Activitas Nervosa Superior Rediviva Volume 65 No. 1 2023

REVIEW ARTICLE

Cognitive dysfunctions in obstructive sleep apnea patients

Jakub Vanek [1], Jan Prasko [1,2,3,4], Samuel Genzor [5], Pavol Pobeha [6], Frantisek Hodny [1], Jozef Visnovsky [1], Milos Slepecky [3], Marie Ociskova [1,4]

[1] Department of Psychiatry, Faculty of Medicine and Dentistry, University Palacky Olomouc,Olomouc, Czech Republic, [2] Institute for Postgraduate Education in Health Care, Prague, Czech Republic, [3] Department of Psychology Sciences, Faculty of Social Science and Health Care, Constantine the Philosopher University in Nitra, Slovak Republic, [4] Rehabilitation Hospital Beroun, Jessenia Inc., Akeso Holding, Mindwalk, s.r.o., Czech Republic, [5] Department of Respiratory Medicine, Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic, [6] Department of Respiratory Diseases and Tuberculosis University Hospital and Faculty of Medicine and Dentistry Pavol Jozef Safarik University Kosice, Slovak Republic.

Correspondence to: Prof. Dr. Jan Prasko, Ph.D. Department of Psychiatry, Faculty of Medicine and Dentistry, Palacky University Olomouc, I. P. Pavlova 6, 77520 Olomouc, Czech Republic
TEL: +420 603 414 930; E-MAIL: praskojan@seznam.cz

Submitted: 2022-12-12 *Accepted: 2023-02-04* *Published online: 2023-02-04*

Key words: **Obstructive sleep apnoea; cognitive dysfunctions; C-PAP; antidepressants; treatment efficacy**

Act Nerv Super Rediviva 2023; **65**(1): 16–24 ANSR65123R02

Abstract

OBJECTIVE: The main objective of the presented narrative review is to assess the contemporary literature regarding cognitive functions and their deterioration in obstructive sleep apnea patients.
METHOD: Articles were acquired via PubMed database via computerized search applying selected keywords in combinations from January 1953 to December 2022. Papers were nominated using including criteria: studies in humans, published in peer-reviewed journals; reviews; English language. The criteria for exclusion were: abstracts from conferences, commentaries, and subjects younger than 18 years. According to the inclusion and exclusion criteria, 80 articles were chosen. Relevant documents from the references of primarily chosen papers were investigated, evaluated and relevant papers were added to the initial list of documents. Review team then assessed full texts and selected and included 110 papers in total in the review.
RESULTS: Studies included in the review documented the dysfunctions in the attention, selected domains of memory, and executive functions in OSA. Verbal functions mostly remain intact, and tests of psychomotor speed show mixed findings. Repeated desaturations caused by airway closure accompanied by hypoxemia and hypercapnia at night and frequent arousals associated with excessive sympathetic activation and sleep fragmentation are presumed to be etiological factors in these cognitive dysfunctions.
CONCLUSIONS: Areas of cognitive function most affected by untreated OSA include attention, memory and executive functions. Studies show that untreated OSA prolongs reaction time and impairs intentional attention and the ability to divide attention between multiple stimuli. Cognition partially improves after CPAP treatment. However there is not enough evidence in the long-term effects of CPAP on cognition and the long-term effect of untreated OSA on cognitive functions.

Introduction

Obstructive sleep apnea (OSA) is one of the most common sleep disorder in general population. Its main features are sleep fragmentation, frequent awakenings, and intermittent hypoxia (Ulander *et al.* 2022; Vardanian & Ravdin 2022). OSA is defined as recurring upper airway block, leading to flow limitation (hypopnea) or full breathing cessation (apnea) (Ryan & Bradley 2005; Feltner *et al.* 2022; Mangione *et al.* 2022). The resulting decrease in blood oxygen saturation, changes in intrathoracic pressure, and other related stimuli (e.g. excessive nocturnal urination, upper airway resistance etc.) trigger the autonomic nervous system, disruption of the sleep architecture, and brief awakening periods. Sleep apnea syndrome is diagnosed with more than five apnea/hypopnea episodes longer than 10 seconds per hour (ICSD-3, 2014). Subjective symptoms are increased daytime sleepiness, fatigue, and impaired attention (De Backer 2013; Feltner *et al.* 2022; Ulander *et al.* 2022).

The gold standard of treatment is pressurized breathing per a continuous positive airway pressure device (CPAP) connected to a face mask. The device keeps the airways open during exhalation and thus prevents their collapse, which is the most common cause of apnea (Sova *et al.* 2015; Genzor *et al.* 2022; Weingarten 2022). Cardiovascular diseases (e.g., cardiac infarctions, arrhythmias, drug-resistant hypertension, pulmonary hypertension), disorders of glucose metabolism, lipid spectrum disorders, and obesity are common risk factors and comorbidity in OSA pathophysiology (Feltner *et al.* 2022; Sovova *et al.* 2011; Sabil *et al.* 2022). These illnesses often worsen sleep apnea (Feltner *et al.* 2022). Other risk factors for developing OSA include male gender, abdominal obesity, smoking, chronic obstructive pulmonary disease, and bronchial asthma (Feltner *et al.* 2022). Furthermore, OSA connects with affective disorders and depressive symptoms and cognitive impairment (Daulatzai 2015; Hobzova *et al.* 2017; Vanek *et al.* 2020a; 2020b; Jiang *et al.* 2021; de Miguel-Diéz *et al.* 2022; Vanek *et al.* 2022; Zhao *et al.* 2022)

Connection between OSA and cognitive deterioration prevalence increase with age and body mass. Several areas of cognitive functions are affected, mainly attention, execution, specific subtypes of memory, and emotional regulation, directly affecting brain health (Vardanian & Ravdin 2022). Increasing evidence links OSA to cognitive deterioration and autonomic dysfunction, a hopeful early marker of cognitive dysfunctions in populations without a diagnosed neurodegenerative disorder (Sabil *et al.* 2022; Bucks *et al.* 2013). OSA can worsen the course and treatment of other diseases, but especially in cognitive deterioration, OSA can significantly affect the progression of atherosclerosis of the cerebral arteries due to inadequate treatment (Feltner *et al.* 2022). That makes the early detection and treatment of OSA a clinical priority.

Method

Articles were acquired via PubMed database via computerized search applying selected keywords in combinations from January 1953 to December 2022. Keywords were "obstructive sleep apnea "and "cognitive function" or "dementia" in successive combination with "CPAP" or "therapy" or "pharmacotherapy" or "surgery" or "quality of life".

Acquired papers were sorted according to inclusion and exclusion criteria. Inclusion criteria were: (1) studies in humans; (2) published in peer-reviewed journals; or (3) reviews on the related topic; (4) accessible in English. The criteria for exclusion were: (1) abstracts from conferences; (2) commentaries; (3) subjects younger than 18 years.

