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CLINICAL REVIEW

Cognitive complaints in obstructive sleep apnea

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SUMMARY

Obstructive sleep apnea (OSA) is associated with impairments in cognitive functioning. Although cognitive complaints are related to quality of life, work productivity and health care expenditures, most research and all reviews have focused exclusively on objective cognitive functioning so far. In this systematic review, we assessed the available literature on subjective measures of cognition in adult OSA patients. Concentration complaints were consistently found to be more severe in untreated OSA patients as compared to primary snorers and healthy controls. The same seems to be true for memory and executive function problems, but firm conclusions cannot be made as of yet, due to methodological limitations of the available studies. Cognitive complaints appear to be at least partially related to subjective sleepiness. Importantly, they are not necessarily a sign of objective cognitive impairment. Additional research is needed to explore the relation between cognitive complaints, sleepiness and mood problems using validated and norm-referenced questionnaires for cognitive complaints. In addition, the impact of continuous positive airway pressure (CPAP) treatment on cognitive complaints in OSA warrants further study.

Introduction

Obstructive sleep apnea (OSA) is a sleep disorder estimated to affect 3–7% of the general population [1–3]. In OSA, episodes of (partial) obstruction of the upper airway cause intermittent hypoxemia and arousals during sleep [4], disrupting the sleep architecture and causing an overall poor quality of sleep. OSA results in significant impairments in daytime functioning, including excessive sleepiness, fatigue and mood problems [5]. Moreover, OSA patients often report cognitive complaints [6–8].

Cognitive functioning in OSA may be assessed objectively -using formal neuropsychological tests to assess cognitive performance- or subjectively, using self-report measures to assess daytime cognitive complaints. So far research in OSA has focussed primarily on objective cognitive functioning. Studies using objective measures of cognition in untreated OSA patients show impairments in memory function [9–12] as well as in attention and executive function [10,13–17]. Effect sizes range from moderate to large depending on the selection of cognitive tests and the control group [10,18]. Treatment with continuous positive airway pressure (CPAP) has been shown to improve performance on objective attention measures with medium effect sizes [19]. Improvements on objective measures for memory and executive function have not been found consistently, indicating that impairments in memory and executive function may persist, even after successful CPAP treatment [19,20].

Although widely used to study cognitive impairments in OSA, the ecological validity of objective measures of cognition is notoriously low [21,22]. Objective cognitive functioning often correlates poorly with cognitive complaints [23–29] and measures of quality of life [30,31]. In contrast, cognitive complaints (i.e., subjective cognitive functioning) have been found to relate to quality of life, health care utilization and work productivity in both the general population [32–34] and several medical conditions such as cancer [24,35,36]. In OSA, subjective daytime symptoms including cognitive complaints, were shown to influence treatment compliance [37] and health service expenditures [38]. Cognitive complaints may therefore serve as an important patient outcome measure next to objective cognitive functioning.

Abbreviations: ADHD, attention deficit hyperactivity disorder; AHI, apnea/hypopnea index; CDS, cognitive difficulties scale; CPAP, continuous positive airway pressure; ESS, Epworth sleepiness scale; OSA, obstructive sleep apnea; RDI, respiratory disturbance index.

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This review will give an overview of our current knowledge of cognitive complaints in patients with OSA, including their prevalence and type in different OSA populations. In addition, possible factors associated with cognitive complaints are reviewed, including objective cognitive functioning, daytime sleepiness and mood problems.

Methods

We reviewed published studies examining cognitive complaints in patients with OSA. Studies were included when adult patients were assessed (18 y and older) with OSA confirmed by polygraphy or polysomnography, in the absence of medical comorbidity, and in whom cognitive complaints were measured with at least one subjective or self-report measure of cognition. Searches were limited to papers written in English. MEDLINE, Cochrane and PsycINFO databases were searched for articles from 1960 until May 2013 using the key terms "sleep apnea/OSAS/sleep disordered breathing/sleep related breathing disorder" in combination with "cognition/memory/attention" or "subjective/neuropsychological/cognitive/neurobehavioural" and "functioning/complaints/symptoms".

The initial search yielded 1997 hits. Titles and abstracts were scanned for the inclusion criteria. If the abstract did not provide sufficient information, a full-text version was collected in which the method section and appendices were assessed. Studies using a quality of life scale as a measure of complaints, were only included if the results from subscales or items directly related to cognition were reported separately. Only 10 studies used a measure for cognitive complaints, all of them meeting our inclusion criteria. The reference lists of these articles yielded an additional two articles. A total of 12 articles were included for the review. Data from the articles were extracted using word processing software.

To assess the quality of the included studies, we constructed a 13-item checklist (see Table 1), based on quality criteria used in recent reviews on cognitive complaints in other medical populations [39,40]. Two authors (TJAV, MMS) rated each item, giving one point for each criterion fulfilled. Disagreement was solved by discussion.

Table 1
Scale for methodological quality assessment.

