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Early View

Original article

Detection of mild cognitive impairment in middle-aged and older adults with obstructive sleep apnea

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Title Page

Title: Detection of mild cognitive impairment in middle-aged and older adults with obstructive sleep apnea.

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Author's contributions: Ms. Gagnon contributed to the study's conception and design and to data acquisition, analysis, and interpretation; she drafted the paper and revised it following author's comments. Ms. Baril and Chami contributed to the study's design, data acquisition and interpretation, and to the critical revision of the work. Drs. Montplaisir, Carrier, Lafond, Gauthier, and Gagnon contributed to the study's conception and to data interpretation, and revised the work critically. Dr. Gosselin contributed to the study's conception and design and to data interpretation; she also helped draft the paper and revised it critically. All authors approved the final version for publication and are accountable for all aspects of the work.

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Summary: Montreal Cognitive Assessment is better to detect cognitive impairment in individuals with obstructive sleep apnea.

Abstract

Obstructive sleep apnea increases the risk for mild cognitive impairment and dementia. The present study aimed at characterizing the ability of two cognitive screening tests, the Mini-Mental State Examination and Montreal Cognitive Assessment, to detect mild cognitive impairment in adults aged 55 to 85 years with versus without obstructive sleep apnea.

We included 42 subjects with mild and 67 subjects with moderate to severe obstructive sleep apnea. We compared them to 22 control subjects. Mild cognitive impairment was diagnosed with a comprehensive neuropsychological assessment. We used receiver operating characteristic curves to assess screening test abilities to detect mild cognitive impairment.

Both screening tests showed similar discriminating abilities in controls. However, among the mild and the moderate to severe obstructive sleep apnea groups, the Mini-Mental State Examination was not able to correctly identify subjects with mild cognitive impairment. The Montreal Cognitive Assessment's discriminant ability was acceptable in both sleep apnea groups and was comparable to what was observed in controls.

The Mini-Mental State Examination should not be used to screen for cognitive impairment in patients with obstructive sleep apnea. The Montreal Cognitive Assessment could be used in clinical settings. However, clinicians should refer to neuropsychology when neurodegenerative processes are suspected.

Keywords (3-10): Sleep-Disordered Breathing, mild cognitive impairment, aging, Montreal Cognitive Assessment, Mini-Mental State Examination, cognition, dementia, neuropsychological deficits.

Introduction

Recent studies showed that obstructive sleep apnea (OSA) is a risk factor for mild cognitive impairment (MCI) and dementia in older adults [1-4]. Hence, being able to easily identify patients at risk of cognitive decline could significantly affect treatment decision for OSA and modify the course of their clinical follow-up, particularly for patients presenting no or mild daytime sleepiness. Clinicians can screen for cognitive decline using patients' subjective report or objective validated cognitive tests. Although subjective cognitive complaint is a good predictor of MCI and dementia in the elderly [5-8], this method is not appropriate for OSA patients. In fact, 23–70% of OSA patients report subjective cognitive complaints, but most of the time, these complaints are not associated with an objective impairment [9]. This suggests that asking OSA patients to evaluate their cognitive status might not reflect objective cognitive decline, which underscores the importance of using screening tests to detect cognitive impairment in this population.

The Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) are cognitive screening tests widely used to identify MCI in older adults [10, 11]. Studies performed in elderly individuals indicated that the MoCA is a better discriminating tool for detecting MCI than the MMSE [12-15]. However, the MoCA seems less able to detect MCI in populations with comorbidities (e.g. Parkinson's disease, chronic obstructive pulmonary disease) compared to populations with no comorbid conditions (area under the curve [AUC] of 0.79-0.84 versus 0.85-0.90, respectively) [11, 16-18]. The same pattern was reported for MMSE [12-14, 17, 18]. These observations raise questions regarding the ability of cognitive screening tests to detect MCI in clinical populations, including OSA.

The present study aimed to compare the validity of the MMSE and the MoCA to detect MCI in individuals aged 55 years and older without (control subjects) or with OSA (mild versus moderate-to-severe). Studies have consistently showed that the MoCA is superior to the MMSE in detecting MCI [12-14, 16-18] and a study demonstrated that the Beijing version of the MoCA was reliable to detect cognitive dysfunction in young OSA patients.[19] Therefore, we hypothesized that the MoCA will be better at identifying MCI in the three groups. We also predicted that the MoCA and the MMSE will have lower discriminant validity in subjects with mild or moderate-to-severe OSA compared to control participants [12-14].