84 articles were selected in primary collection using keywords in different combinations. According to the inclusion and exclusion criteria, 80 articles were chosen. Relevant documents from the references of primarily chosen papers were investigated, evaluated and relevant papers were added to the initial list of documents (n = 44). Review team then assessed full texts and selected and included 110 papers in total in the review (Figure 1).

Results

Potential pathological mechanisms linking cognitive dysfunctions and OSA

Repeated desaturations caused by airway closure accompanied by hypoxemia and hypercapnia at night, together with frequent arousals associated with excessive sympathetic activation and sleep fragmentation, worsen brain tissue oxygenation and regeneration of the brain. The lack of the normal length and depth of sleep essential for proper brain function causes this (Lau *et al.* 2010,; Castronovo *et al.* 2014; Dissanayake *et al.* 2021; 2022). Hypoxia in OSA is intermittent and characterized by blood oxygen desaturations of variable length following respiratory events (Prabhakar *et al.* 2020). Long-lasting intermittent hypoxia in OSA stimulates systemic inflammation, oxidative stress, and endothelial dysfunction, with potential consequences comprising cardiovascular, metabolic disorders, and mental disorders (Ryan & Bradley 2005; Tkacova *et al.* 2014; Burtscher *et al.* 2021). Another possible linking factor is obesity. Obesity is connected with an higher risk of OSA and cognitive dysfunction (Patil *et al.* 2004). Evidence suggests that early to mid-adulthood obesity directly impacts cognitive functioning and increases the likelihood of developing Alzheimer's disease and other types of dementia (e.g. vascular) (Xu *et al.* 2011). Several studies show that as the body mass index (BMI) increases, several cognitive domains (verbal learning, episodic memory or attention) decline (Gunstad *et al.* 2006; Fergenbaum *et al.* 2009). The impairment of cognitive functions is not solely explainable by the

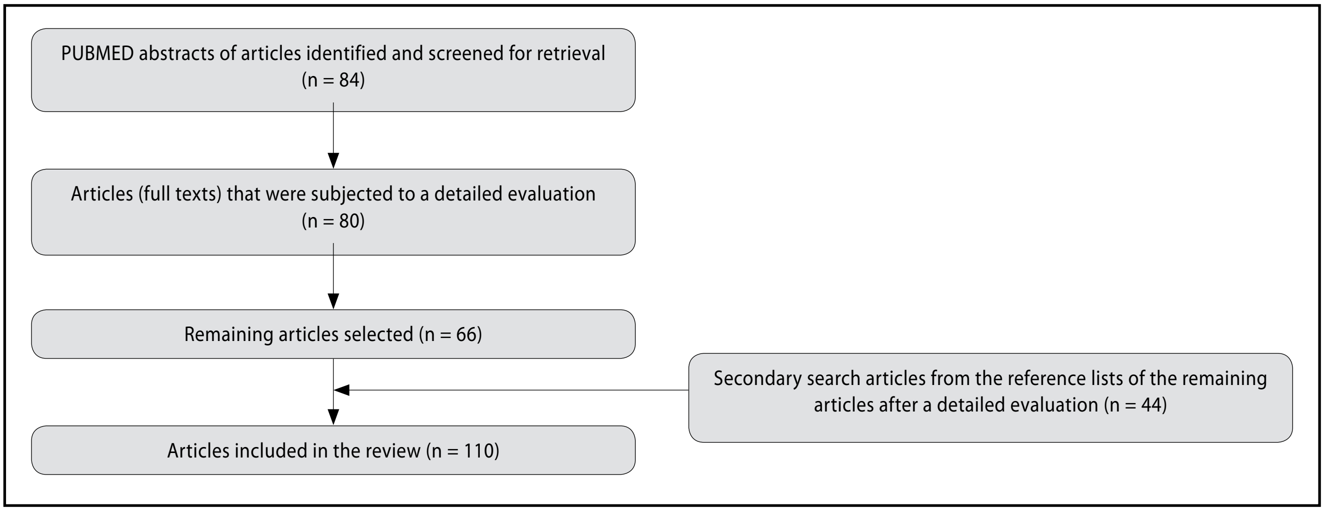

Fig. 1. Summary of the selection process
Keywords: (Obstructive sleep apnea) and (cognitive function or dementia) and (CPAP or therapy or pharmacotherapy or surgery or quality of life) Filters: clinical trials or reviews, and humans and adults 18 + years

presence of OSA or recurrent hypoxia. In the case of dementia (vascular, but also in Alzheimer's), several risk factors have been identified, such as cardiovascular disease, hypertension, high cholesterol or diabetes mellitus (Hugo & Ganguli 2014). Moreover, increased signs of atherosclerosis have been described in the brain vasculature of obese individuals. This results in white matter damage and grey matter atrophy leading to cognitive dysfunction (Dye *et al.* 2017; Morys *et al.* 2021; Quaye *et al.* 2023).

Interestingly, a probable complex link exists between olfactory dysfunction (OD), OSA, and cognitive impairment (Dong *et al.* 2022; Iannella *et al.* 2021). Individuals with OSA commonly suffer from olfactory dysfunction (Iannella *et al.* 2021). Although the exact mechanism is not yet fully explored, it seems that the olfactory cortex is very sensitive to the impairment described above. Additionally, individuals with OD have a higher probability of developing cognitive impairment than those without OD (Dong *et al.* 2022).

Types of cognitive dysfunctions in obstructive sleep apnea patients

Numerous investigations have tested the different cognitive domains in patients with OSA (Davies & Harrington 2016; Liguori *et al.* 2017; Bubu *et al.* 2020; Seda *et al.* 2021, Fernandes *et al.* 2022; Lal *et al.* 2022). Studies have documented the dysfunctions in the OSA's attention, selected subtypes of memory(working and episodic), and executive functions (Greenberg *et al.* 1987; Bedard *et al.* 1991, Decary *et al.* 2000; Beebe & Gozal 2002; Ferini-Strambi *et al.* 2003; Verstraeten & Cluydts 2004; Verstraeten *et al.* 2004; Alvarez & Emory 2006; Jackson *et al.* 2011; Mathieu *et al.* 2008; D´Rozario *et al.* 2022; Li *et al.* 2022). However, most verbal functions stay intact (Beebe & Gozal 2002; Ferini-Strambi *et al.* 2003; Alvarez & Emory 2006; Jackson *et al.* 2011, Naëgelé *et al.* 1998; Barkley 1997; Aloia *et al.* 2004; Lezak *et al.* 2004; Sforza *et al.* 2004; Mazza *et al.* 2005; Shpirer *et al.* 2012; Olaithe & Bucks 2013; Tulek *et al.* 2013; Corrêa *et al.* 2017; Shieu *et al.* 2022; Park *et al.* 2022a). Tests of psychomotor speed show mixed findings (Kilpinen *et al.* 2014; Landry *et al.* 2016; Bhat *et al.* 2018; Lusic *et al.* 2020).

