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Review

Benefits of Treating Obstructive Sleep Apnea in Cognition: Systematic Literature Review

Júlia Montalvão Neves [1,*], Cátia Andreia Maciel [1] and Pedro Alexandre-Sousa [1,2]

[1] Local Health Unit of Leiria's Region, 2400 Leiria, Portugal; camaciel@ulsrl.min-saude.pt (C.A.M.); pesousa@ulsrl.min-saude.pt (P.A.-S.)
[2] Center for Innovative Care and Health Technology (ciTechCare), 2400 Leiria, Portugal
* Correspondence: jsneves@ulsrl.min-saude.pt

Abstract: Introduction: Obstructive sleep apnea syndrome (OSAS) is characterized by intermittent hypoxia, sleep fragmentation, daytime sleepiness, cognitive impairment, and brain cell damage due to brain blood flow reduction, with ischemic damage, increased microvascular reactivity, and brain tissue damage. OSAS is strongly linked to chronic, neurodegenerative, and inflammatory cerebrovascular disease and cognitive impairment. Continuous positive airway pressure (CPAP) is the first-line treatment for OSAS. Objective: This article aims to evaluate the effect of CPAP treatment on neurocognitive performance in OSAS patients with mild cognitive impairment or dementia by reviewing the literature. Methods: We performed a comprehensive review of the Portuguese and English languages without a time limit using the following Mesh terms: dementia, mild cognitive impairment, obstructive sleep apnea, and CPAP. We included randomized controlled trials (RCTs), meta-analyses, and systematic reviews (SRs) where the impact of CPAP on neurocognitive performance was addressed. Results: Five SRs and three RCTs reported significant improvements in neurocognitive performance, especially in verbal, visuospatial, and working memory. Conclusion: CPAP treatment seems to improve cognitive defects associated with OSA.

Keywords: obstructive sleep apnea; cognitive impairment; continuous positive airway pressure

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1. Introduction

Obstructive sleep apnea syndrome (OSAS) is the most common primary sleep disorder in older adults [1], and it is characterized by repetitive episodes of complete or partial collapse of the upper airways during sleep, causing obstruction, chronic intermittent hypoxia, sleep fragmentation, and daytime sleepiness [2].

OSAS is a risk factor not only in several diseases, both in young and older adults, such as hypertension, diabetes, metabolic syndrome, and stroke, but also in cognitive disorders [3], including dementia and Alzheimer's Disease (AD), which has been linked to neuroinflammation [4], intermittent hypoxemia, reduced sleep quality and continuity, and hypercapnia disruption of the hypothalamic–pituitary–adrenal axis mechanisms [5]. Chronic sleep deprivation might also be associated with increased toxic products that induce neurodegeneration. Asthma is another common respiratory disorder that may complicate the clinical course of OSAS, as the pathology and its treatment may increase the collapsibility of the upper airways, contributing to the development and worsening of OSAS. On the other hand, OSAS modifies asthmatic airway inflammation, worsening asthma symptoms and the frequency of exacerbations [6]. The coexistence of both disorders is common as they are highly prevalent and share genetic background and risk factors, such as allergic rhinitis, gastroesophageal reflux disease, and obesity [6].

Due to brain blood flow reduction, which results in ischemic damage, increased microvascular reactivity, and brain tissue damage, OSAS is strongly linked with chronic cerebrovascular, neurodegenerative, and inflammatory disease and cognitive impairment, affecting attention, executive functioning, motor efficiency, working memory, and long-term episodic memory [5].

Continuous positive airway pressure (CPAP), the gold-standard treatment for OSAS, can improve both OSAS and asthma control in patients suffering from both diseases by preventing episodes of upper airway collapse and maintaining a continuous airflow [7,8].

Furthermore, evidence suggests CPAP might have a positive influence on cognitive performance both in young and cognitively impaired patients and improve daily function providing greater independence, quality of life, lower caregiver burden, and need for medical assistance or social support [9]. This association would have a broad impact regarding these patients' quality of life.

With this comprehensive review, we aim to evaluate the existing evidence of CPAP's impact on cognitive function improvement and the prevention of cognitive impairment in OSAS patients with mild cognitive impairment or dementia.

