed a worse performance in the task of thread beads holding the string in the dominant hand and was observed motor impairment in 59% of a sample of 22 dyslexic children. This variability of the different results found in the studies may be related to the evaluation methods of the studies, as well as to the assessment carried out in the sample and the levels of impairment in fine motor skills present in each child. The study by Chaix et al. (2007) showed a variability of 40% to 57% of dyslexic children with motor problems, depending on the severity of the problems. Therefore, motor deficits were present in only a subgroup of dyslexic children, with different levels of impairment. In the comparison between the DD and DC group, there was only one study that investigated these differences in fine motor skills, and the results indicate a large effect size (0.94, 95% CI [0.38; 1.49], Jeffries & Everatt, 2004) with the DC showing a worse performance when compared to the DD group. Anyway, the results found in only four studies show that, although dyslexic children present problems in fine motor skills, it is still a little explored subject in the literature.

Concerning the results found in the handwriting meta-analysis, although no significant differences were found between the DD and DT groups (-0.22, 95% CI [-0.53; 0.09]), nor between the DD and DC (0.31, 95% CI [-0.13; 0.74]), some studies have already shown differences between the DD and DT groups with a negative large effect size: (-1.14, 95% CI [-1.85; -0.43], Berninger et al., 2015), (-1.51, 95% CI [-2.24; -0.78], Lyman et al., 2017), (-0.84, 95% CI [-1.36; -0.32], Sumner & Barnett, 2014), and a positive large effect size: (1.06, 95% CI [0.28; 1.83], Borella et al., 2011). These results indicate that although the overall result of the

handwriting analysis revealed similar results between the DD and the TD, some more specific aspects within each study, such as the accuracy or duration of the pen in the air, for example, may have been more sensitive to demonstrate the differences between these two groups. In the study by Gosse and Reybroeck (2020), the DD and TD groups had equivalent handwriting quality, but differences were found between the groups according to the graphic complexity of the word, in which the DD had poorer handwriting quality and spelling in more complex words. The study by Afonso et al. (2019) also identified differences between the groups according to the complexity and frequency of words, in which the DD produced longer latencies with more complex and little used words, indicating more difficulties with words of low lexical frequency. These increased times to start response and atypical effects of linguistic variables on handwriting latency in dyslexics appear to be a by-product of reading difficulties rather than a manifestation of an additional deficit specifically affecting the spelling system (Afonso et al., 2019). In that regard, the study by Cheng-Lai et al. (2013) identified that more than 60% of dyslexic children had profound difficulties in handwriting while dictating words and about 10% had a lack of legibility in writing. However, the study by Lam et al. (2011) shows that the legibility of writing tends to improve as children grow and experience more writing tasks. This allows them to develop better control with precise movements, adjusting the ideal pen-on-paper strength to produce readable words. This relationship was observed from a negative relationship between the variation in writing pressure exerted on the writing surface with age, that is, over the school years, improvements in kinesthetic and proprioceptive control are expected (Lam et al., 2011). Furthermore, speed also appeared to be related to age development.

Regarding the results found in the manual motor speed meta-analysis, although no significant differences were found between the DD and DT groups (0.19, 95% CI [-0.24; 0.62]), nor between the DD and DC (0.59, 95% CI [-0.30; 1.48]), some studies have already shown differences between the DD and DT groups with a negative large effect size: (-1.33, 95% CI [-2.06; -0.61], Berninger et al., 2015), (-1.44, 95% CI [-2.16; -0.71], Lyman et al., 2017), (-1.55, 95% CI [-2.12; -0.98], Sumner & Barnett, 2014), and a negative medium effect size: (-0.69, 95% CI [-1.28; -0.09], Gosse & Reybroeck, 2020). These results indicate that manual motor speed was not differentiated between the DD and TD groups, corroborated by the study by Afonso et al. (2019), which showed that the DD wrote as fast as the TD group. However, the studies by Gosse and Reybroeck, (2020), and Sumner and Barnett (2014) suggest that the increase in writing time observed in dyslexics was due to the production of more frequent and longer pauses rather than slower writing movements. This suggests that although dyslexic children need more time than the controls to initiate their response, they are not slower once