In order to clarify whether discrepancies in the validity of screening tests could be caused by the different nature of cognitive deficits in mild OSA, moderate-to-severe OSA, and control subjects, we also compared groups based on their MCI subtypes (amnestic versus non-amnestic; single versus multiple cognitive domains impaired). We hypothesized that control participants with MCI will have a cognitive profile typical of preclinical Alzheimer's disease, with a predominance of amnestic MCI [20]. However, more heterogeneous cognitive profiles will be found in mild and moderate-to-severe OSA patients because their cognitive impairments may not be entirely due to neurodegeneration [21-24].

Methods

Detailed methods are described in the online supplement**.** One hundred thirty-one participants were recruited for this study, from 2012 to 2017, and 76% of these participants were included in previous articles on genetics and neuroimaging.[25-27] Recruitment procedure and inclusion/exclusion criteria were extensively described in previous studies [25-27]. Briefly, we included subjects aged 55-85 years with at least 7 years of education. We excluded participants

with a diagnosis of sleep disorders other than OSA, morbid obesity, neurological (e.g. Parkinson's disease, previous stroke, brain tumor, epilepsy) or psychiatric disease (e.g. diagnosed major depression and anxiety disorder), respiratory disorder other than OSA (e.g. chronic obstructive pulmonary disease), and medication that may affect cerebral functioning such as hypnotics, antidepressants, anticonvulsants and opioids. The hospital ethics committee approved the study and all participants gave their written informed consent to participate in the study.

Protocol overview

All participants filled out questionnaires regarding their sleep quality and mood. They underwent one night of in-laboratory polysomnography recording that included electroencephalogram, electromyograms (chin and anterior tibialis), electrooculogram, and electrocardiogram as well as measurements from thoraco-abdominal strain gauges, an oronasal canula, and a transcutaneous finger pulse oximeter.

The next morning, all participants underwent a 3-hour neuropsychological assessment with tests administered in the same order and according to standard procedures [28]. The MoCA and the MMSE were administered first. Detailed procedures for administration and scoring of screening tests and the complete neuropsychological evaluation procedure are displayed in Table E1 in the Online Data Supplement.

We used the three following criteria for MCI diagnosis [29]: 1) An objective cognitive impairment (score under 1.5 standard deviation) on at least two measures of the same cognitive domain (attention and speed processing; executive functions; visual and verbal episodic learning and memory; visuospatial abilities; language); 2) Preserved independence in daily activities according to the Activities of Daily Living Inventory [30]; 3) Psychiatric condition or medication use cannot better explain the presence of cognitive impairments. We categorized MCI according

to four subtypes: amnestic single domain, amnestic multiple domains, non-amnestic single domain and non-amnestic multiple domains [29].

Statistical analyses

We divided participants based on their apnea-hypopnea index (AHI). Subjects with AHI <5 were considered controls; AHI ≥ 5 and <15 were considered mild OSA; and AHI ≥15 were considered moderate-to-severe OSA. [31] They were also divided according to their cognitive status (non-MCI versus MCI). We performed group (control, mild OSA, and moderate-to-severe OSA) by cognitive Status (non-MCI and MCI) ANOVAs on demographic and clinical variables. We decomposed significant interactions using simple effect analysis.

We used receiver operating characteristic (ROC) curve analyses with AUC[confidence interval (CI) of 95%] to determine the MoCA and the MMSE discriminant indices in MCI detection (namely sensitivity, specificity, negative predictive value, positive predictive value, percentage of correctly categorized) in each group separately. We used the Youden Index [y = sensitivity + specificity-1] combined with examination of the balance between sensitivity and specificity to determine optimal cut-offs. Discriminatory abilities of the MoCA and the MMSE were compared between groups using Hanley and McNeil method [32]. Pearson's Chi-squared tests were used to compare groups for MCI subtypes. We performed statistical analyses with SPSS for Mac 20.0 (SPSS Science, Chicago, Illinois, USA). Statistical significance was set at $p<0.05$.