2. Materials and Methods

The present systematic literature review protocol was guided according to the methodological guidelines proposed by the Joanne Briggs Institute (JBI) [10] and registered at PROSPERO with the ID CRD42024622192. We considered the PI(C)O (Population, Intervention, Comparison, and Outcome) framework to formulate the research question [11]: Population—OSAS patients, only adults, diagnosed with mild cognitive impairment or dementia; Intervention—CPAP; Comparison—placebo or CPAP with a low-adherence therapeutic regimen; Outcome—improved neurocognitive performance. In this sense, this review aims to answer the research question: what are the benefits of treating OSAS (I) patients (P) in their cognition (O)?

The literature search was carried out on the electronic PUBMED, Cochrane Library, and NICE evidence databases in July 2024 without a time limit. We used the Medical Subject Heading (MeSH) terms "dementia", "mild cognitive impairment", "obstructive sleep apnea", and "CPAP" and the booleans "AND" and "OR". The inclusion and exclusion criteria adopted are presented in Table 1.

Table 1. Inclusion and exclusion criteria.

	Criteria Code	Description
Inclusion Criteria	IC1	Randomized control trial, systematic review or meta-analysis;
	IC2	The studies included patients with mild cognitive impairment or dementia undergoing treatment for OSAS;
	IC3	SAOS treatment must have an effect in cognition.
Exclusion criteria	EC1	Case reports, editorials, letters to the editor, and clinical trials without a control group;
	EC2	Articles in languages other than Portuguese or English;
	EC3	Full text not available even after contacting the author;
	EC4	The article does not address SAOS and cognition;
	EC5	Does not meet minimum methological quality.

Articles published in Portuguese and English were considered, with no time limit.

All identified citations were uploaded into Zotero 6.0.37 for MacOS, and duplicates were removed. Afterward, titles and abstracts were screened by two independent reviewers for assessment against the inclusion criteria for the review.

The full text of the selected studies was assessed in detail by two independent reviewers, including the quality, quantity, and consistency of evidence using the SORT (Strength of Recommendation Taxonomy) scale [12].

The results of the inclusion process are presented as a PRISMA flow diagram [13] in Figure 1.

