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ORIGINAL ARTICLE

Obstructive sleep apnea, verbal memory, and executive function in a community-based high-risk population identified by the Berlin Questionnaire Akershus Sleep Apnea Project

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Abstract
Purpose Cognitive functions in community-dwelling adults at high risk of obstructive sleep apnea have not been described and nor are associations between cognitive functions and obstructive sleep apnea severity fully understood. The study aimed to describe verbal memory and executive function in community-dwelling adults identified by the Berlin Questionnaire and to investigate associations between these cognitive domains and different obstructive sleep apnea severity indicators.

Methods Among 29,258 age- and gender-stratified persons 30–65 years who received the Berlin Questionnaire by mail, 16,302 (55.7%) responded. From 654 randomly drawn respondents with BQ high risk who were approached for study participation, 290 participants (55.9% males, mean age 48.2 years) were included. Verbal memory was assessed by Rey Auditory Verbal Learning Test and executive function by Stroop test. Obstructive sleep apnea severity indicators were assessed by polysomnography.

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Results Mean (standard deviation) verbal learning score was 42.0 (8.9), mean interference time was 31.1 (12.7), median (25th percentile, 75th percentile) apnea–hypopnea index was 7.7 (2.4–22.2), and mean average oxygen saturation was 94.3 (2.0). Verbal learning score was independently associated with average oxygen saturation (β=0.721, p=0.025) in multivariate linear regression models adjusted for putative confounders. Interference time was only related to OSA severity indicators in bivariate analyses.

Conclusions Verbal memory and executive function impairments were mild in community-dwelling adults at high risk of obstructive sleep apnea. Average oxygen saturation was the indicator of obstructive sleep apnea severity most strongly associated with cognitive function.

Keywords Neurobehavioural manifestations · Polysomnography · Epidemiology · Sleep apnea syndromes · Sleep disordered breathing

Introduction

The association between moderate to severe obstructive sleep apnea (OSA) and impaired neurocognitive function is well-established [1–6]. It is unclear whether this association is related to intermittent oxygen desaturations or the repeated arousals of OSA [1–6]. Neurocognitive function consists of basal processes (i.e., attention, motor speed, and vigilance) and more differentiated cognitive functions, of which impairments in verbal memory [7, 8] and executive functioning [9–11] have been found to be most strongly related to OSA. However, findings of cognitive impairments in patients with moderate to severe OSA have not been consistently reproduced in community-based studies.

We identified seven community-based studies [12–18] and two studies of mild OSA in volunteers [19, 20] that assessed cognitive function with rater-administered instruments in addition to objective sleep measures. Four studies reported associations between OSA and at least one cognitive domain [13, 14, 19, 20]. Affected cognitive domains were verbal memory (Wechsler Memory Scale [13], declarative memory factor [20]), and working memory (composite factor [20]), spatial orientation (Clock Test [13]), executive function (Wechsler Adult Intelligence Scale-Revised Digits Backward Subtest [19]), and cerebral efficiency (composite factor [14]).

Five of the identified studies reported analyses by variables assessing oxygen saturation (4% oxygen desaturation index, lowest oxygen saturation, or percentage time below 90% oxygen saturation [13, 16–18, 20]). In all these studies, the associations with oxygen saturation were at least as strong as the associations reported between cognitive functions and apnea–hypopnea indices (AHIs). The average oxygen saturation during sleep has recently been associated with cerebrovascular regulation in community-dwelling adults [21]. None of the identified community-based studies reported analyses by the arousal index.

In addition to the question of which mechanisms of OSA are associated with cognitive impairment, the relative importance of sociodemography and other potential health-related factors, such as alcohol abuse, sleepiness, use of hypnosedatives, smoking, and asthma [15–17, 19, 20], are not fully understood. The present study is unique in terms of including a large, community-based sample of participants identified by the Berlin Questionnaire (BQ) [22] as being at risk of OSA. The BQ is a widely used screening tool for OSA that has been used as a proxy for OSA diagnosis in nationwide US telephone surveys [23, 24] and validated in the Norwegian general population [25]. We are not aware of any study of cognitive function in a strictly defined probability sample of OSA. We aimed to (1) characterize cognitive function among community-based, BQ high-risk participants; and (2) investigate associations between verbal memory, executive function, and OSA severity as assessed by the AHI, indicators of oxygen saturation, and the arousal index before and after adjustment for putative confounders such as age, gender, comorbid conditions (alcohol abuse, asthma), use of hypnosedatives, sleepiness, smoking, and educational level. We hypothesized that verbal memory and executive function would be more closely related to variables assessing oxygen saturation than the AHI or the arousal index.

