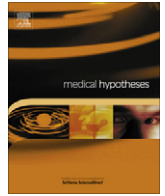


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# Understanding the relationships between breastfeeding, malocclusion, ADHD, sleep-disordered breathing and traumatic dental injuries

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### ABSTRACT

Attention-deficit/hyperactivity disorder (ADHD), one of the most common neuropsychiatric disorders that present at young age, may occasionally be associated with physical problems and disorders. Among them exists a group of oral-pharyngeal conditions with considerable clinical morbidity. Previous research that identified absence or short duration of breastfeeding in ADHD children has been reviewed. Essential nutritional factors in breast milk can affect brain development and regulate the manifestation of ADHD symptoms. Low ferritin levels caused by insufficient breastfeeding may contribute to ADHD susceptibility because of the role of iron in dopaminergic activity. Insufficient breast feeding and subsequently excessive bottle-feeding may lead to increased rates of non-nutritive sucking habits, such as pacifier use and thumb-sucking, all of which are associated with the risk of development of malocclusions. Malocclusion refers to an unacceptable deviation from the ideal relationship of the upper and lower teeth and necessitates orthodontic treatment. Sleep-disordered breathing in children may present with neurocognitive symptoms that resemble ADHD and abnormal craniofacial developments, as well as malocclusions, have been cited as part of the syndrome. Obesity, which is an outcome of insufficient breastfeeding, is a shared comorbidity of ADHD and sleep-disordered breathing. The risk of traumatic dental injury is higher in children with ADHD and presence of malocclusions further increases the likelihood of dental injuries.

In this review, certain oral-pharyngeal conditions relating to ADHD have been reviewed and links among them have been highlighted in a tentative explanatory model. More research that will provide increased awareness and clinical implications is needed.

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### Introduction

Most commonly presenting and diagnosed in childhood, attention-deficit/hyperactivity disorder (ADHD) is a lifelong neuropsychiatric disorder related to various clinically significant conditions. Based on the presentation of the core behavioral symptoms, which are inattention, hyperactivity and impulsivity, three sub-types of ADHD are identified according to the DSM-IV-TR: predominantly inattentive, predominantly hyperactive-impulsive, and a combined sub-type [1]. The onset of symptoms must be before the age of 7 years and impairment in two or more settings is required. About 3 to 8% of children population is affected and boys are more likely to be admitted to clinics than girls [2]. Since ADHD is associated with a high rate of coexisting developmental, psychiatric, genetic and medical disorders, an effective treatment program must be tailored to address all factors involved.

Research evidence has shown that there may be relationships between certain forms of oral-pharyngeal conditions and ADHD. However, although there is significant body of research, the find-

ings are scattered and remain to be integrated into a plausible model. This paper aims to review relevant topics, namely breastfeeding, iron deficiency, malocclusion, traumatic dental injuries and sleep-disordered breathing, from an ADHD perspective and to reach a better understanding of different pathologies involved.

### Breastfeeding and ADHD

There is no source of nutrition in early human life that is more crucial than human milk for the survival of the human being. The World Health Organization recommends initiating breastfeeding within the first hour of life, breastfeeding exclusively for the first 6 months and continuing breastfeeding (along with giving appropriate complementary foods) up to 2 years of age or beyond [3]. The benefits of breastfeeding are manifold, which include prevention of infant morbidity-mortality and chronic diseases, improvement of mental development, positive effects on maternal health and better economic costs, yet more remains to be explored.

A number of studies have focused on duration of breastfeeding in children with ADHD. In the study, which found low fatty acid concentrations in ADHD children, Stevens et al. [4] also noted absence or short duration of breastfeeding in the same subjects.

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Over the last decade, researchers from different parts of the world have devoted more attention to the topic. In 2003, researchers from Turkey reported that the duration of breastfeeding in ADHD children was not only shorter but it adversely affected intelligence scores as well [5]. Following that study, Kadziela-Olech and Piotrowska-Jastrzebska [6] demonstrated significantly shorter duration of breastfeeding in ADHD children than controls and also an increase in the rate of children who were breastfed less than 3 months in the ADHD group. In another study conducted on two prospective population-based birth cohorts in Spain, long-term breastfeeding was found to be associated with fewer attention and hyperactivity symptoms and an improvement in related behavioral areas [7]. Recently, concordant findings were reported in a large epidemiological study of Korean children [8]. To the best of my knowledge, there is no other study that either accepted or rejected an association between ADHD and short duration of breastfeeding. Taken as a whole, the studies cited above indicate a highly significant link between the topics reviewed.