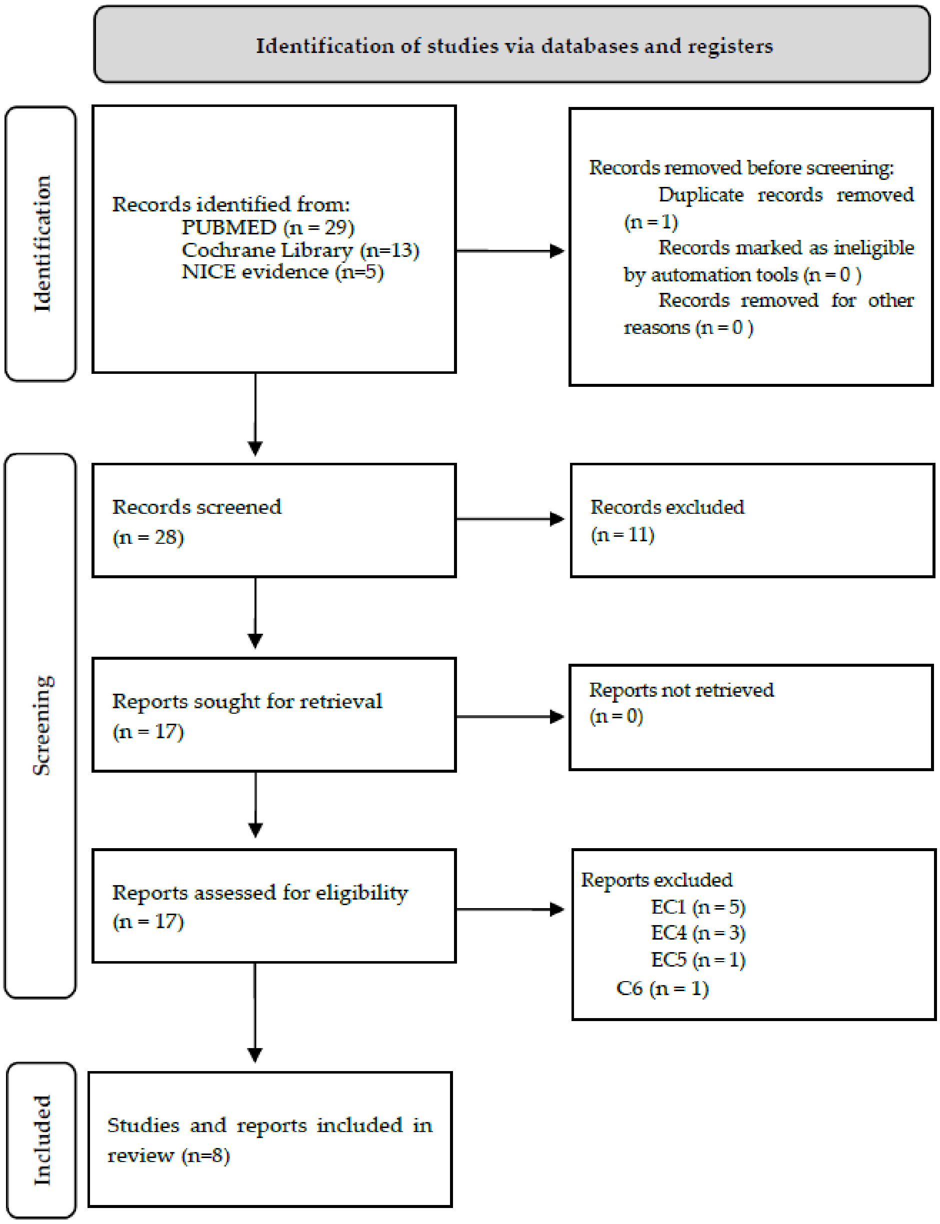

Figure 1. Preferred reporting items for systematic reviews and meta-analysis diagrams.

The articles included in the present review were summarized and presented in a table prepared by the authors.

3. Results

Of the eight selected articles, five were reviews, two were clinical trials, and one was a secondary analysis of a clinical trial. All the articles are from Europe and the United States of America. Table 2 summarizes the data collected from each article, including objectives, participants, evidence level, and key findings regarding our research.

Table 2. Presentation of the studies included in the review.

Authors and Year	Title	Country	Aims/Purpose	Population and Sample Size	Type of Study/Evidence Level	Outcomes
Ancoli-Israel et al. (2008) [14]	Cognitive Effects of Treating Obstructive Sleep Apnea in Alzheimer's Disease: A Randomized Controlled Study	United States of America	To examine whether treatment of OSAS with CPAP in patients with AD would result in improved cognitive function.	52 participants with mild–moderate AD and OSAS	Randomized double-blind placebo-controlled trial	OSAS * may aggravate cognitive dysfunction in dementia and thus may be a reversible cause of cognitive loss in AD* patients. OSAS treatment seems to improve some of the cognitive functioning. post-hoc examination of change scores for individual tests suggested improvements in episodic verbal learning and memory and some aspects of executive functioning such as cognitive flexibility, and mental processing speed. Clinicians who care for these patients should consider implementing CPAP* treatment when OSAS is present.
Richards et al. (2019) [15]	CPAP Adherence May Slow 1-Year Cognitive Decline in Older Adults with Mild Cognitive Impairment and Apnea	United States of America	To determine whether CPAP treatment adherence predicts cognitive and everyday function after 1 year in older adults with MCI and to determine effect sizes for a larger trial.	54 older adults with MCI (MCI + CPAP, n = 29; and MCI–CPAP, n = 25)	Quasi-experimental pilot clinical trial	Statistically significant improvements in psychomotor/cognitive processing speed in the MCI * + CPAP group versus the MCI* − CPAP group were observed at 1 year. There were small to moderate effect sizes for memory, attention, daytime sleepiness, and everyday function favoring the MCI + CPAP.
Bubu et al. (2020) [16]	Obstructive sleep apnea, cognition and Alzheimer's disease: A systematic review integrating three decades of multidisciplinary research	United States of America	To examine OSAS and cognition, MCI and AD, including the effects of CPAP treatment.	-	Systematic literature review	In middle-aged adults, OSAS is often associated with mild impairment in attention, memory, and executive function. In older adults, OSA is not associated with any particular pattern of cognitive impairment at cross-section. OSA is associated with the development of MCI or AD with symptomatic patients who have a higher likelihood of associated disturbed sleep/cognitive impairment. CPAP treatment may be effective in improving cognition in OSAS patients with AD.
Siachpazidou et al. (2020) [17]	Alzheimer's Disease in Patients with Obstructive Sleep Apnea Syndrome	Greece	To collect information concerning OSAS and AD and investigate the effectiveness of CPAP in the treatment of AD.	-	Narrative literature review	The severity of OSAS, as well as the short duration of sleep, is significantly associated with a high risk of developing dementia. Treatment with CPAP seems effective for OSAS and AD patients because it not only treats OSA but also delays cognitive impairment and protects against it.
Wang et al. (2020) [18]	One Year of CPAP Adherence Improves Cognition in Older Adults with Mild Apnea and Mild Cognitive Impairment: A Secondary Analysis of Memories 1	United States of America	To explore the effect of CPAP adherence on cognition in older adults with mild obstructive sleep apnea and mild cognitive impairment.	17 older adults with MCI and OSAS (MCI + CPAP, n = 7; and MCI − CPAP, n = 10)	Secondary analysis of a quasi-experimental pilot clinical trial	A year of CPAP adherence significantly improved psychomotor/cognitive processing speed in older adults with MCI and mild OSAS and shows promise for slowing progression to Alzheimer's Disease.
Cordone et al. (2021) [4]	Sleep-Based Interventions in Alzheimer's Disease: Promising Approaches from Prevention to Treatment along the Disease Trajectory	Italy	To explore sleep disturbances in the different stages of AD, starting from the pre-clinical stage, with particular attention to OSAS.	-	Narrative literature review	The review findings highlight the importance of sleep monitoring and promotion in healthy aging to prevent the development of AD. It suggests that sleep-based therapeutic approaches can positively impact cognitive status in different stages of AD pathology.
Fernandes et al. (2021) [19]	The Importance of Diagnosing and the Clinical Potential of Treating Obstructive Sleep Apnea to Delay Mild Cognitive Impairment and Alzheimer's Disease: A Special Focus on Cognitive Performance	Italy	To summarize the findings of studies that analyzed OSAS as a risk factor for developing MCI and/or AD in middle-aged and older populations, with a special focus on cognition.	-	Narrative literature review	CPAP treatment may delay cognitive decline in patients with MCI or AD, although further evidence should be obtained. CPAP treatment can improve different cognitive deficits in adult OSA patients, namely, executive function, memory, attention, and reaction time. It was highlighted the importance of starting CPAP treatment early and of improving follow-up to monitor compliance to this device.