Materials and methods

Participants

The study population consisted of 29,258 persons (aged 30–65 years, 50% female) of whom 16,302 (55.7%) completed the BQ [22] (Fig. 1). Of them, 3,960 (24.3%) were classified at risk of OSA according to the BQ scoring algorithm [26], which defines three risk categories: (I) snoring, (II) daytime somnolence, and (III) obesity or self-reported hypertension (Table 1). Obesity was defined as a body mass index (BMI) >30 kg/m^2 calculated from self-reported weight and height. High risk on the BQ was defined as any combination of two or three of these categories [26].

From the 3,960 BQ high-risk persons classified at risk for OSA, 1,085 (27.4%) were randomly drawn and 852 of them were asked to participate in the Akershus Sleep Apnea Project (ASAP) for clinical investigations. Persons with established cardiovascular disease, diabetes, or previous otitis media surgery were oversampled. The reason that not all 1,085 were asked to participate was that, after the

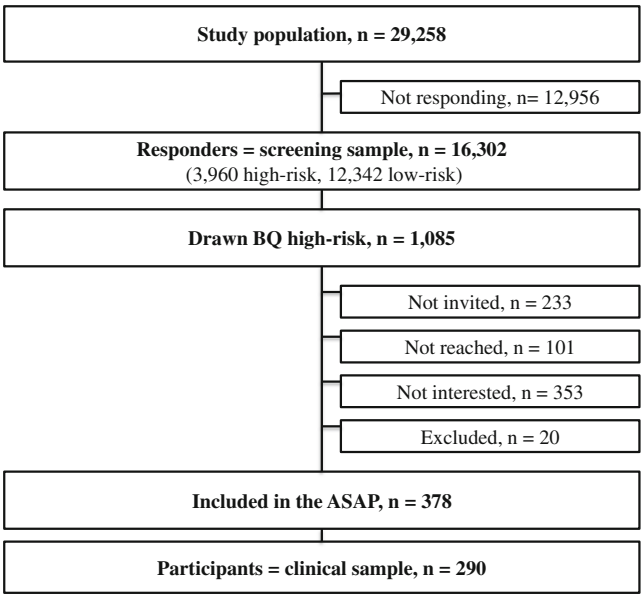

Fig. 1 Diagram to show the flow of persons from the study population to the final inclusion of participants

predefined strata were saturated, the invitation process was stopped. Altogether, 101 persons were not reached by telephone after three attempts; 353 declined participation; 233 not approached, and 20 were excluded according to the following exclusion criteria: use of continuous positive airway pressure (n=10), pregnancy (n=4), inadequate Norwegian language skills (n=4), and severe physical impairment as defined by inability to walk the stairs of our sleep laboratory (n=2). This recruitment procedure resulted in 378 participants which was 44.3% from 852. The present sample comprises consecutive, BQ high-risk persons included in the ASAP between 1 June 2006 and 31 March 2007. During this time, 654 persons had been approached and 290 participants (44.3%) were included.

Measures

Cognitive function

The Rey Auditory Verbal Listening Test (RAVLT) [27] was used to assess verbal memory. The RAVLT score, which is the sum of words retrieved from hearing 15 common words five times (range, 0–75), was calculated.