As there is agreement that ADHD is best viewed as a gene–environment interaction [9,10], breastfeeding appears as one of the factors that regulate the course of the disorder. Therefore, several implications may be drawn ranging from prevention to treatment. For instance, preterm delivery may lead to both insufficient breastfeeding and ADHD symptoms in the child [11,12]. Based on the association demonstrated above, it is also worthwhile to go one step further and think about the impact of early-weaning adversities on ADHD.

### **Breastfeeding, iron deficiency and ADHD**

Since iron plays a central role in the regulation of dopaminergic activity which is implicated in neurobehavioral disorders, there are grounds to look into iron status in ADHD. A number of studies have described deficient iron levels in children with ADHD and suggested iron supplementation during treatment [13–16]. Although some aspects of this topic is still under debate, there is a need to review factors associated with both conditions.

It has been reported that, among children in the developing world, iron is the most common single-nutrient deficiency and can have long-lasting detrimental effects [17]. There is general agreement that exclusive breastfeeding until age 6 months and continuation of breastfeeding after this age, combined with complementary feeding may provide sufficient iron stores to infants [18–20]. Early weaning is associated with early introduction of cow's milk which contributes to iron deficiency by preventing intake of adequate iron-rich foods and increasing gastrointestinal blood loss [21,22].

Although adverse developmental impact of iron deficiency in infancy on central nervous system has been noted by some authors and precautions have been made about the continuity of the effects, a particular emphasis on ADHD does not exist. Based on the research evidence it comes out that, children with ADHD, who have a history of absence or short duration of breastfeeding, might also be at risk for iron-deficiency. Furthermore, a causative role of iron deficiency for ADHD symptoms may be considered in those children. Definitely, more research is needed to identify the interrelatedness of the factors involved.

### **Relationship between duration of breastfeeding, bottle-feeding, non-nutritive sucking habits and development of malocclusions**

Besides the positive aspects mentioned above, breastfeeding has been cited as one of the environmental factors leading to the correct development of dentofacial structures [23,24]. Absence or

short duration of breastfeeding consequently results in longer duration of bottle-feeding which may negatively affect children's oral-facial development [25–27]. Malocclusion, an unacceptable deviation either and/or functionally from the ideal relationship of the upper and lower teeth, is one of the adverse outcomes [28]. Qualitative and quantitative classifications of malocclusion have been developed and many forms require costly and time-consuming orthodontic treatments. Bottle-feeding, even partial, was reported to be associated with changes in certain dimensions of the maxillary dental arch and in inter-arch relationships [29]. In addition to dental malocclusion, bottle-feeding was found to contribute to development of a dolichocephalic Steiner mandibular plane, while breast-fed children displayed a brachycephalic mandible arch [30].

Furthermore, the dyad of insufficient duration of breastfeeding and longer duration of bottle-feeding is significantly linked to non-nutritive sucking habits (NNSH) which refer to another group of factors leading to malocclusion of teeth. NNSH are mentioned when children satisfy their instinctive sucking urge with prolonged use of pacifiers or by sucking their thumbs [31]. Montaldo et al. [32] reported that children with bottle or complementary feeding showed a higher risk of acquiring NNSH after the first year of life which is associated with a greater risk of crossbite, open bite, Class II molar relationship.

Since some children with ADHD have insufficient duration of breastfeeding, there is ground to expect higher rates of dentofacial problems in those children. In a study conducted by Atmetilla et al. [33] although no statistically significant difference was found in relation to occlusal problems in ADHD children, the presence of a different pattern of facial biotype was noted. Following this, Katz-Sagi et al. [34] reported no statistical difference in occlusal relationship between ADHD and control groups. However, emphasizing the importance of awareness of such conditions, a recent study described an abnormal orofacial pattern in ADHD children and more common high arched palate, especially in combined sub-type [35]. In case a child with ADHD has malocclusion, the course of orthodontic treatment is more challenging than a typically developing child which indicates an independent factor for higher prevalences because of the relative increase of uncorrected cases [36]. Definitely more research is needed to fill the gap of knowledge in this field. Malocclusions are further associated with a group of oral-pharyngeal pathologies some of which have aspects relating to ADHD pathogenesis. For this reason, we again need to take steps forward and explore the issues related.

