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# Prevalence of malocclusions and parafunctional habits in pediatric patients with developmental dyslexia

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**Objective:** The study aimed to assess the prevalence of dental malocclusion, orthodontic parameters, and parafunctional habits in children with developmental dyslexia (DD). **Methods:** Forty pediatric patients (67.5% boys and 32.5% girls, mean age:  $11.02 \pm 2.53$  years, range: 6–15 years) with DD were compared with 40 age- and sex-matched healthy participants for prevalence of dental malocclusion, orthodontic parameters, and parafunctional habits. Dental examinations were performed by an orthodontist. **Results:** Pediatric patients with DD exhibited a significantly higher prevalence of Angle Class III malocclusion (22.5% vs. 5.0%,  $P = 0.024$ ), deep bite (27.5% vs. 7.5%,  $P = 0.019$ ), midline deviation (55.0% vs. 7.5%,  $P < 0.0001$ ), midline diastemas (32.5% vs. 7.5%,  $P = 0.010$ ), wear facets (92.5% vs. 15.0%,  $P < 0.0001$ ), self-reported nocturnal teeth grinding (82.5% vs. 7.5%,  $P < 0.0001$ ), nail biting (35.0% vs. 0.0%,  $P < 0.0001$ ), and atypical swallowing (85.0% vs. 17.5%,  $P < 0.0001$ ) compared to that in healthy controls. **Conclusions:** Pediatric patients with DD showed a higher prevalence of Class III malocclusion, greater orthodontic vertical and transverse discrepancies, and incidence of parafunctional activities. Clinicians and dentists should be aware of the vulnerability of children with dyslexia for exhibiting malocclusion and encourage early assessment and multidisciplinary intervention.

**Key words:** Malocclusion, Developmental dyslexia, Orthodontic parameters, Learning disorder

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## INTRODUCTION

According to the 2018 First Step Act Section 3635, the term dyslexia denotes “an unexpected difficulty in reading for an individual who has the intelligence to be a better reader.”<sup>1</sup> Thus, it identifies a brain-based learning disability caused by a difficulty in “phonological processing,”<sup>1</sup> that results in a reading impairment while also affecting the ability to speak and write.<sup>2</sup> Assaf et al.<sup>3</sup> attempted to further clarify the neurobiological origin of developmental dyslexia (DD), which is believed to result from a deficit in the phonological component of language, relative to the patient’s age and educational level.<sup>4</sup> According to a recent systematic review, DD affects one in every five children, thereby accounting for about 20% of the population.<sup>5</sup>

Heterogenous difficulties in reading and phonological processing are only a few of the many symptoms that characterize DD. For instance, motor and sensory changes have also been suggested as characteristic features of children with DD.<sup>6</sup> Specifically, according to a study conducted on 950 individuals with DD, 40–57% of them exhibited some degree of motor impairment that affected coordination, balance, and manual dexterity, thus indicating a cerebellar dysfunction underlying DD symptoms manifestation.<sup>7</sup> An association between cerebellar dysfunction and dyslexia has been confirmed by other studies. Stoodley<sup>8</sup> showed that patients with dyslexia performed worse than controls in a range of cerebellar-related activities, such as balance and eye movement control. A study by Nicolson et al.<sup>9</sup> corroborated the association based on radiological analysis and diagnostic tests, which showed that cerebellar activation is present not only during learning, cognitive, linguistic, and motor tasks in areas of the frontal lobe but also in certain areas of the left hemisphere such as the Broca’s area, fundamental for speech articulation.<sup>10</sup> Specifically, an increased cerebellar activation has been demonstrated in the control of lingual movements and tongue contraction.<sup>11</sup> Noteworthy, children with DD have been suggested to exhibit slower and less accurate reading ability, thereby suggesting an impaired tongue movement and speech-motor development.<sup>12,13</sup> Interestingly, a study investigating the relationship between malocclusion and activation of cerebellar neural circuits suggested an association between unilateral crossbite and the pathway connecting the dorsomedial part of the main sensory trigeminal nucleus to the cerebellum.<sup>14</sup>

