Original Hypothesis

Attention-Deficit/Hyperactivity Disorder Symptoms can be Reduced by Effectively Treating Obstructive Sleep Apnea with Oral Appliances: A Hypothesis

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Abstract

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in children and can persist until adulthood. This disorder negatively affects almost all personal, academic, and work fields and often strains parent-child relationships. On the other hand, obstructive sleep apnea (OSA) is characterized by episodes of partial or complete obstruction of the upper airway during sleep. Some studies have suggested an association between OSA and ADHD in children and adults. **The Hypothesis:** It has been suggested that therapeutic intervention in OSA has a significant improvement in abnormal behaviors such as hyperactivity, inattention, and aggression, and in cognitive and school performance. OSA can lead to ADHD-like symptoms that disappear when OSA is sufficiently treated. The use of oral appliance therapy (OAT) is being studied as a method to control OSA. We hypothesize that the management of OSA with OAT could reduce ADHD symptoms. **Evaluation of the Hypothesis:** In patients who present with OSA and ADHD simultaneously, it should be evaluated whether the treatment of OSA with the use of OAT as rapid maxillary expansion devices or oral mandibular advancement devices reduces the symptoms of both OSA and ADHD, which would allow the establishment of an alternative method of treatment for both pathologies that is less invasive and less expensive.

Keywords: Attention deficit hyperactivity disorder, obstructive sleep apnea, oral appliances

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed neurodevelopmental disorder that affects 8%–12% of children and adolescents, and 2.5% of adults worldwide.[1] It was previously thought that ADHD in children subsides with growth and maturation; however, recent studies have suggested that up to 65% of adults continue to have ADHD symptoms and neuropsychological impairments.[1,2] Three ADHD subtypes have been defined: predominantly inattentive (attention-deficient), predominantly hyperactive-impulsive, and combined.[3] This disorder may impact several aspects of an individual's life, manifesting as academic and social interactions difficulties, and strained parent-child relationships.[3]

The etiology of ADHD is multifactorial. In most cases, it arises from several genetic and environmental risk factors that act independently or synergistically.[4] The diagnosis of ADHD is mainly based on the criteria established in the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM) and the 10th revision of the International Classification of Diseases of the World Health Organization (CIE-10). The DSM and CIE-10 reflect the consensus of experts and extensive research to achieve a better categorization of disorders that do not have a

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biological marker.[5] Both documents cite the same diagnostic criteria for adults and children. However, the predominant features of ADHD in adults differ from those in children, with adults showing less hyperactivity or impulsivity and more inattentive symptoms.[6]

The ADHD diagnostic criteria include three cardinal symptoms under two domains: inattention and hyperactivity/impulsiveness. The diagnosis of ADHD requires at least six of the nine symptoms in each domain or a combination of both[7] and the behaviors must be severe and disproportionate.[8]

To establish a definitive diagnosis, it is necessary to explore other comorbidities, such as learning disorders, tics, anxiety, mood disorders, and autism spectrum disorders.[9]

Furthermore, standard treatment modalities for ADHD in children include medications, behavioral therapy, counseling, and educational services. While these may relieve many symptoms of ADHD, they fail to cure it. Currently, stimulant medications are most prescribed to treat ADHD.[10,11] These medications effectively improve the signs and symptoms of inattention and hyperactivity within a short period. However, treatment responses vary widely in terms of the types of pharmacotherapy and corresponding dosages, tolerability, response rates, and adverse-event profiles.[1]

Association Between ADHD and Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is defined as a breathing disorder during sleep, characterized by prolonged partial airway obstruction, and/or intermittent complete obstruction that interrupts normal ventilation during sleep.[12]

This condition develops because the muscles cannot maintain their tone under the negative pressure generated during inspiration. A narrow airway usually does not result in symptoms during wakefulness but it can become constricted further during sleep when the muscle tone declines, thereby producing occlusion and apnea.[13] Children with this disorder can present a wide range of symptoms and clinical manifestations, such as mild snoring or severe OSA episodes.[13] OSA's most important predisposing factors in children are hypertrophy of the tonsils and adenoids and neuromuscular diseases that favor the loss of pharyngeal muscle tone. Additionally, congenital craniofacial malformations involving shortening of the neck, retrognathia, small chin, nasal obstruction, and obesity are other contributory factors.[13] A complete medical history and polysomnography are crucial for OSA diagnosis.[14]

OSA's treatment modalities may be surgical, such as adenotonsillectomy maxilla-mandibular advancements, soft tissue surgeries, tracheostomies, or medical, such as the use of continuous positive airway pressure (CPAP) or nasal devices and myofunctional therapy.[15] In adults with midfacial hypoplasia and/or micro- retrognathia, reconstructive surgeries can be considered.[14]