writing has started. In contrast, some studies have already shown differences between the DD and TD groups with a positive large effect size: (1.08, 95% CI [0.30; 1.85], Borella et al., 2011), with children aged 7.81, 8.93, 9.91, 10.97, and 11.89 years, respectively (1.29, 95% CI [0.90; 1.69], 0.99, 95% CI [0.58; 1.39], 0.82, 95% CI [0.43; 1.22], 1.23, 95% CI [0.72; 1.74], Lam et al., 2011), and (0.84, 95% CI [0.20; 1.47], Ramus et al., 2003). The study by Lam et al. (2011) showed that the DD wrote significantly slower than the TD group. Cheng-Lai et al. (2013), also identified deficits in the manual motor speed of dyslexic children, as they were slower during the execution of handwriting, in addition the DD group presented several pauses during the handwriting process. According to the study, it was hypothesized the probability that dyslexic children did not have a concrete representation of the various logographemes and their positional regularities in Chinese characters. This may have contributed to their having longer pauses during copying, as they had to repeatedly read the internal structures of the logographemes to copy accurately. Although, the DD group was slower, they had a relatively high accuracy of 80% on the copying task. Even if dyslexic children develop better writing speed with increasing age, this skill is not adequate to meet the age-equivalent writing demand, and this may be due to difficulties in integrating the performance components underlying visual motor and perceptual skills (Lam et al., 2011). It demonstrated that the manual motor speed depends on grade level, which was expected to be a skill that takes practice to become more and more automatic over years of writing experience. However, these findings show that the results cannot be generalized, since a variability in the results between studies was observed, which may be due to differences in the sampling of subjects, as well as differences in the instruments used in the studies.

4.3 Association between working memory and manual dexterity

It was not possible to perform a meta-analysis to verify the association between working memory skills and manual dexterity in dyslexic children and adolescents, since only eleven studies were found in the systematic review that evaluated these two skills, and of these, three presented the results already with a statistical analysis to verify the association (Chaix et al. 2007; Berninger et al., 2008; Marchand-Krynski et al., 2018), and the others evaluated different components of skills, which made this analysis impracticable. However, the results found in the three studies that verified the association between working memory and manual dexterity in children and adolescents with dyslexia are described here.

Regarding the association between working memory skills and manual dexterity, the findings of the study by Berninger et al., (2008) indicate that the graphomotor planning was significantly correlated with the shape factor of words, suggesting that an orthographic loop of the working memory can link the spelled word forms and the hand, just as the phonological loop of working memory connects the phonological forms of words to the mouth. Marchand-Krynski et al. (2018) also found a correlation between visual working memory and manual dexterity, suggesting that working memory along with mathematical fluency are predictors of sequential motor skills in dyslexia. These results support the evidence that cognitive skills play a significant role in the normal development of motor skills, as well as in neurodevelopmental disorders, since working memory is needed to monitor the correction of errors when creating a motor tracing and for control subsequent actions (Diamond, 2000; Seidler et al., 2012; Liao et al., 2014). Chaix et al. (2007) also report findings indicating the existence of a central cognitive deficit that was strongly correlated with writing speed, suggesting that the inability to maintain phonological information in the phonological loop of the working memory system would contribute to a slow writing speed among dyslexic children. Furthermore, this finding may indicate that Chinese children with dyslexia may have particular difficulties in sustaining the distinct visual-orthographic forms of the various Chinese character logographemes in their graphemic buffer, which can lead to frequent substitution errors for logographemes that share visual attributes or similar engines within the Chinese writing system (Chaix et al., 2007). This can prolong copying time, and a possible interpretation is that the observed relationship between cognition and motor skills is specifically applied to sequencing skills, and although motor sequencing skills are impaired, the characteristic deficiency in phonological code automation in dyslexia it is not primarily linked to the decoding of the motor sequence (Marchand-Krynski et al., 2018). Therefore, it is worth emphasizing the importance of not minimizing the relevance of the motor system or the cerebellum in the general phenotype, since it describes motor problems as a secondary deficit that is linked to a more general atypical development measured with non-specific skills, such as working memory.