### **Relationship between malocclusion, sleep-disordered breathing and ADHD**

Sleep-disordered breathing (SDB) in children is a common and serious problem associated with significant morbidity. The spectrum of obstructive SDB may range from habitual snoring to partial or complete airway obstruction, termed obstructive sleep apnea (OSA) [37]. Symptoms may be either nocturnal, such as snoring, observed apnoeas, restless sleep, diaphoresis and enuresis, or diurnal, such as daytime sleepiness, academic problems, headaches and mouth breathing. The physical examination may be normal or may reveal failure to thrive, obesity, enlarged tonsils, adenoid face and hyponasal speech [38]. Questionnaires and scales, home monitoring, and polysomnography (PSG) are among the diagnostic tools used to confirm SDB in children and PSG is accepted as a gold standard evaluation method [38,39]. Although tonsillectomy and adenoidectomy remains the most commonly recommended treatment for pediatric patients with OSA, cautions have been made to define the role of nonsurgical treatments such as nasal continuous positive airway pressure, anti-inflammatory agents, and oral

appliances [40,41]. Controversies still exist regarding diagnosis, evaluation and treatment in the field of SDB which warrant more research.

Abnormal craniofacial development is reported as one of the causes of OSA syndrome [42]. The craniofacial characteristics of OSA patients have been specified as follows: short anterior cranial base, less obtuse cranial base flexure angle, retro positioned mandible, small mandible, small maxilla, steep mandibular plane, long soft palate, decreased airway space, lowered position of hyoid bone and increased anterior facial height [42]. In regard to occlusion, previous research has identified important features. In a study by Cazzolla et al. [43] a statistically significant association between snoring, cross-bite, open-bite and increased over-jet was found in a cohort of 495 school-aged children. A longitudinal study tracking the development of sleep disordered breathing and malocclusion found that cross-bites as well as narrower dental arches were more common among snoring children than non-snoring children, at 4, 6 and 12 years [44]. These findings indicate early-onset nature of malocclusions and the continuity of problem from primary to permanent teeth in SDB. Class II malocclusion was reported to be also more common in a sample of adult OSA patients [45]. Moreover, Miyao et al. [46] argued that as overjet was closely linked to the severity of SDB in adult non-obese patients, malocclusion plays a key role in the development of OSA. In regard to treatment, correction of mandibular retrognathism was found to increase airway space and improve nocturnal breathing in a group of adolescents [47].

Besides several positive effects on health, sufficient duration of breastfeeding has been shown to be associated with a decreased risk of habitual snoring in school-aged children [48]. In a PSG study of children with habitual snoring, those who had been breastfed for at least 2 months were found to have significantly reduced SDB severity on every measure assessed, including apnea-hypopnea index, oxyhemoglobin desaturation nadir, and respiratory arousal index [49]. On the other hand, the same study revealed that breastfeeding for longer than 5 months did not contribute additional benefits. In an interesting study that examined the relationship between breastfeeding, breathing pattern and deleterious oral habits, mouth breathing children not only had a short duration of breastfeeding, but they had significantly more frequent deleterious oral habits compared to nose breathers, as well [50]. This gives support to the view that seemingly different behaviors may be linked to contribute to pathology.

A significant body of research indicates that SDB is associated with neurocognitive impairment, particularly ADHD and learning disorders. In 2002, Chervin et al. [51] reported that inattention and hyperactivity among general pediatric patients are associated with increased daytime sleepiness and – especially in young boys – snoring and other symptoms of SDB. This was followed by another report of a 4-year long prospective cohort study that untreated snoring and sleep disordered breathing are strong risk factors for future emergence or exacerbation of hyperactive behavior [52]. In support of these findings, O'Brien et al. [53] showed that SDB in children can lead to mild ADHD-like behaviors that can be readily misperceived and potentially delay the diagnosis and appropriate treatment. A meta-analysis of 16 sleep studies indicated that children with ADHD had significantly higher night awakenings, sleep disordered breathing and daytime sleepiness compared with the controls [54]. As an objective measure, the apnea-hypopnea index was also significantly higher in ADHD children [54]. There is also PSG evidence that adults who have persistent symptoms of ADHD are more likely to have SDB and sleep fragmentation [55].