Attention

Attention can be characterised by certain basic features – selectivity, sustainability, and distribution. Selective attention allows focusing on or overlooking stimuli according to their subjective importance. Sustained attention contains awareness and receptiveness to stimuli for an prolonged period. Division of attention allows numerous tasks to be fulfilled simultaneously (Lezak *et al.* 2004; Park *et al.* 2022b). Various studies have established that persons with OSA display problems in all these attention modalities (Beebe & Gozal 2002; Mazza *et al.* 2005; Ueno-Pardi *et al.* 2022). Two meta-reviews also support these findings (Olaithe & Bucks 2013; Wang *et al.* 2020). Compared to controls, the individuals with OSA exhibit slower responses and "off the road" actions in situations demanding divided attention, such as driving in a simulator while realizing additional mental assignments (Mazza *et al.* 2005; Wang *et al.* 2020). Given these deficits' degree and magnitude, it is theorized that alertness and attention issues could also impact remaining cognitive areas, e.g. executive functions and episodic memory (Verstraeten & Cluydts 2004; Verstraeten *et al.* 2004; Olaithe & Bucks 2013).

Executive functions

Executive functions represent a multiple diverse cognitive abilities, such as mental flexibility, behavioural inhibition, working memory, fluid reasoning, and problem-solving. They let human beings to practice their skills (e.g., memory, verbal interaction, visuoperception) adaptively to act efficiently in a varying environment (Alvarez & Emory 2006). Two meta-analyses found decreased executive functions in all five subdomains in the patients with OSA: inhibition, shifting, updating/monitoring information in working memory, producing new information and fluid reasoning, and problem-solving (Olaithe & Bucks 2013; Vardanian & Ravdin 2022).

Inhibition - the ability to stop a programmed or current reaction to a stimulus- is crucial for cognitive trials such as Stroop Test or Go-No-Go tasks (Barkley 1997). The patients with OSA make more errors and have prolonged reaction times than healthy controls in these tests. They show reduced brain stimulation in cingulate, frontal, and parietal areas that are usually involved in attention tests (Ayalon *et al.* 2009). Severe OSA patients also showed more impulsive mistakes on a maze accomplishment task (Bucks & Olaithe 2013, Bedard *et al.* 1991; Beebe & Gozal 2002; Archbold *et al.* 2009; Lafreniére *et al.* 2023).

Mental flexibility

Mental flexibility is the capability to shift from one mental task to another. Patients with OSA exhibit more perseverative reactions than healthy subjects in the Wisconsin Card Sorting Test (Bucks & Olaithe 2013; Naëgelé *et al.* 1998; Redline *et al.* 1997; Stranks & Crowe 2016). Reduced mental flexibility was described in several papers using different types of task in which the patients with OSA needed a longer time to complete the tests than controls (Redline *et al.* 1997; Naëgelé *et al.* 1998; Decary *et al.* 2000, Chokesuwattanaskul *et al.* 2021; Macchitella *et al.* 2021).

Working memory

Working memory is a fundamental component of cognitive functions, characterized as the capability to retain, operate, revise, and monitor knowledge for the extent of a task (Miyake & Shah 1999). Redline *et al.* (1997) discovered that working memory was amongst the most commonly damaged executive functions in OSA patients. Investigations utilizing the Digit Backward Test demonstrated that the patients with OSA had worse results on this task compared to healthy controls (Redline *et al.* 1997; Naëgelé *et al.* 1998; Li *et al.* 2022; Franks *et al.* 2022).

Problem-solving

Problem-solving, which includes the assessment and assortment of actions to reach a goal, seems to be decreased in the OSA patients as well (Lezak *et al.* 2004). In a task typically utilized to evaluate this aspect of executive functions, specifically the Tower Tasks, Naëgelé *et al.* (1998) study indicated that OSA patients required additional steps before resolving particular task. Certain executive functions of verbal performance, such as mental processing speed, flexibility, and the ability to synthetize information, are worsened in patients with OSA, regardless of relatively intact language skills (Bedard *et al.* 1991; Naëgelé *et al.* 1998; Ferini-Strambi *et al.* 2003; Sharma *et al.* 2010; Olaithe & Bucks 2013; Saconi *et al.* 2020).

In conclusion, investigations uncovered insufficiencies in almost all executive functioning in OSA individuals. The impairment is present in the processing speed, more perseverative responses or behaviours, impulsivity, and struggle with problem-solving. Nevertheless, the findings are significantly heterogeneous, which could be partially due to differences among samples and methods.

Motor dysfunctions

Tasks including fine coordination and psychomotor tempo are usually utilized to examine motor dysfunctions apart from natural ability for standard locomotion. In patients with OSA, the impairment of manual adroitness was noticeable in the Purdue Pegboard Test (Bedard *et al.* 1991; Naëgelé *et al.* 1998). Fine motor coordination was documented to be more damaged by repeated hypoxemia than by sleep fragmentation (Aloia *et al.* 2004; Landry *et al.* 2016). Unsurprisingly, the OSA patients performed inferior compared to controls in all tasks involving visuomotor coordination (Aloia *et al.* 2004; Koo *et al.* 2020; Lee *et al.* 2022).

Episodic memory

Correspondingly episodic memory was broadly examined in OSA individuals. Episodic memory can memorize verbal or visual information in a spatiotemporal framework. Tasks typically include immediate recollection, total recollection over several trials or learnings, late recollection, and recognition memory. Examples of episodic memory tests include learning and remembering a certain number of words (e.g. Rey Auditory-Verbal Learning Tests, California Verbal Learning Tests). A meta-analysis from 2013 exhibited that OSA individuals have various vocal and visual episodic memory deficit patterns. Most memory components were impaired, namely instant and delayed recollection, learning and recognition (Wallace & Bucks 2013; Patel & Chong 2021). However, the visuospatial episodic memory tasks showed impairment only in immediate and delayed recalls, and their learning curve and recognition were normal (Wallace & Bucks 2013). This deficit was proposed not to be entirely attributed to attention deficits or OSA severity; rather, a complex interplay of multiple factors is viewed as a reason for the memory deficit (Patel & Chong 2021; Seda & Han 2020; Benkirane *et al.* 2021).

Treatment with CPAP and cognitive dysfunctions in OSA

Though positive airway pressure therapy (CPAP) improved some features of cognitive functions, it failed to fully restore all cognitive domains (Vardanian & Ravdin 2022). Moreover, many patients insufficiently adhere to this treatment, which decreased cognitive functions may partly cause (Watach *et al.* 2021; Genzor *et al.* 2022; Avellan-Hietanen *et al.* 2022). Conversely, individuals with better CPAP adherence have significantly larger improvements in cognitive functions if dementia is already present (Costa *et al.* 2022). A meta-analysis presented that the CPAP intervention create at most moderate enhancement in executive functions (Greenberg *et al.* 1987; Aloia *et al.* 2004; Olaithe & Bucks 2013; Costa *et al.* 2022; D´Rozario *et al.* 2022). For example, one study showed an improvement of mental flexibility and semantic fluency in OSA after a brief CPAP intervention (15 days). Longer treatment (4 months) did not produce additional improvement in executive cognitive tests (Ferini-Strambi *et al.* 2003). Moreover, it was reported that the mental flexibility of the OSA patients did not reach the level of control after a three-month treatment (Ferini-Strambi *et al.* 2003; Lau *et al.* 2010).