4.4 Neural correlates of working memory and manual dexterity in dyslexia

Working memory represents the ability to temporarily store, maintain and manipulate information while a certain task is being performed (Baddeley, 1986), and this skill is very important for the performance of daily activities, such as talking, solving problems and writing. Verbal working memory neuroimaging studies suggest that the location of the phonological reserve resides in the inferior parietal lobe, supramarginal gyrus, and articulatory control in the left premotor frontal regions, Broca's area, supplementary motor area and cerebellum (Liao, et al., 2014; Baddeley, 2003). Regarding working memory activation in dyslexic brains, the study by Berninger et al. (2015), showed that overall, had the most functional connectivity with the number of regions connected to the seed point of origin and differed most from others in the nature of the connections' destination. However, more functional connections consume more limited resources and fewer connections can be more efficient in using limited resources to support the brain more at work while learning the written word. Thus, dyslexic brains can be inefficient at creating functional connections during spelling judgments of specific words. The results by Beneventi et al. (2010), corroborate these findings showing that the dyslexic group performed significantly worse in all task conditions, especially in the 2-back from N-back task, and these significant differences between the groups were also observed in the functional magnetic resonance imaging (fMRI) data that indicated differences in brain activation, in that the dyslexic group had less activation of the right inferior frontal gyrus (IFG) and left superior parietal lobule (SPL) areas during task execution. In addition to lower precision, dyslexics showed slower performance compared to controls. As the 0-back phoneme detection tasks do not require the recruitment of working memory resources, deficits of the dyslexic group in this task indicate impaired phonological processing compared to controls (Beneventi et al., 2010). The fMRI data with the combined effects of the 0-back phoneme detection tasks showed significant group differences in activation of the left inferior parietal lobe, bilaterally in the SPL and in the right anterior middle frontal gyrus (MFG), in the left cingulate gyrus and in the precentral gyrus. Differences in the left temporoparietal areas are commonly found in other studies involving phonological processing in dyslexic children (Rischlan et al., 2009; Vandermosten et al., 2012; Lazzaro et al., 2021) indicating an underactivation of this region, which may reflect the phonological impairment, specifically in phoneme-grapheme associations. Bilateral activation in the prefrontal cortex has been shown to be associated with executive processes and it is less likely that lateralized differences in the IFG can be attributed to phonological processing (Beneventi et al., 2010).

Therefore, the results of the 2-back task reveal neural correlates that can be attributed to executive processes, rather than phonological processes, in dyslexic children, as the sign change percentage plots showed a deviant activation pattern in the dyslexic group in the 2-back last phoneme task when both phonological processing loads and working memory load were increased. According to Beneventi et al. (2010), a possible explanation could be that poor verbal working memory in dyslexia could reflect two separate deficits, however this was not supported

in the behavioral results where an opposite pattern was found. Another explanation would be that the phoneme executive processing requirements in the 0-back identification task already addressed, or exceeded the capabilities of the dyslexic group, left no recourse for the more demanding 2-back task. Thus, there is the possibility of a reduction in the absolute amount of central executive capacity or that less effective phonological processing requires more central executive processing which would lead to a relative reduction in capacity. In the control group, the dorsolateral prefrontal cortex and SPL were more strongly activated when the phoneme detection task was added to the working memory load, while the dyslexic group showed no significant differences. No differences were found in the left posterior fusiform area that was associated with visual word form processing. However, it is noteworthy that neural activation detected with functional neuroimaging methods do not always provide simple functional explanations, especially when it comes to the relationship between brain activation and measured behavioral accuracy (Beneventi et al., 2010).

Regarding the neural correlates of manual dexterity deficits remain largely unknown and underexplored in the literature, however, as well as the extent to which handwriting deficits share common neural bases with reading and working memory deficits in dyslexia. The study by Yang et al. (2021) also used fMRI to examine the brain activity of dyslexic children during handwriting and reading tasks compared to age-matched controls. The results showed that dyslexic group exhibited reduced activation during handwriting tasks in brain regions that support sensorimotor processing, including supplementary motor area and postcentral gyrus, and visual-orthographic processing, including bilateral precuneus and right cuneus. It was also observed that the left supplementary motor area and the right precuneus showed a tendency for reduced activation during reading tasks in dyslexics. In addition, increased activation in the left inferior frontal gyrus and anterior cingulate cortex was found in dyslexics, which may reflect more executive control efforts to compensate for motor and visual-orthographic processing deficiencies (Yang et al., 2021). Moreover, the results showed that dyslexic children exhibited aberrant functional connectivity between brain areas to cognitive and sensorimotor processes during handwriting tasks, suggesting that handwriting deficits in dyslexia are associated with functional abnormalities of multiple brain regions implicated in motor execution, visual processing, spelling and cognitive control.

Concerning to brain activations of dyslexic children compared to children with other comorbidities, the findings by Berninger et al. (2015), show brain evidence of convergent functional fMRI connectivity between dysgraphia, dyslexia, Oral and Written Language Learning Disability (OWL), and control groups, differing in the patterns of which local brain

regions of origin are connected to which other regions and how many functional connections are made from the same brain region to other brain regions during a common task of spelling specific words. In general, each of the clinical groups showed some common functional connectivity to the seed point-of-origin destination, as well as distinct patterns of connectivity to each other and four seed-point controls on the same specific word-spelling task. So, common and unique brain bases underlie the same specific word task for dysgraphia, dyslexia and OWL and even controls. Thus, based on behavioral and brain evidence, dyslexia, dysgraphia, ADHD and OWL appear to be unique neurodevelopmental disorders, even though they share some commonalities (Berninger et al., 2015), greater intraindividual variability probably reflects several neural determinants that may be caused by different types of developmental disorders (Borella et al., 2011). Therefore, different students may have different types of neurodevelopmental disorders with different instructional needs, and within diagnostic categories there may also be some individual differences to consider in educational and intervention planning.