Results

Sample characteristics

This sample included non-OSA and OSA participants with a wide range of severity (AHI from 0 to 84) (see Table 1 for group characteristics and statistics). We recruited a similar proportion of MCI in all groups (control: 36.4%; mild OSA: 40.5%; moderate-to-severe OSA: 40.3%), allowing between group comparisons with equivalent cognitive status. No significant differences between the four groups were found for age, sex and education. We found no significant group by cognitive status interactions for demographic variables. However, a cognitive status effect (MCI vs. non-MCI) was found for education, where MCI participants had lower education compared to non-MCI participants (F (1,125) = 12.6; p <0.01).

Questionnaires

We found that the moderate-to-severe OSA group had a significantly higher score on the Pittsburgh Sleep Quality Index compared to the control group (see Table 1). No significant interactions or other group effects were found for the questionnaires.

OSA related variables

We found no significant group by cognitive status interactions on polysomnographic variables. However, we observed group differences that are expected for OSA versus control participants, more specifically for body mass index, sleep fragmentation, percentage of REM sleep and oxygen saturation (see Table 1 for details).

Detection of MCI in moderate-to-severe OSA participants using screening tests

ROC curve analyses are presented in Table 2 and illustrated in Figure 1A. MMSE mean and standard deviation were 28.64 ± 1.32 for moderate-to-severe OSA participants, and the AUC was 0.64 [95% CI; 0.51-0.77]. The optimal MMSE cut-off value was 30 (≤ 29 indicating MCI; 89% sensitivity; 43% specificity; 61% correctly classified). The MoCA mean score in moderate-to-severe OSA participants was 26.48 ± 2.48 and ROC curve analysis showed an AUC of 0.82

[95% CI; 0.71-0.92]. The optimal MoCA cut-off value was 27 (≤ 26 indicating MCI, with a 70% sensitivity, 73% specificity and 72% correctly classified).

Detection of MCI in mild OSA participants using screening tests

The mean score of the MMSE was 28.86 ± 1.35 for mild OSA participants. The ROC curve analysis showed an AUC of 0.74 [95% CI; 0.59–0.90]. The MMSE optimal cut-off was 28 with score ≤27 indicating MCI with 53% sensitivity, 84% specificity and 71% correctly classified. MoCA mean score was 27.02 ± 2.23. We found an AUC of 0.85 [95% CI; 0.74–0.97] (see Figure 1B). The optimal MoCA cut-off was 28, where scores ≤27 indicated MCI with a sensitivity of 88%, a specificity of 76% and 91% of participants correctly classified (see Table 3).

Detection of MCI in control participants using screening tests

The MMSE mean score was 28.36 ± 1.97 for control participants and the ROC curve analysis showed an AUC of 0.94 [95% CI; 0.84–1.00]. The optimal MMSE cut-off was 29 with score ≤28 indicating MCI with 88% sensitivity, 87% specificity and 86% correctly classified. The MoCA mean score was 26.45 ± 3.10. We found an AUC of 0.92 [95% CI; 0.78-1.00] (see Figure 1C). The optimal MoCA cut-off was 27, where scores ≤26 indicated MCI with a sensitivity of 88%, a specificity of 86% and 86% of participants correctly classified (see Table 4).

Between-group comparisons for discriminant validity

When we compared groups for screening tests' discriminant abilities using the Hanley and McNeil method, [32] we found that the MMSE showed significantly higher discriminant validity in the control group compared to the moderate-to-severe OSA group (See tables for AUC and confidence intervals; $p < 0.01$) and a trend for higher discriminant validity when the control group was compared to the mild OSA group ($p = 0.05$). There were no significant differences in the MoCA's discriminant abilities between control subjects and mild or moderate-to-severe OSA participants ($p = 0.23$ and $p = 0.13$, respectively).

Cognitive profile in OSA versus non-OSA participants

The control group showed a higher percentage of amnestic MCI (87.5%) compared to the mild OSA group (64.7%) and the moderate-to-severe OSA group (59.3%), however this difference was non-significant (X^2 (2) = 2.18; p = 0.34). Surprisingly, groups did not differ regarding the proportion of single versus multiple cognitive domains affected (X^2 (2) = 0.99; p = 0.61) (see Figure E1).