Malocclusion and oral anatomical functional abnormalities are highly correlated, and altered muscle function can influence the growth of the bone bases and teeth position.<sup>15</sup> This kinetic relationship is dynamic over time, to the extent that the coordination of the tongue and bases of the jaws changes between 8 and

11 years of age and is further modified during the late stage of adolescence.<sup>12</sup> Recently, children with speech sound disorder and motor speech involvement have been described to present with a higher prevalence of malocclusions compared to that in children with typical speech development.<sup>16</sup> Taken together, given the role of the tongue, masticatory muscles, and their relationship to the bony bases in determining an individual’s occlusion, there may be a relationship between malocclusion and dyslexia. Yet, to the best of our knowledge, only one study to date has examined the presence of orthodontic features in dyslexic children.<sup>13</sup> According to this study, children with DD more frequently exhibit presence of midline diastema and increased overjet and overbite compared to that in healthy controls. Nevertheless, this study did not assess for the presence of parafunctional habits, the investigation of which may be worthy considering a higher prevalence of bruxism is consistently found in children with some degree of neurological and developmental impairment.<sup>17,18</sup>

Therefore, the aim of this study was to analyze the orthodontic parameters and prevalence of dental malocclusion and parafunctional habits in patients with DD. We hypothesized that pediatric patients with DD more commonly exhibit dental malocclusion and alteration in other orthodontic parameters as compared to healthy controls. If this is confirmed, clinicians should be aware of the vulnerability of this specific population in exhibiting malocclusion to encourage an early assessment and multidisciplinary intervention.

## MATERIALS AND METHODS

### Study design

This is a case-control prospective observational study carried out in collaboration between the Child Neuropsychiatry and Pediatric Dentistry Departments of the A. Gemelli Hospital. The study recruited participants over 9 months from July 2022 to March 2023 from patients referred to the Child Neuropsychiatry Unit for learning difficulties. The study was approved by the Ethics Committee of the A. Gemelli Foundation (ID 5023). Written informed consent were obtained by the parents or guardians.

### Sample size calculation

Considering the prevalence of midline diastema in 57% of children with DD compared to 23.5% in healthy controls,<sup>13</sup> a sample size calculated by setting  $\alpha = 0.05$  and power at 80% yielded  $n = 30$  per group ( $n = 60$  total) as the minimum number of participants to be included.

## Participants

Participants were recruited from among patients seeking treatment for learning difficulties at the Child Neuropsychiatry Unit. At their initial appointment, patients underwent a neurophysiological evaluation at the Institute of Child Neuropsychiatry and an orthodontic evaluation at the Department of Paediatric Dentistry of A. Gemelli Hospital, Rome, Italy. Dental examinations were performed by an orthodontist. Pediatric patients (< 18 years of age)<sup>19-21</sup> with a diagnosis of DD from a certified neurologist after a specific neuropsychological assessment and an informed consent signed by the parents or guardians were included in the study. Exclusion criteria were patients > 18 years of age; presence of any other neurological disorder (i.e., epileptic phenomena, neuromuscular disorders), psychiatric (behavioral problems) symptoms, or educational deficit that could cause reading impairment;<sup>22</sup> an intelligence quotient (IQ) of  $\leq 84$ ; hearing and/or visual impairment; speech and/or phonotactory problems;<sup>13</sup> body mass index > 25 kg/m<sup>2</sup>; taking anticonvulsants or psychoactive drugs;<sup>13</sup> history of orthodontic treatment; and/or those not willing to provide informed consent.

An equal number of healthy controls, age- and sex-matched to those with DD (participants without DD) was selected. Participants were chosen based on matching needs, from all consecutive pediatric patients referred to the Department of Paediatric Dentistry and Orthodontics of A. Gemelli Hospital after recruiting patients with DD. Participants did not receive any compensation for partaking in the study.