4.5 Limitations and further research

This review has some important limitations that should be noted. First, our literature search only included data from published articles, which may have limited the results found in the retrieved studies. However, this selection allowed for the study's quality control, which could exclude gray literature that could also bring interesting data for our analyses. Second, meta-analyses are naturally limited by the condition of the studies they are based on. The selected articles differed in study type, research objective, assessment tools, samples, and controls utilized. The heterogeneity between the studies and the protocols used required great care to ensure that the tasks utilized in the studies were assertively combined to avoid incompatibilities and misinterpretations. Third, the selected studies consisted of samples of children diagnosed with dyslexia at the primary or secondary level, that is, there may be a diagnosis of some comorbidity as well as the influence of these comorbidities on the results of the dyslexic sample. Another factor that may have been a limiting factor was the search for studies published only in English language and this may have limited the number of studies retrieved. Although the selected papers were published in English language, the studies were carried out in different nationalities, covering the assessment of dyslexic children in different languages such as Chinese (Lam et al., 2011; Cheng-Lai et al., 2013), French (Chaix et al., 2007; Gosse & Reybroeck, 2020; Maziero et al., 2020), Greek (Mati-Zissi & Zafiropoulou,

2003), Italian (Borella et al., 2011; Menghini et al., 2011), Norwegian (Beneventi et al., 2010) and Spanish (Afonso et al., 2019).

Furthermore, there may be some other limitations, as shown by the authors of the studies, like the total number of participants, which can limit the extent to which results can be generalized (Borella et al., 2011; Lam et al., 2011; Cheng-Lai et al., 2013; Lyman et al., 2017; Sanders et al., 2017; Gosse & Reybroeck, 2020; Maziero et al., 2020), as well as the type of sample and the subtle differences in reading ability, working memory and manual dexterity (Berninger et al., 2008; Beneventi et al., 2010; Afonso et al., 2019), the absence of a control group (Chaix et al., 2007; Berninger et al., 2008; Cheng-Lai et al., 2013). Finally, it is important to highlight that some individual factors can also influence the results of the studies, such as; functional level, biological and anatomical factors, in addition to functional conditions.

Although the results of the present meta-analysis point to a clinical condition of difficulties in working memory tasks and manual dexterity in dyslexia, we cannot assure that these data are not due to the presence of other comorbid disorders that can affect these abilities or the overlapping of primary symptoms that were present in individuals and were underdiagnosed. However, the subjects of the different studies are representative of the heterogeneous nature of neurodevelopmental disorders, as it becomes more evident that overlapping cognitive dysfunctions among the disorders are extremely common. The exclusion of comorbidities would have restricted the sample size of the studies, in addition to not being representative of heterogeneity. Thus, the frequency of deficits in working memory and manual dexterity in dyslexia continues to be a problem, as their assessment depends on the method utilized to detect these disorders and they are often not properly assessed. Studies that evaluated these abilities are important so that from the diagnosis onwards, the necessary follow-up and intervention can be carried out as soon as possible.

4.6 Research desiderata

Children with dyslexia should be evaluated for difficulties in working memory tasks and manual dexterity and, if at risk, early intervention should be undertaken and monitored for progress in cognitive and motor skills. Therefore, this study presents a suggestion that may contribute to the molecular level assessment of the disorder, in an attempt to define and verify dyslexia biomarkers. A very important neurotransmitter for DLPFC functions is dopamine, especially for working memory (Diamond et al., 2004). The dopaminergic system is fundamental for learning, however, variations in the metabolism of this neurotransmitter can
influence both learning and reading skills (Landi et al., 2013), and motor skills (see in the review by Nogueira et al., 2019b). An enzyme involved in cognitive functions related to the dopaminergic system is Catechol-O-methyltransferase (COMT) (Matsumoto et al., 2003; Chen et al., 2004; Nogueira et al., 2019b). The COMT has genetic variants that influences dopaminergic transmission and is involved in motor and cognitive performances related to the prefrontal cortex and to dopamine (Nogueira et al., 2020). The COMT metabolizes dopamine released in the prefrontal cortex, regulating dopamine levels in this region (Landi et al., 2013), and it has a trimodal distribution activity distribution in the human population due to its functional polymorphism known as Val158Met (Nogueira et al., 2019b). The Met allele has a higher level of dopamine in synaptic clefts and may be associated with cognitive stability, while the Val allele has lower concentrations of dopamine, and may be associated with flexibility (Lage et al., 2014; Nogueira et al., 2019a). In contrast, heterozygous individuals exhibit an intermediate enzyme activity (Egan et al., 2001; Tunbridge et al., 2006; Wahlstrom et al., 2007).

