Obstructive Sleep Apnea and Neurocognitive Function

Clete A. Kushida, MD, PhD, Deborah A. Nichols, MS
Sleep Medicine Center, Stanford University, California, USA

Declines in various domains of neurocognitive function are observed in patients with obstructive sleep apnea, and these declines may be reversible with continuous positive airway pressure. However, upon reviewing the literature, a majority of the current studies are limited by small sample sizes and study design constraints. Additional large-scale, randomized clinical trials are needed to explore these relationships as well as to assess the etiology of the neurocognitive decline in obstructive sleep apnea patients and to determine which neurocognitive domain is most affected by obstructive sleep apnea and reversible by continuous positive airway pressure.

Key Words Review, Clinical trial, Positive airway pressure, Treatment outcome.
cognitively impaired than OSA patients without hypoxemia. Data from the large-scale Sleep Heart Health Study (SHHS) have indicated that when nocturnal time spent with oxygen saturations less than 85% (as a percentage of total sleep time) was dichotomized into those participants in the top quartile of the distribution and those in the lower three quartiles, motor speed was significantly impaired in those who were more hypoxic.37 Additionally, the SHHS investigators found that poorer motor speed and processing speed performance were associated with more severe oxygen desaturation despite controlling for variables such as degree of daytime sleepiness, age, gender, and educational level.

Another theory is that the decline in NCF with OSA is related to either sleep fragmentation or the consequent sleepiness. However, this theory also does not appear to be completely supported by the literature. While studies have shown that OSA patients performed worse on neuropsychological tests than both healthy volunteers and patients with other disorders of excessive sleepiness,23 additional studies have demonstrated that subjective sleepiness is absent in many individuals with significant SDB.24-26 In the SHHS, a slight increase in NREM stage 1 (N1) sleep and a higher arousal index were found; however, these factors were not correlated with performance on tests of NCF.37 Epworth Sleepiness Scale total score for SHHS participants predicted processing speed; however, the poorer motor speed and processing speed performance persisted after controlling for these scores.37

Perhaps the most reasonable explanation is that these OSA-related neurocognitive deficits are the result of a combination of both hypoxemia and decreased vigilance due to sleep fragmentation and the resulting sleepiness. Some investigators24,41 found that deficits in OSA patients were associated with both of these factors.

Which Neurocognitive Domain is Most Affected by OSA and What Role does OSA Therapy have on CPAP?

In terms of which domain is most significantly affected by OSA, there is limited evidence to suggest that sleepiness is related to reduced attention and memory functioning.33,42,43 While hypoxemia appears to contribute to deficits in different aspects of executive functioning,33,34 The literature provides scant and mixed evidence to enable the prediction as to which domain (or variables within each domain) of NCF will be most affected by OSA and will result in significant reversal with continuous positive airway pressure (CPAP); this deficiency in the literature, in fact, provided the rationale for the design of the NHLBI-funded Apnea Positive Pressure Long-term Efficacy Study.44 CPAP has been shown to improve deficits in measured variables within the three domains of NCF in a few studies with limited sample sizes,23,28,45 presumably by both enhancing sleep quality/quantity and by increasing oxygenation. Specifically, these studies have demonstrated improvements in A/P tests,46-47 L/M tests,46 as well as in E/F tests.48 However, other investigators have detected persistent deficits in similar measures of psychomotor, short-term memory, and executive function with CPAP use, indicating that some deficits may be due to irreversible anoxic central nervous system damage.49-52

One of the major problems in formulating a response to this section’s question is that many of the prior studies had limitations. Many used only a limited number of tests; e.g., a review of executive function in OSA revealed that of the 40 studies evaluated, half assessed executive function using only one or two tests.53 Additionally, there is very little consistency between the tests selected to study a particular domain by different investigators, and prior attempts to standardize the neurocognitive test battery composition have been largely unsuccessful.53 The possibility that a specific test may evaluate more than one domain of NCF also arises. Further, study administration-related factors such as time-of-day, subject training sessions to minimize learning effects, and experience of the administering psychometricians also vary from study to study. The heterogeneity of the OSA samples assessed in the various studies is also a concern in the review of prior data.

Nevertheless, the available evidence does support the premise that all three domains of NCF are affected by OSA and experience some degree of reversal with CPAP. At this time, it is unclear which domain will be most affected and will reveal the most change with CPAP.

What Role does Individual Variability Play in the Different Results of Past Studies?

A key factor in studies of OSA and NCF is individual variability; there is evidence that deficits in NCF vary significantly among individuals, are independent of sleep history, and may involve a trait-like vulnerability to impairment from sleep loss, of which the neurobiological correlates are presently unidentified.43 The concept of cognitive (or brain) reserve may be used to illustrate these observations: the neural effect of sleep loss may be mediated through cognitive reserve, so that individuals with more reserve are able to withstand a greater insult before performance is detrimentally affected.51

Conclusions

There is a current lack of a comprehensive literature base containing large, well-controlled, and standardized randomized clinical trials that explore OSA and NCF; to the degree that the impact of OSA on NCF cannot be conclusively determined. However, the current literature suggests that OSA may affect three NCF domains, perhaps with differential effects. In parallel, the etiology of the possible NCF impairment related to OSA needs to be further studied, as well as whether there can be a reversal in OSA-related NCF deficits with treatment. Lastly, concepts such as individual variability and cognitive reserve need to be considered in the context of these future studies.
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Conflicts of Interest

The authors have no financial conflicts of interest.

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