Discussion

Main findings

This study aimed at evaluating the ability of two widely used cognitive screening tools, the MMSE and the MoCA, to detect MCI in OSA patients aged 55 years and older compared to a group of non-OSA individuals. We found that the MoCA performed similarly to detect MCI in mild and moderate-to-severe OSA participants and control subjects. More specifically, our results showed that the MoCA was able to correctly identify 81% of mild OSA and 72% of moderate-to-severe OSA patients with MCI, whereas 86% of control subjects were correctly identified as having a MCI. The optimal MoCA cut-off to discriminate MCI in mild OSA was ≤27, and ≤26 for moderate-to-severe OSA individuals, with very good AUC (0.85 and 0.82, respectively) and acceptable sensitivity and specificity. Clinicians can therefore use the MoCA to screen for MCI in older adults with OSA, but they have to be aware that this screening test will correctly identify only 72% of their patients with moderate-to-severe OSA.

Regarding the MMSE in OSA participants, the more balanced MMSE cut-off for detecting MCI was ≤28 for mild OSA and ≤29 for moderate-to-severe OSA and therefore, only OSA patients with a score of 29/30 or a perfect score 30/30 were considered as not presenting MCI in our

sample. This result reflects that MMSE is not a valid screening tool to detect MCI in OSA patients. In fact, in mild OSA participants, we found that the MMSE had a poor sensitivity (53%),a good specificity (84%), and only a fair AUC (0.74%), whereas in the moderate-to-severe OSA group the MMSE had a good sensitivity (89%), but a very poor specificity (43%) and non-acceptable AUC (0.64) [33]. This screening tool should not be used for OSA patients in clinical settings, since it will result in a high number of undetected patients or false positives.

Cognitive screening tests in patients with comorbid conditions

Although the MoCA had a better sensitivity and specificity than the MMSE, this screening test has to be used with caution among patients with OSA and those with comorbid clinical conditions. In fact, our results showed that the MoCA performance to detect MCI in mild and moderate-to-severe OSA tends to be lower than what we found in our control participants as well as in control subjects tested in previous studies [11, 16-18]. We also observed lower discriminant validity in OSA participants for MMSE compared to control participants. Our results therefore confirm previous observations that screening tests have reduced validity in patients with a medical condition [11-18].

Better discriminant ability of the MoCA to screen for cognitive impairment

The higher discriminant ability observed for the MoCA compared to the MMSE in OSA patients is concordant with previous studies that found the MoCA better for detecting MCI compared to MMSE[12-15, 17]. This higher discriminant validity could be explained by the fact that the two screening instruments are not covering the exact same cognitive domains [18]. Indeed, MMSE emphasizes on the evaluation of language and orientation, while MoCA covers more broadly different cognitive domains, including attention and executive functions. In subjects with OSA and MCI, the cognitive profile may not be entirely attributed to ongoing neurodegenerative processes but could also be due to chronic sleep fragmentation and

intermittent hypoxemia that lead to attention, episodic memory and executive dysfunctions even in younger adults [21].

When we compared MCI subtypes between mild OSA, moderate–to-severe OSA and control participants, we found, however, no significant differences for the type (amnestic versus non-amnestic) or number (single versus multiple) of cognitive domains impaired. These MCI subtypes has been created base on the

Low MoCA score and risk of cognitive decline

The prevalence of MCI in individuals with OSA is unknown but is suspected to be high given the common risk factors that OSA shares with MCI (apolipoprotein epsilon 4 allele, hypertension, obesity, and metabolic syndrome) [34]. Moreover, sleep fragmentation and intermittent hypoxemia secondary to OSA may directly increase the risk of abnormal cognitive decline by increasing amyloid depositions and tau hyperphosphorylation in the brain, two main mechanisms in Alzheimer's disease pathogenesis [35]. In the present study, we have recruited our subjects based on their suspected or confirmed diagnosis of OSA at study entry; 40.5% of participants with mild OSA and 40.3% of individuals with moderate-to-severe OSA had MCI, but this proportion of MCI patients has to be confirmed in large cohort studies. Moreover, whether OSA patients with MCI have higher risk than non-OSA adults to develop dementia is unknown. In previous retrospective studies using MoCA to predict dementia, it was observed that 69.1% of MCI convert to dementia over a period of 18 months [36]. Longitudinal studies are needed in order to determine whether low MoCA scores reflect ongoing neurodegenerative processes and will predict progression to dementia in individuals with OSA.

Strengths and limitations

Our sample included a limited number of control subjects. However, when we compared the results obtained in our control subjects to those found in previous studies, we observed that

the discriminant ability of the cognitive tests was similar for our control subjects and those included in the other studies. [11, 16-18] Another weakness of the study is that we did not have longitudinal data that would have allowed a better understanding of the consequences of a low MoCA score over time, as well as the nature (i.e. neurodegenerative or not) of the cognitive impairment observed.