## Screening measures

A neurophysiological assessment was performed at the initial evaluation, which consisted of the following:

### *Cognitive profile*

This was assessed using the Wechsler Intelligence Scale for Children, 4th edition (WISC<sup>®</sup>-IV),<sup>23</sup> a validated questionnaire used to estimate the general intellectual functioning (IQ) and specific aspects of cognitive functioning.<sup>24</sup> The WISC<sup>®</sup>-IV is divided into 10 subtests that contribute to a full-scale IQ. A total of four composite scores can be obtained from the 10 subtests: verbal comprehension index, an overall measure of verbal concept formation; visuospatial index, a measure of visuo-perceptual organization and non-verbal reasoning; working memory index, a measure of memory span and freedom from distractibility; and processing speed index, a measure of fast visuo-motor integration and learning.

### *Academic skills*

These were assessed with different screening instruments. The memory-transfer battery was used to assess

speed and accuracy in reading and text comprehension abilities.<sup>22,25</sup> The Assessment of Writing and Orthographic Competences was utilized to evaluate the writing accuracy in graphology, orthographic competence, and written text production.<sup>26</sup> Lastly, the AC-MT 6-11 (a test for the evaluation of calculating and problem-solving abilities) was administered to assess mathematical performance in terms of number comprehension and calculation skills.<sup>27</sup>

### *Behavioral and emotional profile*

Presence and severity of behavioral and emotional impairment were assessed with the Child Behavior Checklist 6-18 (CBCL/6-18).<sup>28</sup> The CBCL/6-18 is a structured rating proxy-report scale using which the caregivers can rate their child's social and emotional disturbances currently and in the previous 6 months. It consists of 113 behavioral and emotional problems rated on a scale from 0 ("Not true") to 2 ("Very true"). The scale has been validated for individuals aged 6-18 years. In addition to a total score identifying the severity, factor analytic studies yielded two broad-band factors (Internal and Externalizing) and eight narrow-band syndrome scales. The first three narrow-band syndrome scales (i.e., anxious/depressed, withdrawn/depressed, and somatic complaints) constitute the Internal factor; the remaining five (i.e., social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior) constitute the Externalizing factor.<sup>29-31</sup>

## Primary outcomes

During the dental examination performed by a trained orthodontist, the following orthodontic parameters were investigated clinically and classified.

### *Sagittal discrepancy*

Dental malocclusion: Angle classification was used to identify the molar relationship into Class I, II, and III based on the relative position of the mesiobuccal cusp of the maxillary first molar to the mesiobuccal sulcus of the mandibular first molar.<sup>32,33</sup>

### *Vertical discrepancy*

Overbite:<sup>34</sup> This is defined as the vertical overlap and is obtained by measuring the amount of overlap between the upper and lower central incisors in millimeters. Normal values range between 1-2 mm. A negative value is identified as an open bite and values > 2 mm as deep bite.<sup>35</sup>

### *Transverse discrepancy*

Midline deviation: Midline deviation is defined as a discrepancy of  $\geq 2$  mm between the mandibular and the maxillary midline.<sup>32</sup> The coincidence of the maxillary and

mandibular midlines was assessed accordingly.

**Posterior crossbite:** This is assessed at the level of the first molar and is identified by the buccal cusp of the upper molar occluding lingually to the buccal cusp of the lower molar.<sup>32</sup>

**Scissors bite:** This was assessed at the level of the first molar, and is identified by the upper molars occluding buccally to the mandibular molars.<sup>36</sup>

**Midline diastema:** This was assessed in the posterior and anterior regions. A midline diastema is present if there is at least 2 mm of space between the two upper central incisors.<sup>36</sup>

**Secondary outcomes**

Prior to the dental examination, the parents or guardians were asked to complete a questionnaire investigating the presence of parafunctional habits in the participant.