A shortened version of the Comali/Kaplan Stroop test [28] was used to assess response inhibition, which is regarded as a measure of executive function. The score computed was Stroop interference time, the time used on a task requiring response inhibition minus the average time used to name 48 colored patches and to read 48 color

Table 1 Description of the screening sample and the clinical sample

	Screening sample n=3,960	Participants n=290	p Value
Age in years, mean (SD)	48.8 (10.3)	48.2 (11.2)	0.357
Male gender, n (%)	2,198 (55.5)	162 (55.9)	0.899
Higher education, n (%)		80 (28.1)	
Body mass index, mean (SD)	29.1 (5.2)	29.0 (4.9)	0.951
Smoking, n (%)		89 (31.0)	
Alcohol abuse, n (%)		5 (1.7)	
Berlin Questionnaire			
Snoring category, n (%)	3,654 (92.3)	264 (91.0)	0.412
Daytime somnolence category, n (%)	2,498 (63.1)	205 (70.7)	0.005
Hypertension/obesity category, n (%)	2,624 (66.3)	193 (66.6)	0.914
Sleepiness and comorbidities			
Epworth Sleepiness Scale, mean (SD)	8.8 (4.5)	9.5 (4.2)	<0.001
Excessive daytime sleepiness, n (%)	1,336 (33.7)	117 (40.9)	<0.001
Self-reported asthma, n (%)	597 (16.5)	50.0 (18.8)	0.289
Polysomnography indices			
AHI, median (25th and 75th percentiles)		7.7 (2.4, 22.2)	
Arousal index, mean (SD)		19.9 (15.9)	
Nadir oxygen saturation, median (25th and 75th percentiles)		86.0 (82.0, 89.0)	
Average oxygen saturation, mean (SD)		94.3 (2.0)	
Relevant standard blood tests			
Blood hemoglobin[a], mean (SD)		15.1 (1.2)	
Serum ferritin[b], mean (SD)		121.5 (96.0)	

AHI apnea–hypopnea index, *SD* standard deviation

[a] Gram/deciliter

[b] Microgram/liter

names. Thus, a low score (seconds) indicates better executive function.

All assessments were made by the first author (HHS) before sleep registering.

Sleep recordings

Participants underwent in-hospital polysomnography, including two-channel electroencephalography (C4/A1 and C3/A2), two-channel electrooculography, one-channel submental electromyography, leg electromyography (tibialis), measurement of oxygen saturation by finger plethysmography (Nonin, Plymouth, MN, USA), assessment of breathing movements (Respitrace; Ambulatory Monitoring, Ardsley, NY, USA), nasal and oral air flow assessment (Protech, Woodinville, WA, USA), and body position monitoring. All electrophysiological signals were preamplified, stored and subsequently scored at 30-s epochs using the Somnologica 3.2 software package (Flaga-Medcare, Buffalo, NY, USA) in accordance with the Rechtshaffen and Kales scoring manual [29] by two US board-certified polysomnography technicians who were blinded to the result of the BQ. Apneas were scored when airflow dropped below 10% of the reference amplitude for more than 10 s. Hypopneas were scored when airflow dropped below 70% for more than 10 s with a subsequent oxygen desaturation of 4%. Arousals were documented and classified according to standard criteria [30]. The AHI and arousal indices were calculated as the sum of apneas plus hypopneas and the sum of arousals per hours of sleep, respectively. The following variables of oxygen saturation were registered: the 4% oxygen desaturation index (4% ODI) [13], percent time <90% saturation [16, 20], nadir oxygen saturation [20], and average oxygen saturation during sleep [21].

Demographic and clinical characteristics

Demographic data, BQ categories, sleepiness, and medical comorbidities were reported in the screening questionnaire 3–11 months prior to the overnight stay (Table 1). Educational level and smoking were reported during the overnight stay. Higher education was defined as having any college or university degree. A dichotomous variable of current smoking was computed, based on reported daily smoking. Missing information was replaced when possible by answers to other items assessing smoking. Diagnoses of alcohol abuse and/or dependency were determined by the structured clinical interview for Diagnostic and Statistical Manual for Mental Disorders [31] administered by the first author after measurement of cognitive function. The presence of asthma was assessed by self-report (yes/no) in the screening questionnaire. Sleepiness was assessed by a Norwegian translation of the Epworth Sleepiness Scale (ESS) [32, 33]. Excessive daytime sleepiness (EDS) was defined as a score >10 on the ESS. Blood hemoglobin and serum ferritin were analyzed from blood samples obtained in the morning after sleep registration.