Each item is scored 1 (present) or 0 (absent)
Study sample
A. Inclusion and exclusion criteria are reported.
B. OSA is confirmed by poly(somno)graphic evaluation.
C. OSA severity is described using polysomnographic variables (at least AHI or RDI).
D. Demographic variables of participants are described (at least age and gender).
E. If CPAP treatment is studied, dropout rates are included.
Study design
F. Data collection is sufficiently described to replicate the study.
G. Cognitive complaints are a primary or secondary outcome measure.
H. Cognitive complaints are measured using a validated questionnaire.
I. Cognitive complaints in OSA patients are compared to at least one other group.
J. At least one factor associated with cognitive complaints is studied (objective cognitive functioning, sleepiness or mood).
Results
K. Recognized statistical techniques are used to analyze cognitive complaints.

AHI = apnea/hypopnea index; CPAP = continuous positive airway press; RDI = respiratory disturbance index.

Results

Included studies

Study characteristics

The characteristics of the included studies are summarized in Table 2. OSA populations differed across studies. In two studies OSA patients were recruited from the general community [8,41–43] and in 10 studies patients were recruited in sleep centers [6,7,44–51]. Four studies compared cognitive complaints in OSA patients to healthy controls [6,7,45,51], two studies compared OSA patients to a general community sample without OSA [8,41–43] and four studies compared OSA patients to other disorders (narcolepsy [45], attention deficit hyperactive disorder (ADHD) [48], primary snorers [49,50]). Two studies did not include a control group [46,47].

Six studies reported on memory complaints [6–8,44,45,51], seven studies on concentration complaints [6,8,44,48–51] and two on complaints about executive function [6,47]. Two studies only reported on cognitive complaints in general, without differentiating between specific types [43,46].

Demographic and clinical characteristics

Demographic and clinical characteristics are summarized in Table 3, with a separation between community and sleep center studies. As only two studies reported in sufficient detail on nocturnal oxygen desaturations as a marker for OSA severity [7,51], these data are not listed.

There was an important variation in sample size: the majority of studies included between 19 and 65 OSA patients. Three studies included larger numbers with Stoohs et al. including an exceptional number of 1610 patients [49]. In most studies, the number of controls roughly matched the number of patients, except for the studies by Stoohs et al. (OSA patients:controls 10:1) [49] and Jennum and Sjol (OSA patients:controls 1:10) [8].

Of the two community studies, one specifically targeted elderly OSA patients (>60 y old) [42,43]. OSA severity in this study was moderate (apnea/hypopnea index [AHI] = 30.4 ± 13.1 events/h), but with notably low sleepiness scores (Epworth sleepiness scale [ESS] = 6.2 ± 3.7). The second community study included adult patients (>30 y old), but did not provide information on OSA severity. Extrapolation of the findings of the community studies should therefore be made with caution.

The average age of OSA patients from the 10 sleep center studies varied from 41 to 61 y old. Three sleep center studies did not provide information on OSA severity (either AHI, respiratory disturbance index [RDI] or ESS) [44,45,50]. The seven studies reporting information on OSA severity showed moderate to severe OSA based on AHI (study means ranging from 21.4 to 48.9 events/h), RDI (means ranging from 25.6 to 59.2 events/h) and ESS (means ranging from 10.1 to 16.4), indicating that representative samples of OSA patients consulting sleep centers were included.

Methodological quality of studies

For a full overview of the quality ratings of the included studies, see Table 4. All studies reported in- and exclusion criteria, reported the study design in sufficient detail and included cognitive complaints as a primary or secondary outcome. The most common limitations were a lack of a validated questionnaire for cognitive complaints, and a failure to report on the relation between cognitive complaints and objective cognitive functioning, sleepiness or mood problems.

Prevalence of cognitive complaints in OSA

Untreated OSA patients versus general community controls

Jennum and Sjol [8] found a significantly higher number of OSA patients from a community sample to report concentration

Table 2
Study characteristics.

Study	Design	Primary objective	OSA population	Comparison group	Measure	Cognitive domain		
						Memory	Attention	Executive function
Chen et al. (2012) [43]	Case–control	Cognitive complaints in OSA	Sleep center	Healthy control	SCIRS	x	x	x
Daurat et al. (2010) [44]	Case–control	Memory complaints in OSA	Sleep center	Healthy control	MIA	x		
Flemons & Reimer (1998) [45]	Longitudinal, case–control	Change in quality of life in OSA after CPAP	Sleep center	Snorers	Yes/no-item	x		
							x	
Hood & Bruck (1997) [46]	Case–control	Memory complaints in narcolepsy	Sleep center	Healthy control narcolepsy	MIA	x		
Jennum & Sjol (1994) [39]	Case–control	Cognitive complaints in snorers and OSA	Community	Community without OSA	Yes/no-item	x		
					Yes/no-item		x	
Moore et al. (2001) [47]	Descriptive, uncontrolled	PSG measures and quality of life in OSA	Sleep center	–	MOS QOL[a]			
Mulgrew et al. (2007) [48]	Longitudinal, uncontrolled	Sleepiness and work limitations in OSA before and after CPAP	Sleep center	–	WLQ			x
Sangal & Sangal (2004) [49]	Case–control	Inattention and sleepiness in OSA and ADHD	Sleep center	ADHD	ADHDRS		x	
Sforza et al. (2010) [42]	Cross-sectional	Cognition and OSA in healthy elderly	Community	Community without OSA	CDS[a]			
Stoohs et al. (2008) [50]	Case–control	Clinical features of sleep disorders	Sleep center	Snorers and OSA without sleepiness	VAS-scale		x	
Ulfberg et al. (1996) [51]	Case–control	Sleepiness, subjective work performance in snorers and OSA	Sleep center	Snorers	Likert-scale		x	
Vernet et al. (2011) [52]	Case–control	Phenotype of residual sleepiness in OSA	Sleep center	Healthy control	CAARS		x	
					Yes/no-item	x		