*Probable sleep bruxism*

The presence of sleep bruxism was investigated by answering the following ad-hoc questions (“Does your child grind his/her teeth at night?”) with a yes/no an-

swer.<sup>37</sup> During the dental examination, the presence of dental wear facets was recorded. Probable sleep bruxism was considered positive in the presence of a positive self-report by ad-hoc questionnaire and positive signs of wear facets on clinical inspection.<sup>38</sup>

*Nail biting*

The presence of nail biting was investigated by answering the following ad-hoc questions (“Does your child bite his/her nail?”) with a yes/no answer.

*Atypical swallow*

During oral examination, the presence of an atypical swallow was recorded by the orthodontist.

**Statistical analysis**

Demographic data were analyzed using descriptive statistics and are reported as mean ± standard deviation while categorical variables are reported as absolute (or relative) percentages. Shapiro–Wilk test was used to assess for normality distribution. In case of skewness of the data, variables were transformed with logarithmic transformation, as appropriate. Differences in the pro-

**Table 1.** Comparison in orthodontic parameters and prevalence of malocclusion and parafunctional habits between children with DD and healthy controls

	DD children (n = 40)	Controls (n = 40)	P value	Cramer’s V	OR	95% CI
<b>Malocclusion</b>						
Angle’s molar Class I	18 (45.0)	32 (80.0)	0.001***	0.361	0.205	0.076, 0.553
Angle’s molar Class II	13 (32.5)	6 (15.0)	0.067	0.206	2.728	0.916, 8.126
Angle’s molar Class III	9 (22.5)	2 (5.0)	0.024*	0.254	5.516	1.109, 27.429
<b>Vertical dimension</b>						
Normal overbite	22 (55.0)	35 (87.5)	0.001***	0.359	0.175	0.057, 0.538
Open bite	7 (17.5)	2 (5.0)	0.154	0.198	4.030	0.782, 20.760
Deep bite	11 (27.5)	3 (7.5)	0.019*	0.263	4.678	1.193, 18.337
<b>Transverse dimension</b>						
Midline deviation	22 (55.0)	3 (7.5)	< 0.001***	0.512	0.066	0.018, 0.251
Posterior crossbite	7 (17.5)	1 (2.5)	0.057	0.250	8.273	0.968, 70.734
Scissor bite	3 (7.5)	0 (0.0)	0.241	0.197	4.810	0.381, 0.606
Midline diastema	13 (32.5)	3 (7.5)	0.010*	0.313	5.938	1.540, 22.903
<b>Parafunctional habits</b>						
Self-reported nocturnal teeth grinding	33 (82.5)	3 (7.5)	< 0.001***	0.754	58.143	13.892, 243.352
Wear facets	37 (92.5)	6 (15.0)	< 0.001***	0.777	69.889	16.198, 301.551
Nail biting	14 (35.0)	0 (0.0)	< 0.001***	0.461	0.394	0.292, 0.531
Atypical swallowing	34 (85.0)	7 (17.5)	< 0.001***	0.700	32.111	9.410, 109.570

Values are presented as number (%).

DD, developmental dyslexia; OR, odds ratio; CI, confidence interval.

\*Denotes statistically significant difference at P < 0.05; \*\*\*denotes statically significant difference at P < 0.001.

portions of malocclusions and overbite were compared between patients with DD and healthy controls using chi-square for proportion. The orthodontic parameters of midline deviation, posterior crossbite, scissors bite, and midline diastema, as well as the parafunctional habits (i.e., self-report sleep bruxism and wear facets) were dichotomized and assigned a value of 1 if present and 0 if absent. The two groups were compared using the chi-square or Fisher test (for categorical variables). The strength of correlation was ascertained with Cramer's V, and odds ratio (OR) and 95% confidence intervals were calculated for each variable.

Data were analyzed with SPSS (IBM SPSS Statistics Macintosh, Version 27.000; IBM Corp., Armonk, NY, USA). For all analyses, the *P* values were set at *P* < 0.05.