Ethics

The study protocol was approved in 2005 by the Regional Committee for Medical Research Ethics in Eastern Norway, the National Data Inspectorate and the Norwegian Social Science Data Services. All subjects provided written consent before participating.

Statistical analyses

Differences between participants and nonparticipants included in the screening sample were analyzed by Student's *t* test and Chi-square test for normally distributed continuous variables and categorical variables, respectively. The choice of categorization of measures of OSA severity in tertiles was based on the distribution of the AHI with the upper tertile close to the clinical cut-off between mild (AHI 5–14.9) and moderate (AHI 15–29.9) OSA [34]. Differences in cognitive scores between clinical cut-off values of the AHI and these tertiles in other measures of OSA severity were analyzed by one-way ANOVA with Bonferroni post hoc test. Two-sided P values<0.05 were considered statistically significant. Comparisons of cognitive test results between groups of putative confounders were performed with Student's *t* test. Standard multiple regression models adjusting for age, gender and higher education were used to examine the effect of OSA severity on test results. Because of missing information regarding polysomnography data ($n=1$), oxygen saturation data ($n=2$), higher education ($n=5$), RAVLT ($n=4$), and Stroop test ($n=2$), the numbers of participants included in multivariate analyses declined to a minimum of 281. Non-normal variables assessing OSA severity were logarithmically transformed. Standard models were finally adjusted by adding putative confounders and strata variables one by one to these basic models. If a 15% change in the coefficient of the measure of OSA severity was observed, the variable was included in the final model. Interaction analyses and analyses of alternative distributions of measures of OSA severity were performed. All statistical analyses were obtained by using the Statistical Package for Social Sciences, version 16.0.

Results

Sociodemographic and clinical characteristics are displayed in Table 1. There were no significant differences in age, gender, snoring, obesity, or history of hypertension between the 290 participants and the 3,670 nonparticipants. However, a

significantly higher proportion of participants than non-participants were classified in the daytime somnolence category (participants 70.7%, nonparticipants 62.5%), and in the EDS category (participants 43.1%, nonparticipants 33.0%). Five persons fulfilled the diagnostic criteria for alcohol abuse/dependency.

The mean RAVLT score and Stroop interference time among all participants were 42.0 words retrieved (SD=8.9) and 31.1 s (SD=12.7), respectively. Compared with available norms [35, 36], the group performed 1.3 to 1.2 standard deviations below normal mean. Unadjusted mean cognitive test scores by commonly used cut-points for the AHI and tertiles of nadir- and average oxygen saturation are displayed in Table 2. Participants with AHI ≥15 had significantly longer mean interference times on the Stroop test than participants without OSA (p=0.001). A similar pattern with a significant loss of cognitive performance among participants in the tertile with the most severe versus mildest oxygen saturation was seen when categorized by lowest mean nadir oxygen saturation (83.0–54.0) and mean average oxygen saturation (93.8–81.8). Similar but less discriminant patterns were seen for tertiles of the 4% ODI and percent time <90% saturation (data not shown). Cognitive test scores did not differ significantly between tertiles of the arousal index (data not shown).

Bivariate differences in cognitive scores by putative confounders are displayed in Table 3. Correlation coefficients between the Stroop interference times and standard blood samples were not significant. Correlation coefficients between the RAVLT score and blood hemoglobin and serum ferritin were –0.168 (p=0.005) and –0.120 (p=0.046), respectively. The ESS was not significantly related to any of the cognitive tests (data not shown).

The final multiple regression models for the RAVLT score and Stroop interference time with average oxygen saturation as the independent variable assessing OSA severity are presented in Tables 4 and 5. Average oxygen saturation was found to be independently related to the RAVLT score but not to the Stroop test.