Conclusion

Our study showed that MoCA is an effective screening tool for cognitive impairment in OSA. Although MMSE remains widely used in clinical practice [18], our study found that this instrument could not acceptably detect MCI in patients with OSA. Because older OSA patients are more at risk of MCI and dementia, we suggest that clinicians should systematically use the MoCA to identify OSA patients with cognitive impairment and track changes in their cognitive profile depending on whether they use an OSA treatment or not. However, the MoCA should be used with caution because between 19 and 28% of our MCI participants with OSA have not been detected with this screening tool. Consequently, clinicians should refer to a neuropsychologist when a significant cognitive decline is suspected, particularly when the patient is reluctant to use the continuous positive airway pressure treatment or in the case of milder forms of OSA where the decision to treat or not depends more on daytime symptomatology.

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Tables

Table 1. Demographic and clinical characteristics of control, mild OSA and moderate-to-severe OSA participants.

	Control (1)	**Mild OSA (2)**	**Moderate-to-severe OSA (3)**	**F/X^2 values**	**Post-hoc tests**
Demographic					
Participants; n	22	42	67		n/a
Age; yrs	64.0(6.9)	63.5(6.3)	65.0(6.8)	0.7	
Sex; % male	59.1	78.6	79.1	3.9	
Education; yrs	14.7(3.5)	15.5(3.0)	14.7(4.4)	0.5	
Clinical					
BMI; kg/m^2	25.6(3.1)	27.2(4.0)	29.5(3.8)	10.3‡	1,2<3
VBI	0.8(1.0)	1.0(1.2)	1.2(1.2)	1.2	
BDI-II	5.7(5.0)	6.8(6.0)	7.2(5.5)	0.62	
BAI	4.1(4.3)	4.0(4.1)	4.5(4.7)	0.21	
ESS	7.4(5.2)	7.2(4.6)	9.1(4.7)	2.5	
PSQI	3.9(2.8)	4.7(2.9)	5.8(3.3)	3.8†	1<3
MCI; %	36.4	40.5	40.3	0.1	
Sleep					
Stage N1; %	16.6(7.1)	19.6(8.2)	28.1(13.8)	12.1‡	1,2<3
Stage N2; %	58.1(7.8)	56.2(8.4)	51.6(11.0)	5.1‡	1>3
Stage N3; %	9.6(9.0)	8.6(10.2)	6.3(7.2)	1.7	

REM; %	15.6(4.3)	15.7(5.6)	13.0(5.7)	3.8†	2>3
TST; min	366.9(61.1)	363.5(72.8)	355.2(72.3)	0.3	
Awakenings	37.3(13.7)	39.7(13.6)	54.3(26.8)	8.5‡	1,2<3
Efficiency; %	77.6(11.0)	77.9(11.9)	77.5(12.0)	0.0	
AHI	2.3(1.5)	9.5(3.1)	34.5(14.7)	110.9‡	1<2<3
Mean SpO_2; %	95.1(1.1)	94.9(1.1)	93.9(1.2)	13.8‡	1,2>3
SpO_2 <90%; min	0.2 (0.5)	1.9(3.2)	19.0(25.8)	14.8‡	1,2<3

Results are presented as mean (standard deviation). BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II; BMI, Body mass index; ESS, Epworth Sleepiness Scale; MCI, Mild cognitive impairment; OSA, Obstructive sleep apnea; PSQI, Pittsburgh Sleep Quality Index; SpO_2; Oxygen saturation, TST, Total sleep time; VBI, Vascular Burden Index; Yrs, years;. † p <0.05; ‡ p <0.01; n/a, non applicable.

Table 2. Validity of the MoCA and the MMSE in detecting MCI in moderate-to-severe OSA participants.

MoCA						MMSE					
Cut-off	SENS	SPEC	PPV	NPV	% Corr.	Cut-off	SENS	SPEC	PPV	NPV	% Corr.
30/29	100	18	45	100	51	30/29*	89	43	51	85	61
29/28	96	33	49	93	58	29/28	44	65	46	63	57
28/27	89	55	57	88	69	28/27	22	90	60	63	63
27/26*	70	73	63	78	72	27/26	7	93	40	60	58
26/25	59	85	73	76	75	26/25	4	98	50	60	60
25/24	37	98	91	70	73	25/24	4	100	100	61	61
24/23	26	98	88	66	67	24/23	0	100	0	60	60
23/22	11	100	100	63	64	23/22	0	100	0	60	60
AUC (95% CI): 0.82 (0.71 – 0.92)						AUC (95% CI 0.64): (0.51 – 0.77)					

AUC, Area under the curve; CI, Confidence interval; MMSE, Mini-Mental State Examination, MoCA, Montreal Cognitive Assessment; NPV, Negative predictive value; PPV, Positive predictive value; SENS, Sensitivity; SPEC, Specificity. *Optimal cut-off.