Diamond et al. (2004) investigated the relationship between COMT gene polymorphism and cognitive performance in typically developing children using cognitive tasks that depend on the dorsolateral prefrontal cortex and appear to be sensitive to the level of dopamine in this area. Their findings show that children who were homozygous for the Met genotype performed significantly better than children with the Val genotype on a task requiring working memory and inhibition, while heterozygous children performed intermediate. The study by Landi et al. (2013) showed that children with the homozygous Met genotype performed significantly better than Val and heterozygous children in various reading-related skills such as, in Phonological Awareness and Spelling, as well as a marginal effect of better performance in Decoding. Furthermore, homozygous Met children had greater activation in the left prefrontal regions, consistent with the role of COMT in modulating prefrontal function, whereas Val children showed reduced activations. However, homozygous Val individuals showed several brain areas of greater activity than heterozygous individuals, including the parahippocampal gyrus and several small regions of the frontal cortex and the cerebellum. These findings indicate that there is an association between the COMT polymorphism and cognitive functions. In addition to cognition, studies have shown similar results for an association between COMT and motor behavior. The study by Lage et al. (2014) showed that individuals with the Met genotype had better spatial accuracy with the same movement time than Val and heterozygous individuals. In contrast, Val and heterozygous individuals had higher levels of peak velocity. Based on these findings, we suggest that future studies investigate whether there is an association between the COMT polymorphism and dyslexia. Besides that, more specific assessment and treatment options can be adapted to the different profiles found in children with dyslexia to improve the performance of impaired skills. Further research should be carried out to better assess which executive processes are recruited to access working memory in dyslexic children, the speed of cognitive and motor processing, in addition to verifying whether there is a cognitive-motor relationship in dyslexia. Therefore, further exploration of the etiology of these disorders is needed to bring a better understanding of neurofunctional structures and neurodevelopmental disorders.

5. CONCLUSION

Children and adolescents with dyslexia commonly have deficits in working memory tasks and motor problems, with low efficiency in handwriting, accuracy, and spend more time on writing. Thus, working memory problems appear impacting motor problems in children with dyslexia, or vice versa. Functional neuroimaging tests suggest that the cerebellum is important not only for motor functions, but also for cognitive functions for which the dorsolateral prefrontal cortex is required, more specifically, working memory. These findings indicate that cognitive development and motor development may be fundamentally interlinked. The results found in this study suggest that dyslexic children have significantly poorer visuospatial and verbal working memory than controls, with even greater impairments in the phonological loop. However, although differences were observed in fine motor control skills, handwriting and manual motor speed, these differences were not significant between groups and further studies are needed to better explore the area of deficits in manual dexterity in dyslexic children. Therefore, it is worth emphasizing the importance of assessing working memory and manual dexterity skills in children with dyslexia, and if impaired, early intervention should be performed and monitored for progress in cognitive and motor skills. Although some studies suggest that the handwriting skills of children with dyslexia tend to gradually improve with age, without appropriate intervention, these skills may not be sufficiently developed to reach an ageappropriate level. Therefore, it is important that an early therapeutic intervention is carried out in order to improve the basic writing skills of children with dyslexia in order to improve their functionality.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

This study was supported by Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) (grant APQ-03305-15).

APPENDIX

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

Reviewe	rDate				
Author	Year		Record	d Number_	
		Yes	No	Unclear	Not applicable
1.	Were the criteria for inclusion in the sample clearly defined?				
2.	Were the study subjects and the setting described in detail?				
3.	Was the exposure measured in a valid and reliable way?				
4.	Were objective, standard criteria used for measurement of the condition?				
5.	Were confounding factors identified?				
6.	Were strategies to deal with confounding factors stated?				
7.	Were the outcomes measured in a valid and reliable way?				
8.	Was appropriate statistical analysis used?				
Overall appraisal: Include Exclude Seek further info					
Comment	ts (Including reason for exclusion)				

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SUPPLEMENTARY MATERIAL

Table a. Tools used to assess working memory and manual dexterity in the reviewed studies.