Neither logarithmically transformed AHI, nadir oxygen saturation, nor 4% ODI were independently related to the RAVLT score and the Stroop interference time (Online Resource, Tables 1–4). Percent time <90% was not independently related to the RAVLT score but to the Stroop interference time when adjusted for age, gender, and higher education (Online Resource, Tables 7–8). However, this association disappeared when BMI or BQ risk categories were added to the model.

Discussion

To our knowledge, this is the first study to describe verbal memory and executive function in community-dwelling

Table 2 Unadjusted mean cognitive test scores by established cut-off values of the AHI or tertiles of nadir- and average oxygen saturation

Test	Category 1 *n* (range) Mean±SD	Category 2 *n* (range) Mean±SD	Category 3 *n* (range) Mean±SD	*F* test[a] *p* Value	Trend test *p* Value
	AHI	AHI	AHI		
	111 (0.0–4.9)	70 (5.0–14.9)	104 (15.0–104.0)		
RAVLT score[b]	43.2±8.2	41.8±9.4	40.7±9.3	0.109	0.036
Stroop interference time[c]	28.4±12.0*	30.5±11.5	34.5±13.6	0.001	<0.001
	Upper tertile nadir O_2	Mid tertile nadir O_2	Lower tertile nadir O_2		
	85 (95.0%–89.0%)	110 (88.0%–84.0%)	93 (83.0%–54.0%)		
RAVLT score[b]	43.2±8.4*	42.9±8.2*	39.7±9.9	0.010	0.008
Stroop interference time[c]	29.2±12.5*	29.1±11.8*	35.5±13.0	<0.001	0.001
	Upper tertile average O_2	Mid tertile average O_2	Low tertile average O_2		
	97 (97.8%–95.3%)	93 (95.2%–93.9%)	98 (93.8%–81.8%)		
RAVLT score[b]	45.5±8.9*	41.6±8.4	38.8±9.5)	<0.001	<0.001
Stroop interference time[c]	27.2±9.7*	32.7±14.4	33.7±12.8)	<0.001	<0.001

[a] Test for overall model fit

[b] Sum of trials 1–5

[c] Difference in seconds

*p<0.05 for post hoc tests between category 1 and the two other categories identified by Bonferroni post hoc tests

AHI apnea–hypopnea index, *RAVLT* Rey Auditory Verbal Learning Test

Table 3 RAVLT score and Stroop interference time according to cofactors

	Number	RAVLT score[a] Mean±SD	*p* Value	Number	STROOP interference time[b] Mean±SD	*p* Value
Gender						
Male	161	39.8±9.1	<0.001	160	31.8±13.6	0.365
Female	125	44.6±8.0		128	30.5±11.7	
Higher education						
Yes	79	45.8±8.1	<0.001	80	28.9±11.4	0.088
No	203	40.6±8.8		203	31.7±13.0	
Smoking						
Yes	88	41.8±8.7	0.876	89	30.2±12.3	0.327
No	195	42.0±9.1			31.8±13.1	
Self-reported asthma						
Yes	48	42.1±9.9	0.905	49	33.7±14.9	0.134
No	214	42.2±8.7		216	30.6±12.5	
Use of hypnosedatives						
Yes	15	42.1±8.9	0.117	15	38.4±18.2	0.132
No	271	38.4±8.9		273	30.8±12.4	

[a] Rey Auditory Verbal Learning Test, sum of trials 1–5

[b] Difference in seconds

MI myocardial infarction

adults at high risk of having OSA, as identified by the BQ. Verbal memory was found to be independently related to average oxygen saturation, while executive function was not related to OSA severity. The AHI, which is the most commonly used measure when assessing OSA severity, was only related to cognitive function in bivariate analyses. The arousal index was not related to cognitive function in any analysis.

The recruitment of participants by the BQ in this study resulted in a sample of participants with a relatively low median AHI of 7.7 (25th percentile=2.4, 75th percentile=22.2) compared with clinical studies of OSA. However, more than one third of the sample had an AHI of ≥15, which is the criteria for moderate to severe OSA [34]. The cognitive function scores among participants were considerably higher than that reported in "mild cognitive impairment", which is the mildest clinical entity of impaired cognitive function [37]. However, the mean age of participants in this study was considerably lower than the mean age of patients with mild cognitive impairment [37]. Thus, our study adds knowledge to epidemiological factors associated with early cognitive decline rather than being a study of cognitively impaired subjects per se.

