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CLINICAL REVIEW

Neuropsychological functioning after CPAP treatment in obstructive sleep apnea: A meta-analysis

Wytske A. Kylstra [a,e,f], Justine A. Aaronson [b,c,*,f], Winni F. Hofman [c], Ben A. Schmand [c,d]

[a] Heliomare Rehabilitation, Wijk aan Zee, Netherlands
[b] Heliomare Research & Development, Wijk aan Zee, Netherlands
[c] Department of Psychology, Brain and Cognition group, University of Amsterdam, Amsterdam, Netherlands
[d] Department of Neurology, Academic Medical Center, Amsterdam, Netherlands

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SUMMARY

The generally held clinical view is that treatment with continuous positive airway pressure (CPAP) improves cognition in patients with obstructive sleep apnea (OSA). However, the cognitive domains in which recovery is found differ between studies. A meta-analysis was conducted to quantify the effect of CPAP treatment in OSA on neuropsychological functioning. A literature search of studies published from January 1990 to July 2012 was performed. The inclusion criteria were: randomized controlled trial, diagnosis of OSA by poly(somno)graphy, apnea/hypopnea index, duration and compliance of CPAP treatment reported, use of one or more standardized neuropsychological tests. Mean weighted effect sizes of CPAP treatment for seven cognitive domains were calculated, including processing speed, attention, vigilance, working memory, memory, verbal fluency and visuoconstruction. Thirteen studies encompassing 554 OSA patients were included. A small, significant effect on attention was observed in favor of CPAP ($d = 0.19$). For the other cognitive domains the effect sizes did not reach significance. Improvement on measures of sleepiness was modest ($d = 0.30–0.53$) and comparable to prior research. In conclusion, this meta-analysis indicates that the effect of CPAP on cognition is small and limited to attention. Contrary to the general assumption, only slight improvement of neuropsychological functioning after CPAP treatment can be expected.

Introduction

Obstructive sleep apnea (OSA) is characterized by complete cessations (apneas) and partial decreases (hypopneas) in respiration caused by pharyngeal collapse during sleep. The reduction of airflow causes oxygen desaturation, which can lead to sleep fragmentation and hypoxemia. Due to this, patients with OSA often wake up feeling tired, with excessive daytime sleepiness being the most reported complaint. In turn, this can hamper daily functioning.[1] OSA has also been associated with an increased risk for serious medical conditions, particularly cardiovascular diseases, such as hypertension, heart disease and stroke.[2,3]

Extensive research on neuropsychological functioning among adults with untreated obstructive sleep apnea has shown that OSA negatively affects cognitive and psychological functioning.[4] Vigilance, attention, executive functioning, memory and motor coordination have been found to be moderately to markedly affected. No substantial effects on intelligence, verbal functioning, or visual perception have been reported.[1,5,6]

The treatment of choice for OSA is continuous positive airway pressure (CPAP). CPAP corrects the respiratory disturbances and the resultant transient desaturation, leading to less sleep fragmentation during sleep.[7] Consequently, it is expected that when sleep is normalized by CPAP treatment, functioning in daily living, cognitive functioning, and psychological wellbeing of OSA patients will improve. Previous meta-analyses demonstrated significant improvement in sleepiness and self-reported health status with CPAP when compared to placebo treatment or conservative management.[8–10] A number of reviews on cognitive functioning in OSA patients after CPAP treatment have documented partial reversibility of cognitive dysfunction.[1,11,12] The cognitive domains in which recovery was noted, as well as the extent of recovery,

* Corresponding author. Heliomare Research & Development, PO Box 78, 1940 AB Beverwijk, Netherlands. Tel.: +31 88 920 8013.
E-mail addresses: w.kylstra@heliomare.nl (W.A. Kylstra), j.aaronson@heliomare.nl (J.A. Aaronson), w.f.hofman@uva.nl (W.F. Hofman), b.a.schmand@amc.uva.nl (B.A. Schmand).
[e] Tel.: +31 88 920 8328.
[f] These authors contributed equally to this paper.

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Abbreviations

AHI	apnea/hypopnea index
BMI	body mass index
CPAP	continuous positive airway pressure
EF	executive functioning
ESS	Epworth sleepiness scale
HADS	hospital anxiety and depression scale
MSLT	multiple sleep latency test
MWT	maintenance of wakefulness test
OSA	obstructive sleep apnea
PASAT	paced auditory serial addition task
PG	polygraphy
PSG	polysomnography
RCT	randomized controlled trial
RDI	respiratory disturbance index
TMT	trail making test

differed widely across the studies reviewed. This might be due to differences in methods, neuropsychological measures, clinical characteristics and treatment compliance. Importantly, these reviews were qualitative and their conclusions were based on reported statistical significance levels without consideration of the magnitude of any observed effects.