Table 3. Validity of the MoCA and the MMSE in detecting MCI in mild OSA participants

MoCA						MMSE					
Cut-off	SENS	SPEC	PPV	NPV	% Corr.	Cut-off	SENS	SPEC	PPV	NPV	% Corr.
30/29	100	24	47	100	55	30/29	82	52	54	81	64
29/28	100	52	59	100	71	29/28*	53	84	69	72	71
28/27*	88	76	71	91	81	28/27	24	96	80	65	67
27/26	71	80	71	80	76	27/26	6	100	100	61	62
26/25	47	84	67	70	69	26/25	6	100	100	64	62
25/24	29	96	83	67	69	25/24	6	100	100	61	62
24/23	12	96	67	62	62	24/23	6	100	100	61	62
23/22	6	100	100	61	62	23/22	0	100	0	60	60
AUC (95% CI): 0.85 (0.74 – 0.97)						AUC (95% CI) : 0.74 (0.59 – 0.90)					

AUC, Area under the curve; CI, Confidence interval; MMSE, Mini-Mental State Examination, MoCA, Montreal Cognitive Assessment; NPV, Negative predictive value; PPV, Positive predictive value; SENS, Sensitivity; SPEC, Specificity. *Optimal cut-off.

Table 4. Validity of the MoCA and the MMSE in detecting MCI in control participants

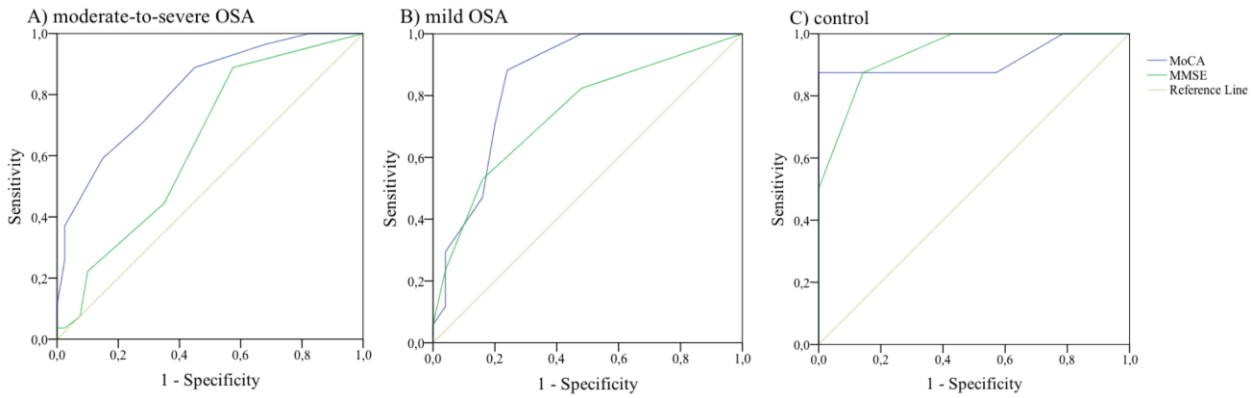
MoCA						MMSE					
Cut-off	SENS	SPEC	PPV	NPV	% Corr.	Cut-off	SENS	SPEC	PPV	NPV	% Corr.
30/29	100	21	42	100	50	30/29	100	57	57	100	73
29/28	88	43	47	86	59	29/28*	88	87	78	92	86
28/27	88	79	70	92	82	28/27	50	100	100	78	82
27/26	88	86	78	92	86	27/26	50	100	100	78	82
26/25*	88	100	100	93	95	26/25	38	100	100	74	77
25/24	28	100	100	93	95	25/24	13	100	100	67	68
24/23	63	100	100	82	86	24/23	13	100	100	67	68
23/22	50	100	100	78	82	23/22	0	100	0	64	64
AUC (95% CI): 0.92 (0.75 – 1.00)						AUC (95% CI) : 0.94 (0.84 – 1.00)					

AUC, Area under the curve; CI, Confidence interval; MMSE, Mini-Mental State Examination, MoCA, Montreal Cognitive Assessment; NPV, Negative predictive value; PPV, Positive predictive value; SENS, Sensitivity; SPEC, Specificity. *Optimal cut-off.