Table 2. *Cont.*

Authors and Year	Title	Country	Aims/Purpose	Population and Sample Size	Type of Study/Evidence Level	Outcomes
Pollicina et al. (2021) [20]	Neurocognitive Performance Improvement after Obstructive Sleep Apnea Treatment: State of the Art	Italy	To analyze the effect of OSAS treatments on neurocognitive performance.	-	Comprehensive review of the English language over the past 20 years	OSAS is strongly associated with cerebrovascular disorders and chronic neurodegenerative and inflammatory diseases, leading to a high risk of cognitive impairment in affected patients. The literature remains doubtful, to date, on the efficacy of OSSA treatment on cognitive functions. CPAP could improve cognitive domains, such as working memory, long-term verbal memory, and short-term visuospatial memory.

* AD: Alzheimer's Disease; CPAP: continuous positive airway pressure; MCI: mild cognitive impairment; OSAS: obstructive sleep apnea syndrome.

Table 3 summarizes the design and evidence of each clinical trial included in the present review. In every trial, the intervention group showed improved results when compared to the control group.

Table 3. Randomized control trials included in the review.

Authors and Year	N *	Age	Patient Characteristics	Treatment		Follow-up	Questionnaires	Evidence Level
				Intervention Group	Control Group			
Richards et al. (2019) [15]	54	55–89	MMSE * 24–30 AHI * > 10	CPAP > 4 h/night	CPAP < 4 h/night	1 year	HVLT-R *, DS *, MMSE	2
Wang et al. (2020) [18]	17	55–89	MMSE 23–30 AHI < 15	CPAP > 4 h/night	CPAP < 4 h/night	1 year	DS, Clinical Dementia Rating scale, Alzheimer's Disease Cooperative Study–Clinical Global Impression of Change Scale	2
Ancoli-Israel et al. (2008) [14]	52	70–86	MMSE > 17 AHI 14–45	CPAP	No treatment	6 weeks	HVLT-R, DS	2

* N: sample; MMSE: Mini–Mental State; AHI: apnea/hypopnea index; HVLT-R: Hopkins Verbal Learning Test Revised; DS: Digit Symbol subtest.