The relationships between OSA and ADHD are complex, multidirectional, and multifactorial. Some studies have suggested an association between OSA and ADHD in children and adults.[16,17] It has been reported that the prevalence of sleep disturbances in individuals with ADHD range from 25% to 55% in children and 50% to 80% in adults.[18] However, it is not known whether sleep disorder is a cause for ADHD or a comorbid disorder. Some studies suggested that sleep disorders might be one of the underlying causes of ADHD[19] and others found a positive association between OSA and ADHD.[20,21]

It is possible that some ADHD-like features in children with OSA may result from repeated sleep disruptions and intermittent hypoxic episodes that affect prefrontal executive functions such as working memory, behavioral control, analysis, organization, and self-regulation of motivation, and other functions such as regulation of arousal, sleep, affect, and attention.[12]

It has been suggested that therapeutic interventions for OSA, such as adenoidectomy and/or tonsillectomy, significantly improve both abnormal behaviors, such as hyperactivity and aggression and cognitive capabilities.[12,21] OSA can lead to ADHD-like symptoms that could disappear when OSA is treated effectively.[22] Hence, parallel diagnoses and effective interventions must be performed to control or eliminate the symptoms associated with both pathologies.

The Hypothesis

Previous studies have shown a close relationship between OSA and ADHD, but whether some OSA characteristics induce ADHD is still poorly understood. The incidence of ADHD is higher than 25%–50% in children with OSA and increases with age, which may be related to OSA's long course and more significant influence on brain function.[23,24] Given that an association between OSA and ADHD has been previously reported, and since OSA can be effectively treated in some patients using oral appliances, we hypothesize that the use of oral appliances therapy (OAT) could reduce the ADHD symptoms associated with the presence of OSA in these patients [Figure 1].

This hypothesis stems from the evidence that obstruction of nasal airflow induces functional changes in the nasomaxillary complex and the mandible.[26]

Following these results and considering that routine procedures for OSA treatment, such as adenotonsillectomy, are insufficient to resolve all the symptoms, additional therapy using OAT has been used in both children and adults. Among the OAT devices used for OSA treatment, oral mandibular advancement devices (MADs) mechanically protrude the mandible to prevent the upper airway's collapse. The other main class of oral appliances includes tongue-retaining devices and appliances for rapid maxillary expansion (RME) in children, which increase the transverse dimensions of the maxilla, widen the nasal

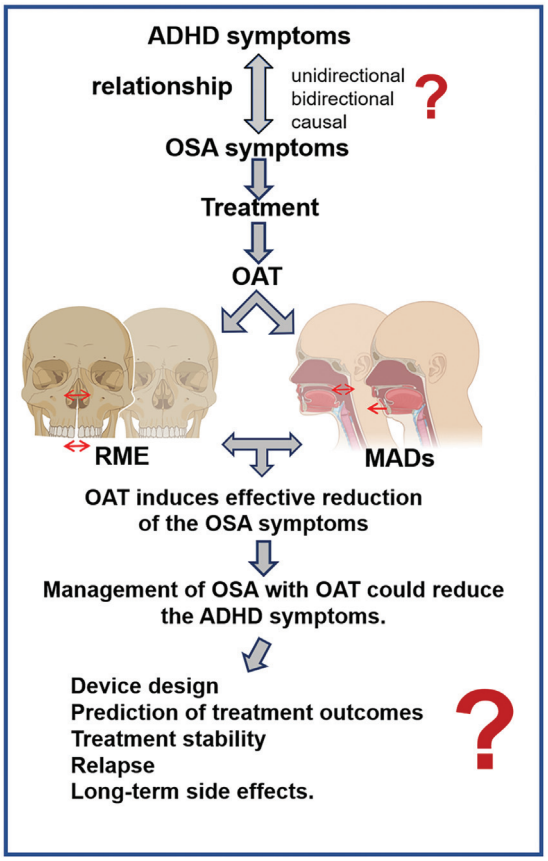

Figure 1: Flowchart showing the hypothesis and unanswered questions: The symptoms of ADHD are related to the presence of OSA; however, it is not clear if this relationship is uni-or bidirectional or causal. For the treatment of OSA, OATs have been used as devices for RME and MADs that effectively reduce symptoms, so we hypothesized that the effective treatment of OSA also reduces the associated symptoms of ADHD. To verify this, questions such as the influence of device design, the need for prediction of treatment outcomes, treatment stability, relapse, and long-term side effects must be considered

cavity, showing improvement in apnea-hypopnea index (AHI), especially in the short term (<3 years of follow-up).[25,27]