As for the treatability of the cognitive decline, an evaluation of cognitive changes related to the CPAP intervention described that 11 of the 17 investigations found a substantial improvement in attention and vigilance (Aloia *et al.* 2004). However, regardless of the significant improvement in attention, attention processes often do not return to their premorbid levels (Fernandes *et al.* 2022). According to the investigation of Lau *et al.* (2010), discriminatory and divided attention impairment was still present evern after three months of the CPAP in comparison to healthy controls.These findings propose that hypoxemia and sleep fragmentation partly cause attention deficits in OSA but that OSA also might cause a permanent damage in the brain areas responsible for attention processing (Lau *et al.* 2010). One of the factors causing attention deficits in OSA is the presence of excessive daytime sleepiness (EDS). EDS has been described in 40.5–58% OSA patients (number varying according to severity of the disorder) at the time of diagnosis but can remain present even in patients with CPAP therapy (residual EDS) in 9-22% of patients (Gasa *et al.* 2013; Lal *et al.* 2021)

Following similar results from studies worldwide, we compared the results of cognitive tests after one month of continuous CPAP therapy (at least 4.5 hours per day) in our research, with treated individuals showing a substantial improvement in attention and short-term memory together with subjective improvement in depressive symptoms as tested by Beck's Depression Inventory (Hobzova *et al.* 2017). When compared, the control group exhibited a slight non-significant deterioration in concentration, worse short-term memory, and further progression of depressive symptoms during the month (Hobzova *et al.* 2017).

In summary, presented literature propose that only a particular part of executive functions recovers after a CPAP intervention and they tend not reach the levels found in healthy controls (Ferini-Strambi *et al.* 2003, Lau *et al.* 2010, Vardanian & Ravdin 2022). Additional cognitive domains, such as attention and attentiveness, are essential to complete most tasks. Untreated OSA is probably causing lasting damage to the prefrontal cortex, which could clarify part of the inconsistency in studies examining the effects of CPAP on cognitive functions (Shu *et al.* 2022).

Unlike previous cognitive area, psychomotor speed and fine coordination are not significantly increased after CPAP intervention, suggesting that OSA is probably responsible for lasting impairments to cortical and subcortical regions engaged in motor skills (Shu *et al.* 2022; Vardanian & Ravdin 2022).

A review of the outcomes of the CPAP interventions described an improvement in memory in about half of the investigations (Aloia *et al.* 2004; Seda & Han 2020). Even though all verbal episodic memory mechanisms are affected in OSA, a 3 months CPAP intervention normalizes immediate and delayed recollection and visuospatial learning performances (Ferini-Strambi *et al.* 2003; Lau *et al.* 2010; Wallace & Bucks 2013).

CPAP is the main treatment intervention in OSA, but there are other treatment modalities for patients who do not tolerate this treatment. Oral appliances (OAs) are one of the alternative types of treatment. Studies in OSA compared the effectiveness of CPAP and OAs and found that the CPAP-treated cohort achieved better effects in improving OSA polysomnographic parameters. However, the results of both modalities were comparable in other clinical outcomes, including improvement in cognitive function (Loredo *et al.* 1999; Li *et al.* 2022).

Exercise and cognitive functioning in OSA

Compromised glucose metabolism suggests neuronal/synaptic dysfunction and cognitive function deterioration in OSA (Longlalerng *et al.* 2021; Park *et al.* 2022a; Ueno-Pardi *et al.* 2022). Ueno-Pardi *et al.* (2022) investigated how exercise recovers cerebral metabolic glucose rate and cognitive functions in OSA individuals. When they compared patients with the control group, the trained group had improved exercise capacity, decreased AHI, had fewer oxygen desaturations, increased attention and observed and improvement in cognitive functions, and increased cerebral metabolic glucose turnover in the frontal lobe (Ueno-Pardi *et al.* 2022). Bughin *et al.* (2020) assessed the effect of customised exercise with informative sessions versus education alone on OSA severity indicators over in a randomized, controlled, parallel-design study with 64 patients. Compared to the control group, exercise led to a larger reduction in AHI. When compered to education only group, distinctive differences were found in the severity of fatigue and insomnia, depressive symptoms, and weight reduction. (Bughin *et al.* 2020).

Surgical treatment and other therapeutic modalities

Although there is a very probable positive influence on cognitive functions in the case of successful surgical interventions, the evidence is still sparse (Pollicina *et al.* 2021). The surgical treatment may be applicable, particularly in non-obese individuals with treatable obstruction (e.g. enlarged palatal tonsils or retrognathia), where uvulopalatopharyngoplasty and maxillomandibular advancement are the most effective options for OSA treatment (Randerath *et al.* 2021). Lojander *et al.* (1999) tested both CPAP and surgical treatment to improve basic cognitive tests. The study involved 50 individuals (27 in CPAP treatment, 23 treated surgically). Any effective treatment decreased sleepiness and improved the Bourdon-Wiersma Wakefulness Dot Cancellation test, but the study did not found significant improvement in the basic cognitive test after 12 months of therapy (Lojander *et al.* 1999). Alkan *et al.* (2021) tested the cognitive functions and vigilance of 32 OSA individuals before and after surgical treatment. All the tests were repeated during the follow-up after 3-6 months. The Epworth Sleepiness Scale decreased from 13.7 to 8.1 ($p=0.043$) and reduced the time to complete the Color Trail Test (part 1: 21.4 to 18.7s; part 2: 48.8 to 40.5s, all with statistic significance). Similarly, according to the Useful Field of Vision Scale, there were confirmed improvements in selective attention response time (Alkan *et al.* 2021).

Mandibular advancement devices (MAD) might be an effective tool in non-obese individuals with poor tolerance of CPAP or surgery contraindications (Randerath *et al.* 2021). However, evidence of improvement in cognitive functions is missing. We have identified only a prospective study involving 15 patients – Galic *et al.* (2016). The study group consisted of mild to moderate OSA subjects who were followed up for 3 and 12 months of therapy use. The AHI decreased significantly (mean 22.9 dropped to mean 9.7), resulting in improved reaction time (measured by a computer-based system) and overall quality of life (Li *et al.* 2013; Galic *et al.* 2016).

Among other therapeutic modalities should be noted hypoglossal nerve stimulation, which may also be applicable for similar patients to MAD, including those with difficult dentition or other complications resulting in poor effectivity or tolerance of MAD (Li *et al.* 2013; Randerath *et al.* 2021) However, despite great efficiency in properly selected individuals, the evidence about effectivity on cognition is yet to be found (Dzierzewski *et al.* 2021).