Figure Title and Captions

Figure 1. ROC curve comparisons between the MoCA and the MMSE in detecting MCI in (A) moderate-to-severe OSA, (B) mild OSA, and (C) control participants.

Moderate-to-severe OSA participants (A) had a significant higher AUC for the MoCA (AUC 0.82 [CI 95%; 0.71-0.92]) compared to the MMSE (AUC 0.64 [CI 95%; 0.51-0.77]). For mild OSA participants (B), the ROC curve had higher AUC for the MoCA (AUC 0.85 [CI 95%; 0.74–0.97]) compared to the MMSE (AUC 0.74 [CI 95%; 0.59–0.90]). Among (A) control participants, the ROC curve had a similar AUC for the MoCA (0.92 [CI 95%; 0.75–1.00)] compared to the MMSE (AUC 0.94 [CI 95%; 0.84–1.00]).


A) moderate-to-severe OSA
B) mild OSA
C) control
Sensitivity
1 - Specificity
0,0
0,2
0,4
0,6
0,8
1,0
MoCA
MMSE
Reference Line

Online Data Supplement

DETAILED METHODS

Participants

The following recruitment methods were used: reference from the Department of Pulmonology of the Hôpital du Sacré-Coeur de Montréal (n=35), newspaper ads asking volunteers for a study on sleep and cognitive health (n=63) and reference from other laboratories based on suspected obstructive sleep apnea (OSA) (n=33). We included participants aged between 55 and 85 years, with at least 7 years of education, without neuropsychological evaluation in the last year, and with French or English as their mother tongue. We excluded participants with a diagnosis of dementia based on the neuropsychological assessment (see Table E1), sleep disorders other than OSA (e.g. insomnia, restless leg syndrome, narcolepsy, rapid eye movement sleep behavior disorder), morbid obesity (body mass index >40 kg/m^2), and neurological (e.g. Parkinson's disease, previous stroke, brain tumors, epilepsy) or psychiatric disorders (e.g. diagnosed major depression and anxiety disorder). The use of medication (e.g., hypnotics, antidepressants, anticonvulsants, opioids) and/or drugs known to affect cognition, sleep, or cerebral functioning also led to exclusion.

Questionnaires

Because they may be associated with increased risk of MCI [1-9], we documented conditions such as depression and anxiety symptoms, poor sleep quality and cardiovascular diseases using the following instruments: the Beck Depression Inventory-II [10], the Beck Anxiety Index [11], the Pittsburgh Sleep Quality Index [12], and the Epworth Sleepiness Scale

[13, 14], the Activities of Daily Living Inventory filled by patients themselves and/or relatives [15], and the Vascular Burden Index [16].

Sleep data acquisition and analysis

All participants had a full-night in-laboratory polysomnographic recording. This protocol was extensively described in previous studies [17-19]. Briefly, we used 18 electroencephalographic channel montage combined with electrooculograms, electromoyograms and electrocardiogram. We monitored respiration with thoraco-abdominal strain gauges, an oronasal thermistor and a canula, in addition to a transcutaneous finger pulse oximeter to measure oxygen saturation. Sleep and respiratory events were scored according to the standard method [20, 21]. Apneas and hypopneas were summed and divided by the total hours of sleep to create the apnea-hypopnea index.

Neuropsychological procedure

We first administered the Montreal Cognitive Assessment (MoCA), followed by the Mini-Mental State Examination (MMSE) and all other neuropsychological tests. Questions related to orientation, such as date, month, year, day of the week, place, and city, were asked only during the MoCA. We then added the orientation score to the MMSE. According to the MoCA standard procedure, an extra point was given to participants with 12 years of education or less. Neuropsychological tests and measures were selected to assess five cognitive domains: 1) attention and speed processing; 2) executive functions; 3) visual and verbal episodic learning and memory; 4) visuospatial abilities; 5) language. All neuropsychological tests, normative data and selected measures, as well as criteria to define mild cognitive impairment (MCI) are presented in Table E1.