OAT offers a noninvasive method by using intraoral devices in patients suffering from OSA and snoring. These appliances are worn during sleep and are used in OSA patients, particularly those with additional structural defects, such as retrognathia, micrognathia, cleft palate, and facial dysplasia.[28] For the American Academy of Sleep Medicine, OAT is an alternative to CPAP for all OSA patients' treatment.[29] Although, CPAP is an effective treatment, there is a need for other modalities because CPAP's clinical effectiveness is often limited by low patient acceptance and tolerance, and suboptimal compliance.[30] Additionally, more recent investigations demonstrating incomplete resolution of abnormal oropharyngeal growth by adenotonsillectomy have led to the use of orthodontic appliances to help treat sleep-disordered breathing. [31] These findings suggest that OSA's effective treatment with OAT may jointly reduce the symptoms of ADHD due to the previously established relationship between these two pathologies.

Evaluation of the Hypothesis

MADs are the most common oral appliances used for the treatment of OSA. They improved the AHI and OSA symptoms in 92% of the patients.[32] However, RME devices have also been shown to induce a reduction of symptoms in individuals with OSA by early treatment.[25] Hence, based on their efficacy, they would be ideal devices for evaluating this hypothesis.

Treatment of OSA with an oral appliance requires a multidisciplinary approach involving a dental practitioner and a sleep expert physician. Initially, a medical assessment should be performed to confirm the OSA diagnosis, the severity of the condition, and decide whether OAT is the treatment of choice. Polysomnography should be performed as a part of the evaluation, and the AHI must be determined by measuring the mean number of apneas and hypopneas during sleep. According to the AHI system, OSA can be classified as mild (AHI 5–15), moderate (AHI 16–30), or severe (AHI > 30).[33] A dental assessment should follow, along with the selection and fitting of the device. It is essential to consider the severity of OSA because some studies do not recommend OAT for individuals with severe OSA, and in general, there are limited indications of OAT for such patients.[34] However, patients with less severe forms of OSA, who are intolerant to CPAP or surgery, require alternative therapies that must be evaluated. In addition to the OSA diagnosis, patients must have a positive diagnosis of ADHD based on the criteria established in the DSM-5 and CIE-10.

Custom-made appliances should be used, and the degree of mandibular advancement or maxillary expansion should be determined individually for each patient.

To assess the outcome of OAT's efficiency in OSA reduction, follow-up polysomnography should be performed, along with patient interviews, to understand subjective outcomes regarding the quality of life, daytime sleepiness, and compliance. For the same patients, changes in ADHD induced by OAT should be evaluated, and it should be determined whether these changes were associated with a reduction in OSA symptoms through two commonly used diagnostic criteria established in DSM-5 and CIE-10.

According to the DSM-5 criteria, six (or more) symptoms of each subtype are required to diagnose a child, while for older adolescents and adults (over 17 years of age), the presence of at least five symptoms is required. The symptoms should persist for at least 6 months, with a severity that surpasses the child's development level and should compromise social, academic, and professional activities. These criteria are widely used and are evaluated using the following tests: the SNAP-IV, BAARS-IV, ADHD assess scale-IV, and

Kiddie-Sads-actuality and Life Version.[34] The DSM-5 does not allow for diagnosis in patients <12 years of age. According to the CIE-10 criteria, children must present at least six inattention symptoms, three of hyperactivity, and one of impulsiveness, to be diagnosed with a hyperkinetic disorder or ADHD. However, the number of symptoms required to make a diagnosis is not dependent on age in the case of CIE-10. Like DSM-5, CIE-10 requires that these symptoms have been present for at least six months to a degree incompatible with the typical level of development at that age and cause problems in more than one life situation of the patient. CIE-10 does not allow for diagnosis in patients younger than 7 years of age.[5] Changes in symptoms should be evaluated periodically to monitor changes in the condition. The study's follow-up period should be a minimum of 12 months after regular nighttime use of MADs or RMEs. The recommended period of device use or follow-up after treatment has not been reported in the literature. However, patients need to undergo OAT for an extended period until OSA symptoms and possibly ADHD decrease. To determine OAT's effectiveness, it would be of interest to quantitatively evaluate the anatomical changes at the level of the oropharynx that may be induced over time in patients using this type of device. Said changes might favor the permeability of the upper pathways and contribute to reducing or eliminating the need for other OSA treatment modalities.

OAT contributes to a significant reduction in AHI and the symptoms in OSA patients and could, in turn, reduce the symptoms associated with ADHD in these patients, resulting in a previously unexplored improvement.

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Conflicts of interest

There are no conflicts of interest.

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