Discussion

OSA is rarely a solitary disease; in many patients, it is one of their many comorbidities, such as cardiovascular disorders, diabetes mellitus or cognitive diseases. CPAP is the main OSA therapeutic intervention. As we do not expect this treatment to reverse somatic components of the sleep disorder, it is understandable that it will not eliminate cognitive dysfunctions. One of the reasons might be that the long-term effect of sleep apnea (at the time of diagnosis, OSA could have been present for many years) on the brain led to partially irreversible damage, and the treatment corrects only reversibly damaged parts of the cerebral features. Therefore, we cannot rely solely on one albeit fundamental treatment modality, but to manage the patient comprehensively, including proper lifestyle changes and adjustments and comprehensive cognitive rehabilitation program and physical training.

Conclusion

In summary, areas of cognitive function most affected by untreated OSA include attention, memory, and executive function, while verbal tasks are preserved. Studies show that untreated OSA prolongs reaction time and impairs intentional attention and the ability to divide attention between multiple stimuli. Research attention is then paid to the degree of adjustment and improvement of cognitive functions in CPAP therapy. Cognition improves after CPAP treatment and exercise, but it's improvement is mostly limited – probably because OSA causes irreversible brain damage making the deterioration persistent. Additional studies are necessary to assess the long-term outcomes of CPAP treatment on cognition and the long-term outcome of untreated OSA on cognitive functions.

Disclosure

The authors state no conflicts of interest in this paper.

REFERENCES

1 Alkan U, Nachalon Y, Weiss P, Ritter A, Feinmesser R, Gilat H, et al. (2021). Effects of surgery for obstructive sleep apnea on cognitive function and driving performance. *Sleep Breath.* **25**(3): 1593–1600.

2 Aloia MS, Arnedt TJ, Davis JD, Riggs RL, Byrd D (2004). Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: A critical review. *J Int Neuropsychol Soc.* **10**: 772–785.

3 Alvarez JA & Emory E (2006). Executive function and the frontal lobes: a meta-analytic review. *Neuropsychol Rev.* **16**: 17–42.

4 Archbold KH, Borghesani PR, Mahurin RK, Kapur VK, Landis CA (2009). Neural activation patterns during working memory tasks and OSA disease severity: preliminary findings. *J Clin Sleep Med.* **5**(1): 21–27.

5 Avellan-Hietanen H, Aalto T, Maasilta P, Ask O, Bachour A (2022). Adherence to CPAP therapy for sleep apnea in patients aged over 70 years old. *Sleep Breath.* **26**(1): 325–331.

6 Ayalon L, Ancoli-Israel S, Aka AA, McKenna BS, Drummond SP (2009). Relationship between obstructive sleep apnea severity and brain activation during a sustained attention task. *Sleep.* **32**(3): 373–381.

7 Barkley RA (1997). Behavioral inhibition sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychol Bull.* **121**: 65–94.

8 Bedard MA, Montplaisir J, Richer F, Malo J (1991). Nocturnal hypoxemia as a determinant of vigilance impairment in sleep apnea syndrome. *Chest.* **100**: 367–370.