## RESULTS

The total sample consisted of 80 participants. Forty pediatric patients with DD (67.5% boys and 32.5% girls, mean age:  $11.02 \pm 2.53$  years, range: 6–15 years) were compared with 40 sex- and age-matched healthy controls. All the participants were Caucasian and belonged to the same geographical area.

Table 1 and Figure 1 show the difference in prevalence of malocclusion, orthodontic parameters, and parafunctional habits between patients with DD and healthy controls.

### Prevalence of dental malocclusion in pediatric patients with DD vs. healthy controls

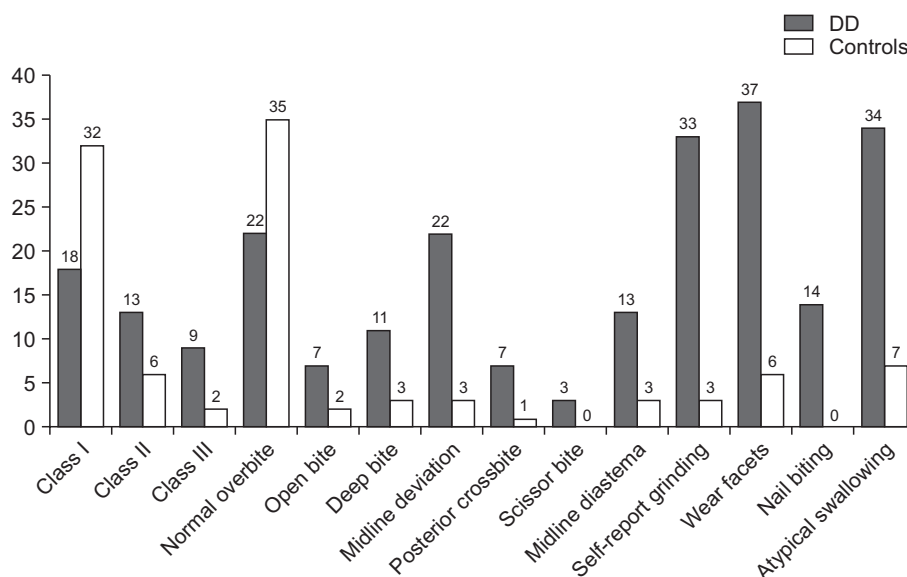
Patients with DD had a significantly higher prevalence of Angle Class III malocclusion compared to healthy controls (22.5% vs. 5.0%,  $X^2(1) = 5.100$ , *P* = 0.024). On the contrary, healthy controls had a higher prevalence of Angle Class I (80.0% vs. 45.0%,  $X^2(1) = 10.323$ , *P* = 0.001).

### Comparison of orthodontic parameters between pediatric patients with DD and healthy controls

Patients with DD exhibited a significantly higher prevalence of deep bite (27.5% vs. 7.5%,  $X^2(1) = 5.541$ , *P* = 0.019), midline deviation (55.0% vs. 7.5%,  $X^2(1) = 20.741$ , *P* < 0.001), and midline diastema (32.5% vs. 7.5%,  $X^2(1) = 7.813$ , *P* = 0.010) compared to that in healthy controls. Conversely, healthy controls more frequently exhibited normal values of overbite (87.5% vs. 55.0%,  $X^2(1) = 10.184$ , *P* = 0.001). The remaining orthodontic parameters were not significantly different between the two groups (Table 1).

### Comparison of parafunctional habits between pediatric patients with DD and healthy controls

Patients with DD exhibited significantly higher prevalence of wear facets (92.5% vs. 15.0%,  $X^2(1) = 48.322$ , *P* < 0.001) and reported greater prevalence of sleep grinding activity than that in healthy controls (82.5% vs. 7.5%,  $X^2(1) = 45.455$ , *P* < 0.001). Moreover, patients with DD reported significantly higher prevalence of nail biting (35.0% vs. 0.0%,  $X^2(1) = 16.970$ , *P* < 0.001) and atypical



**Figure 1.** Bar chart displays the difference in orthodontic parameters, prevalence of malocclusion, and parafunctional habits between children with DD and controls. DD, developmental dyslexia.



swallow (85.0% vs. 17.5%,  $\chi^2(1) = 39.200$ ,  $P < 0.001$ ) compared to the healthy controls.