TABLES

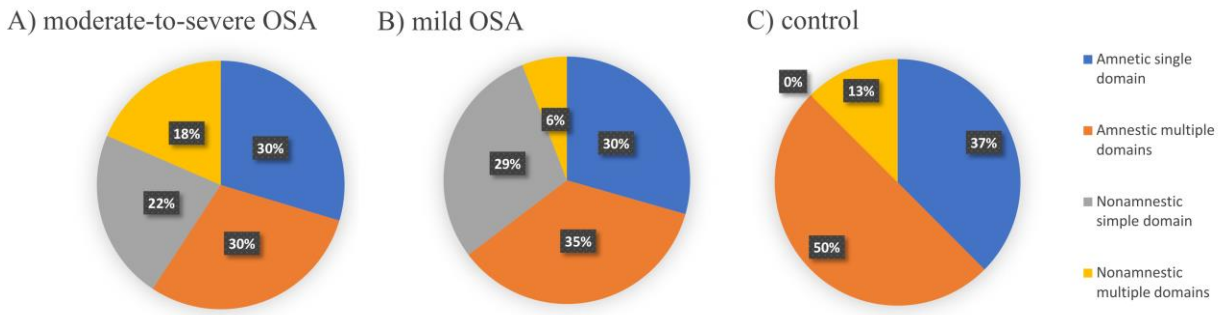
Table E1. Neuropsychological tests and variables used to identify MCI.

Tests	Variables	Criteria for domain impairment
Attention and speed processing		
CPT-II [22]	Omission % (T score) [22]	
	Variability of standard error (T score) [22]	
CWIT [23]	Part 1 (time) [23]	2/5 results ≥1.5 SD
Coding [24]	Scale score [24]	
TMT [25]	Part A (time) [26]	
Executive functions		
Digit Span [24]	Backward (scale score) [24]	
TMT [25]	Part B - Part A (time) [26]	
CPT-II [22]	Commission % (T score) [22]	
CWIT [23]	Part 3 – Part 1 (scale score time) [23]	2/7 results ≥1.5 SD
	Part 4- Part 3 (scale score time) [23]	
TOL [27]	Total move [27]	
	Total time [27]	
Verbal and visual episodic learning and memory		
RAVLT [28]	Sum of trials 1 to 5 [29]	
	List B [29]	2/7 results ≥1.5 SD
	Delayed recall [29]	
	Delayed recognition [29]	

BVMT-R [30]	Total recall (trials 1 to 3) [30]	
	Delayed recall [30]	
	Discrimination index [30]	
Visuospatial abilities		
ROCF [31]	Copy score [32, 33]	2/4 results ≥1.5 SD
BLOJ [34]	Number of correct answers [34]	
Bells test [35]	Number of omission [35]	
Blocs [24]	Scale score [24]	
Language		
BNT [36]	Number of correct answers [36]	2/4 results ≥1.5 SD
Vocabulary [24]	Scale score [24]	
Verbal fluency [23]	Phonemic (number of words) [23]	
	Semantic (number of words) [37]	

BLOJ, Benton Line Orientation Judgment; BNT, Boston Naming Test; BVMT-R, Brief Visuospatial Memory Test-revised; CPT-II, Continuous Performance Test – II, CWIT, Color-Word Interference test; MCI, mild cognitive impairment; RAVLT, Rey Auditory Verbal Learning Test; ROCF, Rey-Osterrieth Complex Figure; SD, standard deviation; TMT, Trail Making Test; TOL, Tower of London.

Figure E1. Proportions of MCI subtypes in (A) moderate-to-severe OSA, (B) mild OSA, and (C) control participants.



We observed a similar proportion of amnestic single domain between (C) the control (37%), (B) mild OSA (30%) and (A) moderate-to-severe OSA (30%) groups. The proportion of nonamnestic simple domain was similar in the mild OSA (29%) and the moderate-to-severe OSA (22%) groups, but there was no nonamnestic simple domain in the control group (0%). A higher proportion of amnestic multiple domains was observed for the control group (50%) compared to the mild OSA (35%) and the moderate-to-severe OSA (30%) groups. Inversely, we observed a lower proportion of nonamnestic multiple domains for the control and mild OSA participants compared to the moderate-to-severe OSA group. However, we found no significant group differences according to the type (amnestic versus non-amnestic) or number (single versus multiple) of cognitive domains impaired.

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