Assessments tools of Working Memory		Assessments tools of Manual Dexterity			
Visuospatial working memory	Verbal working memory	Fine motor control	Handwriting	Manual motor speed	
BAS-II - British Abilities	Forward block-tapping test;	BDT - Bangor Dyslexia Test:	Alphabet task;	BHK;	
Scales–II;	Block design;	the pointing task;	Batteria per la valutazione delle	CHAT - Chinese Handwriting	
Foward digit span;	Maze memory;	BOT-2 - Bruininks–Oseretsky	competenze ortografiche nella	Assessment Tool;	
CTOPP - Comprehensive Test	Picture span;	test of motor proficiency—	scuola dell'obbligo;	DASH;	
of Phonological Processing;	PRI-WISC-IV Perceptual	2nd edition;	Handwriting;	Finger to thumb	
Listening recall;	Reasoning Index;	DST - Dyslexia Screening	DASH;		
Non-word list recall span;	Prove di Memoria e Apprendimento	Test: the bead-threading task;	The Rey-Osterrieth Complex		
Prove di Memoria e	per l'Età Evolutiva by Vicari's	MABC-2 - Movement	Figure;		
Apprendimento per l'Età	battery of tasks. (Visuospatial span	Assessment Battery for	Timed letter formation;		
Evolutiva by Vicari's battery of	task);	Children—2 nd edition;	BHK		
tasks. (Verbal span task)	The Rey-Osterrieth Complex	Purdue Pegboard test			
_	Figure (Drawing it from memory)	-			

Table b. Description of tools used to assess working memory and manual dexterity in the reviewed studies.

	Working Memory	Manual Dexterity		
Assessments tools	Task description	Assessments tools of	Task description	
Alphabet writing 15 task	The task is to write the alphabet from memory in readable letters in alphabetical order as quickly as possible within 15 seconds.	Alphabet task	It consists of handwriting (unjoined letters) the lowercase letters of the alphabet from memory as quickly as possible in alphabetical order.	
Forward and Backward block- tapping test	In this task, ten cubes are presented on a board. The examiner touches the cubes one after the other and the participant is asked to repeat the series in the same order (forward) or in the reverse order (backward).	Annett´s pegboard task	In this task, the participant must place a series of 10 pins into small holes as quickly as possible. Three blocks of attempts are performed with each hand.	

BAS-II - British Abilities Scales–II	In this task, the participant repeats, in the order of presentation, a sequence of digits presented orally.	Batteria per la valutazione delle competenze ortografiche nella scuola dell'obbligo	This task consists of handwriting a continuous repetitive alternating sequence of cursive letters ((1) and "E") in a time interval of 180 s on a sheet of paper.
Block recall span	The task starts with a small number of blocks and gradually increases in length up to nine blocks. The test measures the number of correct sequences and the longest sequence remembered.	BDT - Bangor Dyslexia Test: the pointing task	It consists of indicating different right or left parts of your own body according to the examiner's request.
Block design	This task requires the participant to view a constructed model or image in the Stimulus Book and use one- or two-color blocks to recreate the drawing within a specified time limit.	BHK test Handwriting speed and quality	This task consists of handwriting words as quickly as possible.
Coding	In this task the participant copies symbols that are paired with simple geometric shapes or numbers. Querying a key, the participant draws each symbol in the corresponding shape or cell, within a specified time interval.	BOT-2 - Bruininks–Oseretsky test of motor proficiency–2nd edition	It consists of tasks to assess the development of fine motor skills in school activities, such as handwriting and drawing.
Comes From	This task consists of judging whether or not a word is derived from a base word. Sample items include the following: Does corner come from corn? Does builder come from build?	CHAT - Chinese Handwriting Assessment Tool	It consists of a task in which the participant must copy a standardized 90-character template displayed on the computer screen as quickly and accurately as possible.
CTOPP - Comprehensive Test of Phonological Processing	The task is to listen to an audio recording of non- words, which are uttered one at a time, and then exactly repeat the spoken non-word heard, which contains sounds in English but has no meaning.	DASH - Detailed Assessment of Speed of Handwriting	This task consists of copying a sentence with all the letters of the alphabet under contrasting instructions.
Digit Span	In this task, the participant repeats a sequence of digits presented orally, in the same order (forward) or in the reverse order (backward).	DST - Dyslexia Screening Test: the bead-threading task	This task consists of passing a string on 15 beads in 30 seconds.