4. Discussion

Using the VOSviewr version 1.6.20 software for MacOS, we analyzed biometric networks between all included studies. Figure 2 presents the network visual map obtained by VOSviewr.

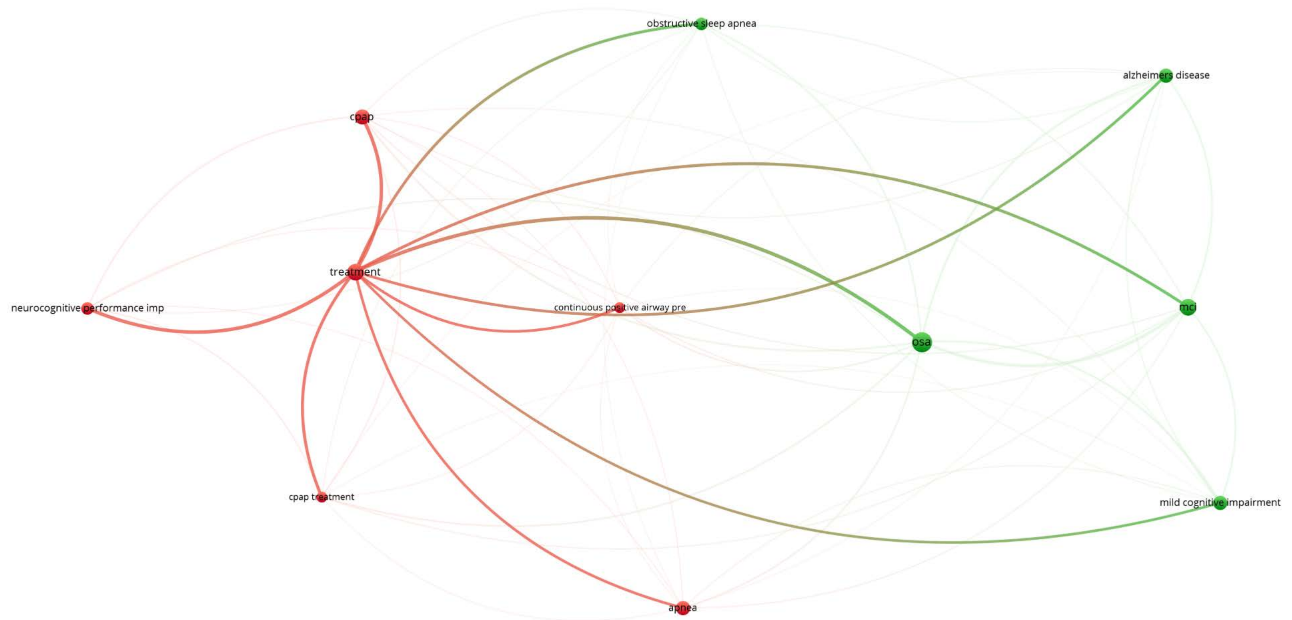

Figure 2. Visual map of included studies cluster analysis.

The cluster analysis focusing on the "treatment" concept connects it to OSAS, CPAP, MCI, AD, and neurocognitive performance impairment.

The gold standard for treating OSAS is CPAP [7,8,14–20], which is consistent in the studies included in this review and in the evidence from the literature. CPAP is proven to prolong N3 sleep and increase the power and amplitude of slow electroencephalographic waves during N3 sleep, indicating improved sleep quality [21]. Additionally, CPAP can improve sleep-related symptoms, the apnea–hypopnea index, and quality of life [7,8], although poor adherence can compromise its results [22]. People with allergic rhinitis, moderate to severe nasal congestion at bedtime, rhinorrhoea, sinus opacification, and high nasal septum deviation have higher rates of CPAP initial adherence problems, leading to treatment discontinuation unless adequately treated before CPAP initiation [23,24]. A systematic review regarding CPAP adherence suggests home calls, phone calls, CPAP therapist support, patient education, motivational interviews, and follow-up visits as CPAP adherence interventions [22]. Also, nurses can play an important role in managing respiratory diseases and treatment compliance [25]. In some countries, adherence is continuously monitored with devices attached to the CPAP system, and its non-use can lead to the removal of the device from the national health system or the insurance company.