The mechanism through which SDB produces ADHD-like symptoms is postulated to be the impact of SDB specifically on “executive functions”, which include cognitive flexibility, task initiation, self-monitoring, planning, organization, and self-regulation of

affect and arousal [56]. In children with SDB who underwent PSG and neurocognitive assessment, increased arousal during sleep was described as a defensive mechanism that may preserve cognitive function by counteracting the respiratory events, at the expense of sleep maintenance and further, ADHD-like symptoms [57].

With regard to treatment effects, significant improvements on behavior after adenotonsillectomy have been reported by researchers. Using a screening questionnaire, Weber and colleagues [58] compared the impact of adenotonsillectomy on the domains of inattention, hyperactivity and impulsivity, and found significant improvements in particular in children aged 8 to 10. In a similar comparison study involving children who underwent adenotonsillectomy, the apnea-hypopnea index in PSG, attentional scores and 8 of 9 individual domains of the Child Behavior Checklist scores were found to have improved after surgery [59]. Likewise, on the Conner's Parent Rating Scale and Pediatric Sleep Questionnaire, 71 children diagnosed as having SDB were reported to have improved in both sleep and behavior after adenotonsillectomy [60]. Beyond the use of psychometric questionnaires and scales, children with clinically confirmed diagnosis of ADHD and comorbid SDB were compared for the effects of methylphenidate treatment and adenotonsillectomy [61]. Children who underwent surgery not only had lower post-surgery ADHD ratings, but they were also significantly better than the children who received only methylphenidate treatment and who had no treatment.

#### **Relationship between duration of breastfeeding, ADHD, SDB and obesity**

Another dimension worth mentioning is the protective effect of breastfeeding on obesity and related health problems, as revealed by previous research [62–64]. There is also evidence that comorbidity exists between ADHD and obesity [65,66]. SDB appears to be one of the mechanisms that mediate the comorbidity between ADHD and obesity [67,68].

#### **Relationship between traumatic dental injuries, ADHD and malocclusion**

Traumatic dental injuries (TDI) constitute a prevalent and serious health problem among children worldwide. Previous epidemiological and hospital-based studies revealed that one third of all preschool children and one fourth of all school children may suffer from dental trauma [69]. Anterior teeth fractures, which account for the majority of cases, lead to both functional, aesthetic and emotional consequences [70]. Complications that may arise include tooth discoloration, loss of vitality, root resorption and/or abscess formation [71]. Falls and collisions during sports and games are the major causes of TDIs [72]. Among the structural determinants considered, incisor overjet of more than 3 mm and incompetent lips were described as significant factors predisposing to dental trauma [73]. The estimated cost of TDIs ranged from US\$2–5 million per million inhabitants per year irrespective of age [74].

It is the Health Survey for England 1997 that provided the initial data regarding the association between hyperactivity as a symptom and major injuries affecting face and/or teeth [75]. Soon after this, Sabuncuoglu et al. [76] compared the frequency of TDIs among children with ADHD and non-ADHD diagnoses and found a significant association between TDIs and ADHD. This laid the ground for the proposal of an explanatory model for TDIs. Sabuncuoglu also reviewed previous studies in the field of dental traumatology which provided indirect evidence of ADHD [72]. Since