Table 4 Final model for RAVLT score fitted by age, gender, education, average oxygen saturation, and covariates

n=281 (adjusted R^2=0.199; p<0.001)[a]	β[b]	SE[c]	*p* Value
Intercept	−19.278	32.969	0.559
Gender (0=female, 1=male)	−3.251	1.033	0.002
Age[d]	−0.168	0.047	<0.001
Higher education[e]	4.722	1.076	<0.001
Average oxygen saturation	0.721	0.320	0.025
Body mass index	0.066	0.106	0.535

[a] Results from multiple regression analysis. Inclusion of the variables smoking, self-reported myocardial infarction, sleepiness, use of antidepressants, and use of hypnosedatives in the model did not affect the relationship between any covariate on the dependent variables

[b] β is the unstandardized regression coefficient of the variable

[c] SE is the standard error of β

[d] Unit of age, 5 years

[e] College or university

Studies in the last 5 years have confirmed that verbal memory is particularly affected by OSA pathology [7, 8]. On the other hand, the association between OSA and the complex executive function may be spurious [8, 11, 17] and potentially influenced by attention [5, 38]. Unfortunately, no objective measures of attention were available in the ASAP. Accordingly, the Stroop interference time test, which provides adjustment for baseline speed [5], was chosen.

We have not identified any previous studies that have reported test results from the RAVLT or the Comali/Kaplan Stroop test in community-based OSA populations. We therefore compared the RAVLT score with general population norms [35] and the Stroop interference time with an available clinical sample [36]. Both results indicate mildly impaired cognitive function. RAVLT scores are equivalent with general population norms of persons 20–30 years older than the actual age of participants of the study [35].

The salient finding of the second aim of this study was the support of our hypothesis that oxygen saturation, rather than the AHI or the arousal index, was associated with

Table 5 Model for Stroop interference time fitted by age, gender, education, average oxygen saturation and covariates

n=282 (adjusted R^2=0.223, p<0.001)[a]	β[b]	SE[c]	p Value
Intercept	35.389	48.319	0.465
Gender (0=female, 1=male)	0.105	1.507	0.944
Age[d]	0.494	0.068	<0.001
Higher education[e]	−3.047	1.551	0.051
Average oxygen saturation	−0.360	0.470	0.444
Body mass index	0.206	0.156	0.189
Self-reported asthma	2.331	1.857	0.211

[a] Results from multiple regression analysis. Inclusion of the variables smoking, logAHI, myocardial infarction, sleepiness, use of antidepressants, and use of hypnosedatives in the model did not affect the relationship between any covariate on the dependent variables

[b] β is the unstandardized regression coefficient of the variable

[c] SE is the standard error of β

[d] Unit of age, 5 years

[e] College or university

verbal learning and executive function after adjusting for age, gender, higher education, and putative confounders. Smoking, alcohol consumption, and subjective sleepiness were not related to cognitive test scores and thus were not putative confounders of the associations examined.

Regarding the AHI, the fact that cognitive test scores differed significantly by tertiles of the AHI only in bivariate analyses (Table 2) suggests that the association between AHI and cognitive function was potentially mediated by covariates included in the final multiple regression analysis. On the other hand, this is unlikely because the association between the AHI and both cognitive test scores disappeared when age, gender, and higher education, which are unlikely mediators of this association, were adjusted for. Regarding potential effect modification between the AHI and these covariates, no interaction terms were significant when added, one pair at a time, to the multivariate models of AHI and verbal memory and executive function, respectively.

Regarding oxygen saturation, a novel finding in our study was that average oxygen saturation, rather than the commonly used variables, explained most of the variation in cognitive function. The effect of average oxygen saturation has, somewhat surprisingly, not been reported in any of the eight identified previous community-based studies or studies of mild OSA [12–17]. Studies of cognitive function in clinical samples of moderate to severe OSA have reported a similar level of average oxygen saturation as our study [7, 39, 40], and a recent study also found that average oxygen saturation was an independent predictor of cognitive decline in middle-aged adults with moderate to severe OSA [41]. This finding was age-dependent.