9 Beebe DW &, Gozal D (2002). Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *J Sleep Res.* **11**: 1–16.

10 Benkirane O, Neu D, Schmitz R, Dehon H, Mairesse O, Peigneux P (2021). Reversible Verbal Memory Integration Deficits in Obstructive Sleep Apnoea. *Psychol Belg.* **61**(1): 131–144.
11 Bhat S, Gupta D, Akel O, Polos PG, DeBari VA, Akhtar S, et al. (2018). The relationships between improvements in daytime sleepiness, fatigue and depression and psychomotor vigilance task testing with CPAP use in patients with obstructive sleep apnea. *Sleep Med.* **49**: 81–89.
12 Bubu OM, Andrade AG, Umasabor-Bubu OQ, Hogan MM, Turner AD, de Leon MJ, et al. (2020). Obstructive sleep apnea, cognition and Alzheimer's disease: A systematic review integrating three decades of multidisciplinary research. *Sleep Med Rev.* **50**: 101250.
13 Bucks RS, Olaithe M, Eastwood P (2013). Neurocognitive function in obstructive sleep apnoea: a meta-review. *Respirology.* **18**: 61–70.
14 Bughin F, Desplan M, Mestejanot C, Picot MC, Roubille F, Jaffuel D, et al. (2020). Effects of an individualized exercise training program on severity markers of obstructive sleep apnea syndrome: a randomized controlled trial. *Sleep Med.* **70**: 33–42.
15 Burtscher J, Mallet RT, Burtscher M, Millet GP (2021). Hypoxia and brain aging: Neurodegeneration or neuroprotection? *Ageing Res Rev.* **68**: 101343.
16 Castronovo V, Scifo P, Castellano A, Aloia MS, Iadanza A, Marelli S, et al. (2014). White matter integrity in obstructive sleep apnea before and after treatment. *Sleep.* **37**(9): 1465–1475.
17 Chokesuwattanaskul A, Chirakalwasan N, Jaimchariyatam N, Pitakvej N, Sarutikriangkri Y, Chunharas C, et al. (2021). Associations between hypoxia parameters in obstructive sleep apnea and cognition, cortical thickness, and white matter integrity in middle-aged and older adults. *Sleep Breath.* **25**(3): 1559–1570.
18 Corrêa CC, Cavalheiro MG, Maximino LP, Weber SA (2017). Obstructive sleep apnea and oral language disorders. *Braz J Otorhinolaryngol.* **83**(1): 98–104.
19 Costa YS, Lim ASP, Thorpe KE, Colelli DR, Mitchell S, Masellis M, et al. (2022). Investigating changes in cognition associated with the use of CPAP in cognitive impairment and dementia: A retrospective study. *Sleep Med.* **101**: 437–444.
20 Daulatzai MA (2015). Evidence of neurodegeneration in obstructive sleep apnea: Relationship between obstructive sleep apnea and cognitive dysfunction in the elderly. *J Neurosci Res.* **93**: 1778–1794.
21 Davies CR & Harrington JJ (2016). Impact of Obstructive Sleep Apnea on Neurocognitive Function and Impact of Continuous Positive Air Pressure. *Sleep Med Clin.* **11**(3): 287–298.
22 De Backer W (2013). Obstructive sleep apnea/hypopnea syndrome. *Panminerva Med.* **55**(2): 191–195.
23 de Miguel-Díez J, Lopez-de-Andres A, Jimenez-Garcia R, de Miguel-Yanes JM, Hernández-Barrera V, Carabantes-Alarcon D, et al. (2022). National Trends in Prevalence of Depression in Men and Women with Chronic Obstructive Pulmonary Disease Hospitalized in Spain, 2016-2020. *J Clin Med.* **11**(21): 6337.
24 Decary A, Rouleau I, Montplaisir J (2000). Cognitive deficits associated with sleep apnea syndrome: a proposed neuropsychological test battery. *Sleep.* **23**: 369–381.
25 Dissanayake HU, Bin YS, Sutherland K, Ucak S, de Chazal P, Cistulli PA (2022). The Effect of Obstructive Sleep Apnea Therapy on Cardiovascular Autonomic Function: A Systematic Review and Meta-Analysis. *Sleep.* **45**(12): zsac210.
26 Dissanayake HU, Bin YS, Ucak S, de Chazal P, Sutherland K, Cistulli PA (2021). Association between autonomic function and obstructive sleep apnea: A systematic review. *Sleep Med Rev.* **57**: 101470.
27 Dong J, Zhan X, Sun H, Fang F, Wei Y (2022). Olfactory dysfunction is associated with cognitive impairment in patients with obstructive sleep apnea: a cross-sectional study. *European Archives of Oto-Rhino-Laryngology.* **279**(4): 1979–1987.
28 D'Rozario AL, Hoyos CM, Wong KKH, Unger G, Kim JW, Vakulin A, et al. (2022). Improvements in cognitive function and quantitative sleep electroencephalogram in obstructive sleep apnea after six months of continuous positive airway pressure treatment. *Sleep.* **45**(6): zsac013.
29 Dye L, Boyle NB, Champ C, Lawton C (2017). The relationship between obesity and cognitive health and decline. *Proceedings of the nutrition society.* **76**(4): 443–454.
30 Dzierzewski JM, Soto P, Vahidi N, Nord R (2021). Clinical Characteristics of Older Adults Seeking Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea. *Ear Nose Throat J.* Doi 10.1177/01455613211042126. Epub ahead of print.
31 Feltner C, Wallace IF, Aymes S, Cook Middleton J, Hicks KL, Schwimmer M et al. (2022). Screening for Obstructive Sleep Apnea in Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA.* **328**(19): 1951–1971.
32 Fergenbaum JH, Bruce S, Lou W, Hanley AJ, Greenwood C, Young TK (2009). Obesity and lowered cognitive performance in a Canadian First Nations population. *Obesity.* **17**(10): 1957–1963.
33 Ferini-Strambi L, Baietto C, Di Gioia MR, Castaldi P, Castronovo C, Zucconi M, Cappa SF (2003). Cognitive dysfunction in patients with obstructive sleep apnea (OSA): partial reversibility after continuous positive airway pressure (CPAP). *Brain Res Bull.* **61**(1): 87–92.
34 Fernandes M, Mari L, Chiaravalloti A, Paoli B, Nuccetelli M, Izzi F, et al. (2022). 18F-FDG PET, cognitive functioning, and CSF biomarkers in patients with obstructive sleep apnoea before and after continuous positive airway pressure treatment. *J Neurol.* **269**(10): 5356–5367.
35 Franks KH, Rowsthorn E, Nicolazzo J, Boland A, Lavale A, Baker et al. (2022). The treatment of sleep dysfunction to improve cognitive function: A meta-analysis of randomized controlled trials. *Sleep Med.* **101**: 118–126.
36 Galic T, Bozic J, Pecotic R, Ivkovic N, Valic M, Dogas Z (2016). Improvement of cognitive and psychomotor performance in patients with mild to moderate obstructive sleep apnea treated with mandibular advancement device: a prospective 1-year study. *J Clin Sleep Med.* **12**(2): 177–186.
37 Gasa M, Tamisier R, Launois SH, Sapene M, Martin F, Stach B, et al. (2013). Residual sleepiness in sleep apnea patients treated by continuous positive airway pressure. *J Sleep Res.* **22**(4): 389–397.
38 Genzor S, Prasko J, Vanek J, Asswad AG, Nadjarpour S, Sova M (2022). Adherence of obstructive sleep apnoea syndrome patients to positive airway pressure therapy - 10-year follow-up. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* **166**(4): 441–446.
39 Greenberg GD, Watson RK, Deptula D (1987). Neuropsychological dysfunction in sleep apnea. *Sleep.* **10**: 254–262.
40 Gunstad J, Paul RH, Cohen RA, Tate DF, Gordon E (2006). Obesity is associated with memory deficits in young and middle-aged adults. *Eat Weight Disord.* **11**(1): e15–e19.
41 Hobzova M, Hubackova L, Vanek J, Genzor S, Ociskova M, Grambal A, et al. (2017a). Cognitive function and depressivity before and after CPAP treatment in obstructive sleep apnea patients. *Neuro Endocrinol Lett.* **38**(3): 145–153.
42 Hobzova M, Prasko J, Vanek J, Ociskova M, Genzor S, Holubova M et al. (2017b). Depression and obstructive sleep apnea. *Neuro Endocrinol Lett.* **38**(5): 343–352.
43 Huang Y, Hennig S, Fietze I, Penzel T, Veauthier C (2020). The Psychomotor Vigilance Test Compared to a Divided Attention Steering Simulation in Patients with Moderate or Severe Obstructive Sleep Apnea. *Nat Sci Sleep.* **12**: 509–524.
44 Hugo J & Ganguli M (2014). Dementia and cognitive impairment: epidemiology, diagnosis, and treatment. *Clin Geriatr Med.* **30**(3): 421–442.
45 Iannella G, Magliulo G, Maniaci A, Meccariello G, Cocuzza S, Cammaroto G, et al. (2021). Olfactory function in patients with obstructive sleep apnea: a meta-analysis study. *Eur Archf Otorhinolaryngol.* **278**(3): 883–891.
46 International Classification of Sleep Disorders. 3rd ed. Darien, IL USA: American Academy of Sleep Medicine. 2014.
47 Jackson ML, Howard ME, Barnes M (2011). Cognition and daytime functioning in sleep-related breathing disorders. *Prog Brain Res.* **190**: 53–68.