D-KEFS - Delis Kaplan Executive Functions	It consists of reading orally a color word in black and then naming the ink color for a written word where the ink color conflicts with the word color name (for example, the red word written in green ink).	Finger to thumb	This task consists of placing the index finger of one hand on the thumb of the other hand and vice versa. Then, keeping the top thumb and index finger together, they rotate one hand clockwise and the other counterclockwise until the finger and thumb touch each other again, and so on.
Freedom from distractibility	It consists of an index score composed of the sum of scores on the Arithmetic and Digit Span subsets of the WISC test.	LOMDS - Lincoln-Orseretsky Motor Development Scale	It consists of a 36-item scale that assesses a wide range of motor skills, such as finger dexterity, hand-eye coordination, and gross hand, arm, leg, and trunk activity.
Listening recall	It consists of a sequence of sentences that is verbally presented, each of which requires a true/false decision to be made. After each sequence of sentences, the participant must name, in the order of presentation, the last word of each sentence in the sequence.	MABC-2 - Movement Assessment Battery for Children—2 nd edition	The manual dexterity component includes three tasks: a one-handed post task, a timed two-hand assembly task, and an untimed drawing task.
Maze memory	This task consists of a route through a maze where the participant is asked to make a pencil copy of the same route in an empty maze.	Purdue Pegboard test	This task consists of a board with two parallel rows with 25 holes into which cylindrical metal pins are placed by the participant for a total of four trials.
Non-word list recall span	It consists of sequences composed of non-words presented verbally one after the other, with the participant being asked to verbally repeat these non-words in the order presented.	SRT task simple reaction time	The stimuli consist of a white cross located in one of five positions corresponding to the tips of an invisible five-branch star in the center of a computer screen. Participants should mark as soon as possible when the cross appears after a fixation point (d) by pressing a button box with their dominant hand.
Picture span	The participant views the visual stimuli with one or more photos and then selects the images in the correct order from the response page.	The Rey-Osterrieth Complex Figure Copying the shape	In this task, the participant observes a figure that contains 18 elements and tries to draw it with all the details that can be remembered.
PRI-WISC-IV Perceptual Reasoning Index	This task consists of trying to understand visual information and solving new abstract visual problems.	Time estimation	This task consists of the successive presentation of two tones in which the participant has to say whether the second is longer or shorter than the first.

Prove di Memoria e Apprendimento per l'Età Evolutiva by Vicari's battery of tasks.	The verbal task consists of a list of eight low- frequency words of two syllables that are read by the examiner and must be repeated by the participants in the same order. Then four additional two-word strings are presented. The visuospatial task consists of a non-verbalable geometric shape that appears for two seconds in one of seven possible positions on the computer screen. After one second, the same geometric shape appears in a second position and disappears after two seconds, and the participant must indicate the order in which the stimuli appeared.	Timed letter formation task	The task consists of writing alternate symbols 0 (zero) and + (plus) as fast as possible for 1 minute.
RAN - Rapid Automatic Letter Naming	This task consists of naming tiny printed letters arranged in lines as quickly as possible.		
RAS - Rapid Automatic Switching	This task consists of naming letters printed in alternate lowercase and written numerals arranged in lines as quickly as possible.		
The Rey-Osterrieth Complex Figure Drawing it from memory	In this task, the participant observes a figure that contains 18 elements and after a period this observation is interrupted, and the participant has to draw the figure with all the details that can remember.		
TOSWRF - Test of Silent Word Reading Fluency	This task consists of marking the word boundaries in a series of letters arranged in lines over a period of three minutes.		
WMI-WISC-IV	It consists of a measure of the participant's ability to respond to information presented verbally and to formulate a response.		

4. CONSIDERAÇÕES FINAIS

Crianças disléxicas comumente apresentam prejuízos em uma série de habilidades, dentre elas, na memória de trabalho e na destreza manual, que por sua vez, podem acarretar em dificuldades nas tarefas funcionais diárias, como memorizar a forma das letras ou um número de telefone, além dos impactos em tarefas que exijam destreza para abotoar uma camisa ou amarrar os cadarços de um tênis, até o ato motor da escrita à mão. Diante disso, o presente estudo objetivou realizar uma revisão sistemática e metanálise para averiguar as habilidades de memória de trabalho e destreza manual e a existência de uma relação entre alterações nessas duas habilidades em crianças e adolescentes disléxicos.

Os resultados indicam que crianças disléxicas apresentam prejuízos em tarefas que exigem memória de trabalho, tanto no esboço visuoespacial quanto na alça fonológica, porém, em acordo com a literatura, esses prejuízos são ainda maiores na alça fonológica. Além disso, encontrou-se que as crianças disléxicas produziram latências de escrita mais longas e cometeram mais erros do que o grupo de desenvolvimento típico, sugerindo que o grupo disléxico teve uma velocidade de processamento particularmente lenta, indicando alguma dificuldade em reconhecer palavras rapidamente, incluindo palavras curtas. Assim, uma velocidade de processamento mais lenta indica que mais esforço mental é necessário para realizar tarefas simples, com menos recursos disponíveis para níveis mais elevados de aprendizagem e processamento cognitivo, como compreensão de leitura (FUCHS et al., 2001; PERFETTI; LANDI; OAKHILL, 2005) e habilidades perceptivas. O grupo disléxico também apresentou um desempenho pior nas tarefas de apontar, que indicam evidências de má coordenação visuoespacial/motora, além de déficits de memória de trabalho, uma vez que a tarefa de apontar exige que sejam seguidas certas sequências de comandos verbais, déficits na memória de trabalho podem prejudicar o desempenho nestas tarefas de sequenciamento e apontamento.