## DISCUSSION

The current study aimed to assess the difference in orthodontic parameters and the prevalence of malocclusion and parafunctional habits between a cohort of children with DD and healthy controls. The results of this study suggested that pediatric patients with DD exhibited a significantly higher prevalence of Angles Class III malocclusion, greater vertical (deep bite) and transverse discrepancies (midline deviation and midline diastema), and higher prevalence of wear facets and parafunctional habits (self-reported sleep bruxism, nail-biting, and atypical swallowing).

DD is a multisymptomatic and heterogeneous disorder, characterized by a broad range of cognitive and neurological signs. Over time, several studies have assessed the ability of patients with dyslexia to perform certain tasks (muscular control, speech control, etc.) in comparison with that in healthy patients and have observed impaired functioning. The majority of these studies are based on the cerebellar hypothesis, which links dyslexia to abnormalities in the cerebellum. This hypothesis likely explains the poor performance of patients with dyslexia compared to healthy controls since the cerebellum is responsible for tasks, such as maintaining posture, the ability to initiate and sustain complex voluntary movements, and maintenance of muscle tone, among others.<sup>39-41</sup> The cerebellum is not only involved in motor control and coordination, but it has also been implicated in the cognitive processes responsible for reading and language processing.<sup>42</sup> As such, it is plausible to speculate that a dysfunction of the cerebellum in children with dyslexia may contribute to the development of malocclusion and cognitive difficulties associated with dyslexia. Similarly, it is possible to postulate that the cerebellum plays a role in controlling tongue movements, and consequently, abnormalities in this control mechanism may contribute to disturbances in the tongue. This could explain the higher prevalence of atypical swallow and altered orthodontic parameters, such as midline deviation, midline diastema, deep bite, and crossbite observed in this cohort of children with DD than in healthy controls. In literature, several studies have analyzed the correlations between malocclusion, tongue position, and speech distortion. In fact, a recent systematic review indicated an association between atypical swallow and malocclusions.<sup>43</sup> Assaf et al.<sup>3</sup> in a sample of 547 children observed that open bite, deep bite, and posterior crossbite were associated with altered lingual posture. Thus, the results of the present study could explain the possible alteration in lingual kinetics in patients with DD. These data

may be particularly useful in guiding clinicians in the diagnosis of DD in a multidisciplinary context. Moreover, for clinical implications, it should be noted that a recent study suggested adjustments in clinical care when treating patients with DD, including providing dyslexia-friendly written information; avoiding asking patients to multi-task; and using the tell-show-do technique and distraction if anxiety is present.<sup>44</sup> To the best of our knowledge, only one other study has investigated the difference in malocclusion and orthodontic features between children with DD and healthy controls. This was a case-control study of Perillo et al.<sup>13</sup> where a group of 28 children with DD was compared to 51 sex- and age-matched healthy controls. Similar to our results, this study confirmed a higher prevalence of midline diastema and increased overbite and overjet in children with DD. The results of our study revealed a higher prevalence of Angles Class III malocclusion, midline diastema, midline discrepancy, and atypical swallow among pediatric patients with DD. Particularly for Class III malocclusion and atypical swallow, it is possible to speculate that in addition to an altered lingual kinetics, the cerebellum plays a role in balancing the external sensory input and motor commands. In other words, the cerebellum is responsible for translating sensory information into temporally relevant motor commands.<sup>45</sup> As a result of abnormalities in the functioning of the cerebellum in patients with dyslexia, the mechanism that causes the form to adapt to the function according to a precise pattern of automatisms and balances may be impaired. This could lead to difficulties in coordinating both jaws and lips during growth.