48 Jiang X, Wang Z, Hu N, Yang Y, Xiong R, Fu Z (2021). Cognition effectiveness of continuous positive airway pressure treatment in obstructive sleep apnea syndrome patients with cognitive impairment: a meta-analysis. *Exp Brain Res.* **239**(12): 3537–3552.
49 Kilpinen R, Saunamaki T, Jehkonen M (2014). Information processing speed in obstructive sleep apnea syndrome: a review. *Acta Neurol Scand.* **129**: 209–218.
50 Koo DL, Kim HR, Kim H, Seong JK, Joo EY (2020). White matter tract-specific alterations in male patients with untreated obstructive sleep apnea are associated with worse cognitive function. *Sleep.* **43**(3): zsz247.
51 Lafreniére A, Lina JM, Hernandez J, Bouchard M, Gosselin N, Carrier J(2023). Sleep slow waves' negative-to-positive-phase transition: a marker of cognitive and apneic status in aging. *Sleep.* **46**(1): zsac246.
52 Lal C, Ayappa I, Ayas N, Beaudin AE, Hoyos C, Kushida CA, et al. (2022). The Link between Obstructive Sleep Apnea and Neurocognitive Impairment: An Official American Thoracic Society Workshop Report. *Ann Am Thorac Soc.* **19**(8): 1245–1256.
53 Lal C, Weaver TE, Bae CJ, Strohl KP (2021). Excessive Daytime Sleepiness in Obstructive Sleep Apnea. Mechanisms and Clinical Management. *Ann Am Thorac Soc.* **18**(5): 757–768.
54 Landry S, O'Driscoll DM, Hamilton GS, Conduit R (2016). Overnight Motor Skill Learning Outcomes in Obstructive Sleep Apnea: Effect of Continuous Positive Airway Pressure. *J Clin Sleep Med.* **12**(5): 681–688.
55 Lau EY, Eskes GA, Morrison DL, Rajda M, Spurr KF (2010). Executive function in patients with obstructive sleep apnea treated with continuous positive airway pressure. *J Int Neuropsychol Soc.* **16**: 1077–1088.
56 Lee MH, Lee SK, Kim S, Kim REY, Nam HR, Siddiquee AT, et al. (2022). Association of Obstructive Sleep Apnea With White Matter Integrity and Cognitive Performance Over a 4-Year Period in Middle to Late Adulthood. *JAMA Netw Open.* **5**(7): e2222999.
57 Lezak M, Howieson D, Loring D (2004). Neuropsychological assessment. 4th edition. Oxford University Press.
58 Li J, Yan W, Yi M, Lin R, Huang Z, Zhang Y (2022). Efficacy of CPAP duration and adherence for cognitive improvement in patients with obstructive sleep apnea: a meta-analysis of randomized controlled trials. *Sleep Breath.* Doi: 10.1007/s11325-022-02687-y. Epub ahead of print.
59 Li W, Xiao L, Hu J (2013). The comparison of CPAP and oral appliances in treatment of patients with OSA: a systematic review and meta-analysis. *Respir Care.* **58**(7): 1184–1195.
60 Liguori C, Mercuri NB, Izzi F, Romigi A, Cordella A, Sancesario G, Placidi F (2017). Obstructive Sleep Apnea is Associated With Early but Possibly Modifiable Alzheimer's Disease Biomarkers Changes. *Sleep.* **40**(5). doi: 10.1093/sleep/zsx011.
61 Lojander J, Kajaste S, Maasilta P, Partinen M (1999). Cognitive function and treatment of obstructive sleep apnea syndrome. *J Sleep Res.* **8**(1): 71–76.
62 Longlalerng K, Nakeaw A, Charawae AE, Reantong P, Prangyim U, Jeenduang N (2021). Effects of six weeks high-intensity interval training and resistance training in adults with obesity and sleep-related breathing disorders. *Sleep Sci.* **14**(Spec 1): 41–48.
63 Loredo JS, Ancoli-Israel S, Dimsdale JE (1999). Effect of continuous positive airway pressure vs. placebo continuous positive airway pressure on sleep quality in obstructive sleep apnea. *Chest.* **116**: 1545–1449.
64 Lusic Kalcina L, Pavlinac Dodig I, Pecotic R, Valic M, Dogas Z (2020). Psychomotor Performance in Patients with Obstructive Sleep Apnea Syndrome. *Nat Sci Sleep.* **12**: 183–195.
65 Macchitella L, Romano DL, Marinelli CV, Toraldo DM, Arigliani M, De Benedetto M, Angelelli P (2021). Neuropsychological and socio-cognitive deficits in patients with obstructive sleep apnea. *J Clin Exp Neuropsychol.* **43**(5): 514–533.
66 Mathieu A, Mazza S, Décary A, Massicotte-Marquez J, Petit D, Gosselin N, et al. (2008). Effects of obstructive sleep apnea on cognitive function: a comparison between younger and older OSAS patients. *Sleep Med.* **9**(2): 112–120.
67 Mazza S, Pepin JL, Naegele, B, Plante J, Deschaux C, Levy P (2005). Most obstructive sleep apnoea patients exhibit vigilance and attention deficits on an extended battery of tests. *Eur Respir J.* **25**: 75–80.
68 Miyake A, Shah P (1999). Models of working memory: Mechanisms of active maintenance and executive control. United Kingdom: Cambridge University Press.
69 Morys F, Dadar M, Dagher A (2021). Association Between Midlife Obesity and Its Metabolic Consequences, Cerebrovascular Disease, and Cognitive Decline. *J Clin Endocrinol Metab.* **106**(10): e4260–e4274.
70 Naëgelé B, Pepin JL, Levy P, Bonnet C, Pellat J, Feuerstein C (1998). Cognitive executive dysfunction in patients with obstructive sleep apnea syndrome (OSAS) after CPAP treatment. *Sleep.* **21**: 392–397.
71 Olaithe M & Bucks RS (2013). Executive dysfunction in OSA before and after treatment: a meta-analysis. *Sleep.* **36**: 1297–1305.
72 Park HR, Cha J, Joo EY, Kim H (2022a). Altered cerebrocerebellar functional connectivity in patients with obstructive sleep apnea and its association with cognitive function. *Sleep.* **45**(1): zsab209.
73 Park SH, Bae WY, Kim S, Kim YG, Yun YB, Lee HG et al. (2022b). Parameters affecting improvement of excessive daytime sleepiness in obstructive sleep apnea patients. *Am J Otolaryngol.* **44**(1): 103683.
74 Patel A & Chong DJ (2021). Obstructive Sleep Apnea: Cognitive Outcomes. *Clin Geriatr Med.* **37**(3): 457–467.
75 Patil S, Schneider H, Gladmon E, Magnuson T, Smith PL, O'Donnell CP, et al. (2004). Obesity and upper airway mechanical control during sleep. *Am J Respir Crit Care Med.* **169**: A435.
76 Pollicina I, Maniaci A, Lechien JR, Iannella G, Vicini C, Cammaroto G, et al. (2021). Neurocognitive performance improvement after obstructive sleep apnea treatment: state of the art. *Behav Sci.* **11**(12): 180.
77 Prabhakar NR, Peng YJ, Nanduri J (2020). Hypoxia-inducible factors and obstructive sleep apnea. *J Clin Invest.* **130**(10): 5042–5051.
78 Quaye E, Galecki AT, Tilton N, Whitney R, Briceño EM, Elkind MSV, et al. (2023). Association of Obesity With Cognitive Decline in Black and White Americans. *Neurology.* **100**(2): e220–e231.
79 Randerath W, Verbraecken J, de Raaff CA, Hedner J, Herkenrath S, Hohenhorst W et al. (2021). European Respiratory Society guideline on non-CPAP therapies for obstructive sleep apnoea. *Eur Respir Rev.* **30**(162): 210200.
80 Redline S, Tishler PV, Hans MG, Tosteson TD, Strohl KP, Spry K (1997). Racial difference in sleep disordered breathing in African Americans and Caucasians. *Am J Respir Crit Care Med.* **155**: 186–192.
81 Ryan CM & Bradley TD(2005). Pathogenesis of obstructive sleep apnea. *J Appl Physiol.* **99**: 2440–2450.
82 Sabil A, Blanchard M, Annweiler C, Bailly S, Goupil F, Pigeanne T, et al. (2022). Pays de la Loire Sleep Cohort study group. Overnight pulse rate variability and risk of major neurocognitive disorder in older patients with obstructive sleep apnea. *J Am Geriatr Soc.* **70**(11): 3127–3137.
83 Saconi B, Yang H, Watach AJ, Sawyer AM (2020). Coping Processes, Self-Efficacy, and CPAP Use in Adults With Obstructive Sleep Apnea. *Behav Sleep Med.* **18**(1): 68–80.
84 Seda G & Han TS (2020). Effect of Obstructive Sleep Apnea on Neurocognitive Performance. *Sleep Med Clin.* **15**(1): 77–85.
85 Seda G, Matwiyoff G, Parrish JS (2021). Effects of Obstructive Sleep Apnea and CPAP on Cognitive Function. *Curr Neurol Neurosci Rep.* **21**(7): 32.
86 Sforza E, Haba-Rubio J, De Bilbao F, Rochat T, Ibanez V (2004). Performance vigilance task and sleepiness in patients with sleep-disordered breathing. *Eur Respir J.* **24**: 279–285.
87 Sharma H, Sharma SK, Kadhiravan T, Mehta M, Sreenivas V, Gulati V, Sinha S (2010). Pattern & correlates of neurocognitive dysfunction in Asian Indian adults with severe obstructive sleep apnoea. Indian J Med Res. **132**: 409–414.