It is well established that OSAS is strongly associated with cerebrovascular and neurodegenerative diseases, which may aggravate cognitive dysfunction such as dementia, AD, psychomotor speed, memory, attention, and daytime sleepiness [14,16,17,20,22]. Evidence from analyzed studies in this review supports that treating OSAS seems to have a positive impact on MCI [14–20], improving cognition, protecting against MCI, and slowing its progression. In this sense, some of the MCI improvements mentioned were (i) memory (including long-term verbal memory and short-term visuospatial memory) [4,14,16,18–20], (ii) attention [15,16,18–20], (iii) daytime sleepiness [15–18,20], and (iv) language [16,19]. Corroborating this evidence, a clinical trial conducted by Hong et al. (2000) revealed that OSAS patients treated with CPAP for two months showed significant improvements in daytime sleepiness, logical memory, and face memory compared to those patients without CPAP treatment [21]. A study from Malik and Patrik (2001) also concluded that good CPAP adherence improves cognitive memory and attention [26]. Many patients with OSAS experience excessive daytime sleepiness, which can improve with CPAP treatment [27], although a substantial proportion of patients may continue to experience this symptom despite receiving optimized primary OSA therapy [28]. OSAS may affect language abilities, especially those that involve efficient retrieval of lexical–semantic representations [29], but the evidence is not clear about this.

On the other hand, we could also find studies that did not find MCI improvements over OSAS treatment [30], suggesting the correlation is not linear and that more studies should be conducted. In a systematic review, Bubu et al. (2020) suggest that decreased neural plasticity and neural loss and atrophy seen in AD patients may explain the lack of significant results on some cognitive dysfunction improvements with CPAP therapy [16]. In return, the same author stated that in young and middle-aged OSAS patients, CPAP treatment played a significant role in cognitive function improvement, suggesting potential benefits on brain tissue damage prevention and AD, as significant improvements in memory, attention, and executive function paralleled white matter changes after 12-month treatment, found in middle-aged patients.

According to the studies analyzed, treating OSAS also seems to have a positive impact on neurocognitive performance in areas such as (i) executive function [4,14–20], (ii) psychomotor speed [14–16,18], (iii) cognitive process speed [4,14–16,18], and (iv) reaction time [16,19,20]. A study by Malik and Patrick (2021) found significant executive performance differences between patients with OSAS, improved by correct compliance with CPAP treatment [26]. Evidence is divided concerning psychomotor speed and reaction time improvement with OSAS treatment. OSAS patients reveal impaired results in minimum single-task solving time in the speed of solving simple arithmetic operations [31], where CPAP treatment appears to mitigate and slow the rate of cognitive decline and may improve information processing speed [9]. On the other hand, a study conducted by Vanek et al. (2020) stated that, in contrast to other cognitive areas, psychomotor speed and fine coordination do not significantly improve after CPAP treatment [32]. However, all authors agree that treating OSAS is necessary to prevent neurocognitive and psychomotor performance declination.

Education, prevention, and early diagnosis are the most effective ways to mitigate the impact of OSAS both on patients and the health system, whereas CPAP adherence can be treated as a secondary prevention measure that aims to reduce the overall impact of OSAS [33]. Furthermore, OSAS prevention includes physical activity, obesity treatment, reducing the frequency of supine sleep, reducing alcohol consumption, treating dental and maxillofacial pathology, and reducing the use of sedatives such as opioids and benzodiazepines [33]. All these aspects should be addressed in treating OSAS in order to achieve better results in cognition, not forgetting to treat comorbidities and MCI accordingly.

Our search resulted in only two primary studies, suggesting that the impact of treating OSAS on cognition has not yet been thoroughly explored. Also, most reviews on the subject rely on the same limited clinical trials. In that sense, we cannot assure a high evidence level for the results, and we recommend more primary studies concerning the effect of OSAS treatment on cognition.

5. Conclusions

The literature shows that CPAP treatment in OSAS is associated with significant benefits in neurocognitive performance, such as executive function and cognitive process speed, as well as neural recovery, in the long term. It can also be an important tool in preventing cognitive impairment in OSAS patients, as it can improve memory and attention and reduce daytime sleepiness. Treatment compliance is essential, and certain issues must be addressed, such as allergies, nasal problems, and other comorbidities.

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