In order to quantify the magnitude of the overall effect of CPAP treatment in OSA on neuropsychological functioning, we carried out a meta-analysis of the randomized controlled trials of CPAP treatment in OSA.

Methods

Literature search

We initially performed a literature search of Medline, PsycInfo, Embase and Cochrane Library covering the period from January 1990 to December 2011. In August 2012 we updated our search. Search terms for OSA were *apnea (MeSH), apn*ea, obstructive sleep apn*ea, OSA, hypopn*ea* and *SAHS*. Treatment search terms included *positive pressure respiration (MeSH), continuous positive airway* pressure, CPAP, bilevel positive airway pressure, BiPAP, positive pressure therapy* and *nocturnal ventilation*. Search terms for cognitive measures were *mental processes (MeSH), neuropsychol*, mental status, cogniti*, memory, attention, vigilance, executive* and *psychomotor*. Searches for all possible combinations of OSA, treatment and cognitive measures were conducted. We identified additional published studies by scanning the reference lists of the identified papers and checking for journal publications of conference abstracts. Two independent assessors identified relevant studies based on title and abstract that included empirical data related to the treatment effect on neuropsychological functioning in OSA.

Inclusion criteria

Studies had to meet the following criteria to be included in the meta-analysis:

- The diagnosis OSA was made by polysomnography (PSG) or polygraphy (PG) and the number of apneas and hypopneas per hour sleep was stated by apnea/hypopnea index (AHI) or respiratory disturbance index (RDI).
- The treatment of CPAP was investigated within a randomized controlled design.
- Duration and compliance of CPAP treatment for both the experimental and control group was reported. In case this information was not originally reported, we contacted the study authors to obtain relevant data.
- Assessment using at least one standardized neuropsychological test was employed as a dependent variable.
- Test scores were reported for both the experimental and control group at baseline and after treatment (mean and standard deviation), or other statistics that could be converted to effect sizes. In case this information was not originally reported, we contacted the study authors to obtain relevant statistics.

When articles reported overlapping samples of participants, the article with the largest sample size was included.

The quality of the randomized controlled trial (RCT) in the final selection was judged using the Jadad rating score assessing randomization procedure, blinding and description of dropout.[13]

Exclusion criteria

Studies were eliminated according to the following exclusion criteria: monographs, letters, book chapters, commentaries, review articles, case studies, dissertations, abstracts, studies within pediatric (<18 years) or elderly populations (>65 years) and studies within special medical populations with OSA (e.g., dementia, stroke or Down's syndrome).

Outcome measures

Primary outcome measures

Multiple neuropsychological tests were used across studies to assess cognitive functioning. All neuropsychological tests were classified into seven cognitive domains following two standard textbooks of neuropsychological assessment[14,15]: processing speed, attention, vigilance, working memory, memory, verbal fluency and visuoconstruction. Appendix 1 lists the included tests per cognitive domain.

Secondary outcome measures

For subjective sleepiness, the Epworth sleepiness scale (ESS), a self-rating of recent sleepiness behavior, was used, as it was employed in the majority of studies reviewed. For similar reasons, objective sleepiness was quantified by the multiple sleep latency test (MSLT), a measure of the time taken to fall asleep, and the maintenance of wakefulness test (MWT), a measure of the ability to stay awake. Mood was assessed by the hospital anxiety and depression scale (HADS), a self-report questionnaire consisting of an anxiety and a depression subscale.

Participant and study variables

We recorded variables that are considered important risk factors for OSA such as age and body mass index (BMI). BMI was classified according to the World Health Organization criteria as normal (BMI 20.0–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2) or obese (BMI ≥30 kg/m^2).[16] We registered the AHI in order to quantify the severity of OSA. By convention OSA severity is classified as mild, moderate or severe (AHI, >5; >15; >30 events/h, respectively).[17]

We recorded the average number of hours usage of CPAP per night. Patients were considered compliant when using CPAP for more than five days a week and for more than 4 h a night, as defined by Kribbs et al.[18] Duration of treatment was registered in weeks as noted in the study designs.