Embora não tenha sido possível realizar uma metanálise para verificar a associação entre as habilidades de memória de trabalho e destreza manual em crianças e adolescentes disléxicos, foram analisados três estudos que verificaram a associação entre essas duas habilidades. Os achados dos estudos de Chaix *et al.* (2007), Berninger *et al.* (2008) e de Marchand-Krynski, Bélanger e Morin-Moncet (2018) mostraram que o planejamento grafomotor foi significativamente correlacionado com o fator de forma das palavras, sugerindo que o loop ortográfico da memória de trabalho faça a ligação entre as formas das palavras com a escrita à mão, assim como o laço fonológico da memória de trabalho conecta as formas fonológicas das

palavras à boca. Além disso, o estudo de Chaix *et al.* (2007) indica a existência de um déficit cognitivo central fortemente correlacionado com a velocidade de escrita, sugerindo que a dificuldade em manter a informação fonológica na alça fonológica, contribuiria para uma baixa velocidade de escrita em crianças disléxicas. Esses resultados apoiam a evidência de que as habilidades cognitivas desempenham um papel significativo no desenvolvimento das habilidades motoras, uma vez que a memória de trabalho é necessária para monitorar a correção de erros ao criar um traçado motor e para controlar as ações subsequentes (DIAMOND, 2000; SEIDLER; BO; ANGUERA, 2012; LIAO *et al.*, 2014). Portanto, vale ressaltar a importância de não minimizar a relevância do sistema motor no desenvolvimento da criança, e embora as crianças com dislexia nem sempre apresentem dificuldades óbvias de escrita, elas parecem ser mais sensíveis a complexidade gráfica do que crianças com desenvolvimento típico. Isso significa que quanto mais difícil fica a tarefa, tanto a precisão da ortografia quanto a qualidade da escrita podem ficar comprometidas. Estes resultados destacam a necessidade de considerar a escrita como uma atividade em que a habilidade motora e o ato ortográfico da escrita podem influenciar uns aos outros.

Como a avaliação motora é um elemento importante para avaliar o desenvolvimento geral de crianças, é necessário que os aspectos quantitativos e qualitativos dos movimentos motores finos e globais sejam investigados, uma vez que estes podem refletir a integridade e a maturidade do cérebro e podem, provavelmente, fornecer indícios de alterações no desenvolvimento motor, como os observados nos escolares com dislexia. Essas alterações motoras quando presentes no quadro de dislexia e não evidenciadas no processo diagnóstico fazem com que as condutas, tanto terapêuticas quanto psicoeducacionais em relação a esses escolares, sejam inadequadas para suas necessidades, podendo desencadear problemas de baixa autoestima, fracassos escolares e desmotivação para a aprendizagem.

Em sua revisão, Medina, Minetto e Guimarães (2017) verificaram que os trabalhos que avaliaram as funções executivas na dislexia são escassos, além disso, a maioria dos estudos encontrados, foram realizados com população estrangeira (estadunidenses, alemães, italianos, ingleses, holandeses, israelenses e portugueses), sendo apenas quatro trabalhos realizados com a população brasileira. Há, pois, a necessidade de se ampliar os estudos na área no Brasil de forma atualizada, aprofundada e sistemática, tanto no que se refere ao construto, quanto à elaboração de instrumentos que sejam validados e padronizados para a nossa população. A dislexia existe, é diagnosticável, mas nem todas as dificuldades de leitura são dislexia. Portanto, em uma perspectiva diagnóstica, crianças com dislexia devem ser avaliadas quanto às suas habilidades cognitivas e motoras, além das fonológicas, por uma equipe multiprofissional. Em

caso de prejuízos, uma intervenção precoce nas funções deficitárias deve ser realizada até que as habilidades de leitura e escrita atinjam o nível esperado. A conduta terapêutica necessita de um enfoque clínico e educacional, voltado para a minimização do impacto das manifestações comportamentais e cognitivo-linguísticas inerentes à dislexia, visando a uma melhor qualidade de vida social e escolar destas crianças. Para tal, é necessário que estudos futuros possam elaborar um protocolo de avaliação para o diagnóstico de dislexia que englobe tarefas cognitivas que avaliem a memória de trabalho, bem como, tarefas motoras que avaliem a destreza manual, para que assim, a partir de um protocolo de avaliação, também possam ser elaborados protocolos de intervenção que visem trabalhar essas habilidades.

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