We believe that the lack of an association between the arousal index and measures of cognitive function should be understood in relation to our finding of an independent association with oxygen saturation. Objective sleep quality has traditionally been more strongly associated with memory consolidation than hypoxia [42]. However, regarding OSA, accumulating evidence from studies applying neuroimaging techniques [43–45] and studies of animal models [46, 47] indicates that intermittent hypoxia is the most important cause of neural injury related to this disorder over time.

Finally, it should be kept in mind that different variables assessing intermittent hypoxia or oxygen saturation might be related to other aspects of chronic disease than OSA, such as the nonlinear oxygen dissociation curve, abdominal obesity limiting the functional residual capacity, or other lung diseases. It is therefore interesting that the relations between average oxygen saturation and cognitive function were not altered by the inclusion of blood hemoglobin and serum ferritin in the multivariate models. Regarding obesity, BMI only slightly altered the association between average oxygen saturation and the cognitive test results. The multiple regression model for Stroop interference time was adjusted for potential confounding by self-reported asthma. Asthma was not found to be related to the association between average oxygen saturation and the RAVLT score.

In summary, the finding of an independent association between oxygen saturation, rather than the AHI or the arousal index, with early cognitive decline in participants with high risk of OSA emphasizes that future studies should specify variables of OSA severity prior to analysis. Future studies should also include enough subjects to allow adjustment for putative confounders. Regarding which variables to assess, we argue that average oxygen saturation and other variables assessed through the whole night (4% ODI, percentage time below 90% saturation) should be considered in community-based samples or studies of mild OSA because of the advantage of being less vulnerable to artifacts than, for example, the nadir oxygen saturation.

Strengths and limitations

The use of polysomnography to assess OSA severity in a large, community-based sample is an obvious strength. However, the use of only a single, hospital-based polysomnography recording is a potential limitation of the study [48]. Therefore, the possible first night effect could not be controlled for. It remains unknown what, if any, effect it may have had on indicators of OSA severity.

Another strength of the study is that cognitive tests were performed by the same physician at identical time points the day prior to the polysomnography. Both tests were suggested by Decary et al. [2] for use in OSA patients, although the

limited number of tests increased the probability of a type 2 statistical error (i.e., finding no association when the association is truly present). The cognitive tests should ideally have been performed after the sleep studies, but with the chronic nature of OSA, we consider this to be only a minor weakness.

Regarding potential limitations, the relatively low response, and participation rates biased the sample towards including participants with more daytime impairments. However, we believe that this mechanism did not significantly affect our findings because daytime impairments did not contribute to the multivariate models displayed in Tables 4 and 5.

The multivariate models should ideally have been adjusted for diagnosed asthma rather than self-reported asthma and more putative confounders such as better measures of attention [9] or inflammation [49]. However, the statistical models in this study are adjusted for more putative confounders than most previous community-based studies of the relation between OSA and cognitive function.

Finally, the cross-sectional design and the lack of a control group were limitations to causal interpretations. The cross-sectional design also limited us from including variables in the multivariate models that assessed psychological distress because it could not be determined whether psychological distress would be a cause or a consequence of cognitive impairment.

Conclusion

Verbal memory and executive function were mildly impaired in community-dwelling adults at high risk of OSA. The data supported the hypothesis that memory decline in OSA, as measured by the RAVLT score, is more strongly related to oxygen desaturation than the AHI or the arousal index. Average oxygen saturation during sleep, rather than traditional variables assessing oxygen saturation related to OSA, was the variable that was most strongly related to the RAVLT score. No independent relations were found between executive function, as measured by the Stroop interference time, and variables of OSA severity. The effect of average oxygen saturation on cognitive function should be explored in future studies.

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Conflicts of interest All authors except Torbjørn Omland declare that they have no conflict of interest. Torbjørn Omland has received speaker honoraria from Roche and Abbott (<10.000 USD).

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