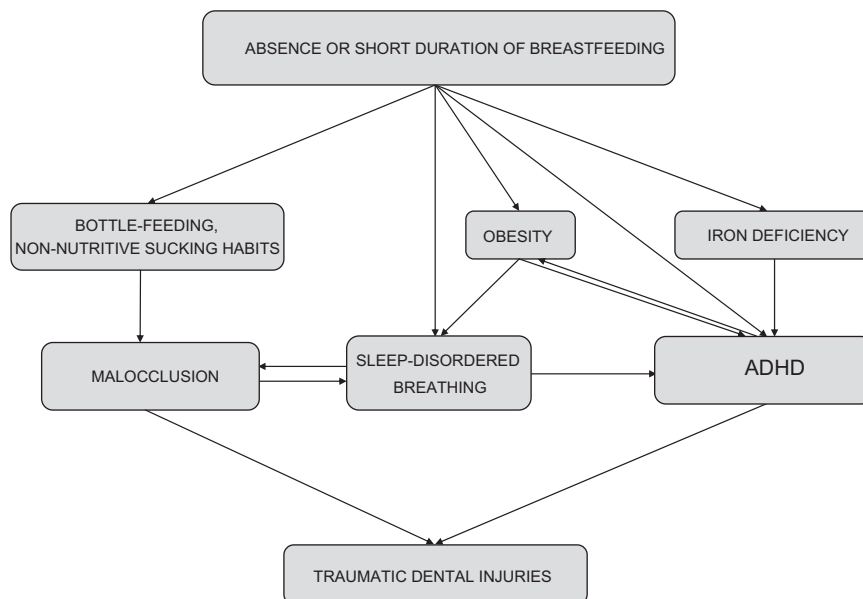


Fig. 1. Summary chart for the relationships between certain oral-pharyngeal conditions and ADHD symptoms.

then, controlled studies from different parts of the world have confirmed the link between ADHD and TDIs [34,77,78].

It is important to emphasize that incisor overjet, which is a structural predisposing factor for TDIs, is a form of malocclusion as highlighted in relation to various factors in the sub-section of this review. It is highly possible that ADHD, besides behavioral risk factors it poses, may also have a role in the occurrences of dental injuries through the structural risk factor it may be related to. Several developmental mechanisms that may link ADHD and malocclusions have been pointed out in this review. As pointed above, children with combined sub-type of ADHD, which is the most common sub-type, are more likely to present with high arched palate [35]. Prevalences of malocclusions and in particular, overjet are high in the general child population [79–81]. Despite the fact that we need more data regarding the association between malocclusions and ADHD, projected general population rates enable us to estimate that a significant percentage of ADHD children may be affected by malocclusions. To put it brief, malocclusion in a child with ADHD may not be simply a dental anomaly unrelated to the pathogenesis of ADHD.

The relationships between the factors highlighted in this article are shown in Fig. 1, which enables to grasp the complexity of the model at a glance.

## Discussion

In this review, relationships and causality between symptoms of ADHD and certain oral-pharyngeal conditions have been investigated. A multidisciplinary approach has been employed which connects work from different disciplines such as pediatrics, child and adolescent psychiatry, otorhinolaryngology, pediatric dentistry, orthodontics and endodontics. At the beginning of the article, studies reporting an association between ADHD and insufficient breastfeeding duration has been highlighted and the need to understand the possible consequences of this finding has been underlined (Fig. 1). Early weaning leads to increased use of cow's milk which is thought to be a cause of early-life iron deficiency. Mentioning the role of iron in the pathogenesis of ADHD, this mechanism may be postulated as one of the factors that may affect the manifestation of ADHD. Absence or short duration of breastfeeding is highly associated with longer duration of bottle-

feeding and higher frequency of non-nutritive sucking habits all of which lead to development of malocclusions. Although malocclusion seems to be an expected outcome in children with ADHD, there's only few research in the literature. In this review, studies reporting a high degree of correlation between SDB and malocclusion have also been cited. Furthermore, this point of evidence has been linked to the high rates of SDB in children with ADHD. In addition to this, research evidence suggesting an association between insufficient duration of breastfeeding and mouth breathing has been underlined. Obesity, which is related to insufficient breastfeeding, has been highlighted as a shared comorbidity of ADHD and SDB. As a further point of interest, previous work reporting a relationship between ADHD and TDIs has been reviewed. Having described incisor overjet as a form of malocclusion and a well-established risk factor for TDIs, how insufficient breastfeeding may relate to the development of both overjet and ADHD symptoms has been explained.

To the best of my knowledge, this is the first attempt to bring together existing studies and knowledge on various aspects of oral-pharyngeal conditions in a framework relating to ADHD. Besides the genetic explanation of ADHD, a parallel environmental model has been proposed based on previous research findings. It is very remarkable to see that how an early life experience, namely breastfeeding, may impact long-term mental and physical well-being.

For the professionals who are in clinical work with ADHD children, it is not uncommon to see children who have clinical features highlighted in this article. An important question worth raising is whether this complicated ADHD presentation constitutes a subtype. Definitely more research is needed for a thorough understanding of the topics reviewed and subsequent clinical implications for the betterment of children who are in need.

## Conflict of interest statement

None.

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