88 Shieu MM, Dunietz GL, Paulson HL, Chervin RD, Braley TJ (2022). The association between obstructive sleep apnea risk and cognitive disorders: a population-based study. *J Clin Sleep Med.* **18**(4): 1177–1185.
89 Shpirer I, Elizur A, Shorer R, Peretz RB, Rabey JM, Khaigrekht M (2012). Hypoxemia correlates with attentional dysfunction in patients with obstructive sleep apnea. *Sleep Breath.* **16**(3): 821–827.
90 Shu Y, Chen L, Li K, Li H, Kong L, Liu X, et al. (2022). Abnormal cerebellar-prefrontal cortical pathways in obstructive sleep apnea with/without mild cognitive impairment. *Front Neurosci.* **16**: 1002184.
91 Sova M, Sovova E, Hobzova M, Zapletalova J, Kamasova M, Kolek V (2015). The effect of continuous positive airway pressure therapy on the prevalence of masked hypertension in obstructive sleep apnea patients. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* **159**(2): 277–282.
92 Sovova E, Sova M, Hobzova M, Kaminek M, Kolek V, Taborsky M, et al. (2011). Complicated course of ischemic heart disease in a patient with obstructive sleep apnea. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* **155**(1): 51–54.
93 Stranks EK & Crowe SF (2016). The Cognitive Effects of Obstructive Sleep Apnea: An Updated Meta-analysis. *Arch Clin Neuropsychol.* **31**(2): 186–193.
94 Tkacova R, McNicholas WT, Javorsky M, Fietze I, Sliwinski P, Parati G, Grote L, Hedner J; European Sleep Apnoea Database study collaborators (2014). Nocturnal intermittent hypoxia predicts prevalent hypertension in the European Sleep Apnoea Database cohort study. *Eur Respir J.* **44**(4): 931–941.
95 Tulek B, Atalay NB, Kanat F, Suerdem M (2013). Attentional control is partially impaired in obstructive sleep apnoea syndrome. *J Sleep Res.* **22**: 1–8.
96 Ueno-Pardi LM, Souza-Duran FL, Matheus L, Rodrigues AG, Barbosa ERF, Cunha PJ, et al. (2022). Effects of exercise training on brain metabolism and cognitive functioning in sleep apnea. *Sci Rep.* **12**(1): 9453
97 Ulander M, Hedner J, Stillberg G, Sunnergren O, Grote L (2022). Correlates of excessive daytime sleepiness in obstructive sleep apnea: Results from the nationwide SESAR cohort including 34,684 patients. *J Sleep Res.* **31**(6): e13690.
98 US Preventive Services Task Force, Mangione CM, Barry MJ, Nicholson WK, Cabana M, Chelmow D, Rucker Coker T, et al. (2022). Screening for Obstructive Sleep Apnea in Adults: US Preventive Services Task Force Recommendation Statement. *JAMA.* **328**(19): 1945–1950.
99 Vanek J, Prasko J, Genzor S, Ociskova M, Holubova M, Sova M, et al. (2020a). Insomnia and emotion regulation. *Neuro Endocrinol Lett.* **41**(5): 255–269.
100 Vanek J, Prasko J, Genzor S, Ociskova M, Kantor K, Holubova M, et al. (2020b). Obstructive sleep apnea, depression and cognitive impairment. *Sleep Med.* **72**: 50–58.
101 Vanek J, Prasko J, Ociskova M, Genzor S, Sovova E, Sova M, et al. (2022). Screening for obstructive sleep apnoea in high-risk patients with mood disorders. *Neuro Endocrinol Lett.* **43**(4): 218–226.
102 Vardanian M & Ravdin L (2022). Cognitive Complaints and Comorbidities in Obstructive Sleep Apnea. *Sleep Med Clin.* **17**(4): 647–656.
103 Verstraeten E & Cluydts R (2004). Executive control of attention in sleep apnea patients: theoretical concepts and methodological considerations. *Sleep Med Rev.* **8**: 257–267.
104 Verstraeten E, Cluydts R, Pevernagie D, Hoffmann G (2004). Executive function in sleep apnea: controlling for attentional capacity in assessing executive attention. *Sleep.* **27**: 685–693.
105 Wallace A & Bucks RS (2013). Memory and obstructive sleep apnea: a meta-analysis. *Sleep.* **36**: 203–220.
106 Wang ML, Wang C, Tuo M, Yu Y, Wang L, Yu JT, et al. (2020). Cognitive Effects of Treating Obstructive Sleep Apnea: A Meta-Analysis of Randomized Controlled Trials. *J Alzheimers Dis.* **75**(3): 705–715.
107 Watach AJ, Hwang D, Sawyer AM (2021). Personalized and Patient-Centered Strategies to Improve Positive Airway Pressure Adherence in Patients with Obstructive Sleep Apnea. *Patient Prefer Adherence.* **15**: 1557–1570.
108 Weingarten JA (2022). Cost-Effectiveness of Continuous Positive Airway Pressure Therapy Versus Other Treatments of Obstructive Sleep Apnea. *Sleep Med Clin.* **17**(4): 559–567.
109 Xu WL, Atti AR, Gatz M, Pedersen NL, Johansson B, Fratiglioni L (2011). Midlife overweight and obesity increase late-life dementia risk: a population-based twin study. *Neurology.* **76**(18): 1568–1574
110 Zhao Z, Zhang D, Sun H, Chang D, Lv X, Lin J et al. (2022). Anxiety and depression in patients with chronic obstructive pulmonary disease and obstructive sleep apnea: the overlap syndrome. *Sleep Breath.* **26**(4): 1603–1611.