Contrary to our findings, the study by Perillo et al.<sup>13</sup> did not observe any statistically significant difference in the prevalence and type of dental malocclusion. These contradictory results may be due to the difference in the age range of participants included by Perillo et al.,<sup>13</sup> (age range: 7–10 years) from the present investigation (age range: 6–15 years). It is well known that the prevalence of malocclusion differs according to the age group analyzed and may progress over time. Another possible reason for the difference in results may be related to the difference in the specific geographic area from where the participants were recruited. It is established that the prevalence of malocclusion differs not only between different ethnicities but also according to the geographic area.<sup>46</sup>

Lastly, our study revealed a higher prevalence of parafunctional activities among children with DD, all of which were characterized by strong associations (Cramer's V between 0.461 and 0.754) and significantly high OR. Especially, self-reported nocturnal teeth grinding (OR = 58.143) and clinically visible wear facets (OR = 69.889) combined contribute to the proposed diagnosis of prob-

able sleep bruxism.<sup>38</sup> These findings are consistent with a high prevalence of sleep bruxism observed in children with attention deficit and hyperactivity disorder.<sup>47</sup> In addition to the higher prevalence of nail biting in children with DD, these findings tentatively point to an impaired control of movements, both voluntary and involuntary, and in automatism that leads the growing patient to assume a functional occlusion. Yet, this hypothesis is only speculative as the etiopathogenesis of sleep bruxism and other body-focused repetitive behavior disorders is multifactorial and far from being clear.<sup>48,49</sup>

### Strength and limitations

The strength of this study lies in an adequate power of the comparison between pediatric patients with DD and healthy controls. To ensure sufficient inferential statistics, a minimum sample size of  $n = 30$  per group was deemed necessary. The current study was able to recruit and compare  $n = 40$  participants per group, thus supporting the validity and reliability of our findings.<sup>50</sup> Another important strength of this study is that it provides valuable and novel insights into a potential relationship between malocclusion and psychological health, which is still an unexplored area. Moreover, this study is one of the few investigations in the scientific literature that investigates the orthodontic features that characterize a cohort of pediatric patients with DD, thus greatly contributing to this area of research.

Nevertheless, it is important to acknowledge the following limitations. The sample included in the analysis was derived from a pediatric population of a specific geographical area; as such, the results may not be generalizable to other ethnicities or any other geographical area. Although the two groups were similar in age and sex, the results presented in this study consisted of aggregated data. Therefore whether there was a difference between girls and boys or across different age groups cannot be inferred. Moreover, these findings reflect the data collected at one single timepoint, and did not show the progression of the observed results over time. The orthodontic analysis included only a clinical examination, with no radiographic exam; as such, it is possible that the two groups were also different in other orthodontic or dental parameters, which were not evaluated in the current study. Even though radiographic examination would have been important to provide skeletal descriptions, it should be noted that it is unethical to let patients undergo radiographic examinations for research purposes only; and analyzing only images of patients interested in undergoing orthodontic treatment after the initial evaluation would represent a major bias. Finally, although an altered lingual kinetics has been hypothesized in children with dyslexia the current study did not assess for tongue posture and function. Future studies

should include the assessment of lingual kinetics in this patient population to possibly elucidate the role of the tongue in relation to orthodontic parameters.

## CONCLUSIONS

Within its limitations, the present study provides evidence of a relationship between orthodontic parameters, dental malocclusion, and parafunctional habits with DD in pediatric patients. These results encourage a multidisciplinary approach involving speech therapists/neuropsychiatrists and pediatric dentists/orthodontists for early diagnosis, interception, and management of dyslexic difficulties.

## AUTHOR CONTRIBUTIONS

Conceptualization: AAB, PG. Data curation: GG. Formal analysis: LS. Investigation: FG, GG. Methodology: FG, AAB. Project administration: PG. Software: FG, LS. Supervision: PG. Validation: PG. Writing–original draft: FG. Writing–review & editing: AAB, LS.

## CONFLICTS OF INTEREST

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

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