CAARS = Conners' adult attention deficit hyperactivity disorder rating scale; SCIRS = subjective cognitive impairment rating scale; CDS = cognitive difficulties scale (McNair-R); FLP = functional limitations profile; MIA = metamemory index for adults; MOS QOL = medical outcome study quality of life; PSG = polysomnography; WLQ = work limitations questionnaire.

[a] Only assesses cognitive complaints in general, without specifying type of cognitive complaint.

problems (23%) compared to a community sample without OSA (14%). The percentage of OSA patients reporting memory problems was not significantly higher (OSA: 59%, non-OSA: 45%). The generalizability of the findings of this study may be limited, as no validated questionnaire was used for cognitive complaints and details on OSA severity were not provided. Flemons and Reimer [44] found 69% of OSA patients from a sleep center reporting concentration difficulties and 58% experiencing memory problems. Unfortunately, no formal comparisons were made for these problems with their control group. Sforza et al. administered the validated cognitive difficulties scale (CDS) in an elderly community population (age over 60 y), and did not find a difference between OSA patients and subjects without OSA [43]. It should be noted however that the CDS evaluates aspects of cognition that are typically affected in dementia or stroke patients, such as praxis and temporal orientation. This may have resulted in underestimating or masking cognitive complaints more typically related to OSA.

Untreated OSA patients from sleep centers versus healthy controls

Findings on cognitive complaints in sleep center samples comparing OSA to healthy controls are summarized in Table 5. Compared to healthy controls OSA patients were more likely to report difficulties concentrating on new tasks, performing monotonous tasks [50] and reported their life to be more impacted by problems with attention and vigilance [6]. Also OSA patients experienced more difficulties with memory, learning in general [6] and learning new tasks [50]. Findings on more specified memory complaints were inconsistent. Daurat et al. [7] found OSA patients to experience a decline in memory over time and to be more anxious about their memory compared to healthy controls. Hood and Bruck [45] could not replicate these findings however using the same questionnaire in their study design. Both studies failed to find a significant difference in subjective memory capacity between OSA patients and healthy controls. The inconsistent findings for these more specified memory complaints may be attributed to lack of statistical power in both studies due to small sample sizes ($N = 26$ and $N = 23$ respectively). With regard to executive function Chen et al. [6] found OSA patients to report more complaints regarding emotional control and motivation, but not regarding abstract thinking and problem solving.

Untreated OSA versus other disorders

Findings on OSA patients compared to other disorders are summarized in Table 6. Compared to primary snorers, OSA patients reported more concentration complaints, complaints performing monotonous tasks [49,50] and complaints learning and concentrating on new tasks [50]. Compared to narcolepsy patients, OSA patients perceived their memory to have a higher capacity and experienced less memory decline over time [45]. The only study comparing OSA patients to a non-sleep disorder group found that OSA patients experienced less inattention complaints than people with ADHD [48]. It should be noted that even though a validated questionnaire was used, this questionnaire is not designed to assess general attention complaints but attention complaints typically found in ADHD.

Table 3
Demographic and clinical characteristics.

Study	Group	*N*	Age (y)	Diagnostics	AHI (events/h)		RDI (events/h)	ESS	
Community studies									
Jennum & Sjol [39]	OSA	65	30–60	PG, RDI ≧5 events/h	–		–	–	
	COM	683							
Sforza et al. [42]	OSA	445	>68	PG, AHI >15 events/h	30.4 ± 13.1		–	6.2 ± 3.7	
	COM	382			8.7 ± 4.1			5.1 ± 3.4	
Sleep center studies									
Chen et al. [43]	OSA	19	41,7 ± 7.5	PSG, RDI >15 events/h	–		59.2 ± 24.5	12.6 ± 2.4	
	HC	19	41.6 ± 8.3					5.8 ± 3.0	
Daurat et al. [44]	OSA	26	52.7 ± 1.5	PSG, AHI >5 events/h	24.2 ± 17.2			12.4 ± 3.8	
	HC	27	50.6 ± 1.2					8.9 ± 4.8	
Hood & Bruck [46]	OSA	23	48.5 ± 11.8	Sleep laboratory, not specified	–		–	–	
	HC	29	49.6 ± 12.7						
	NC	33	55.2 ± 14.4						
Flemons & Reimer [45]	OSA	113	49.5 ± 10.6	Sleep laboratory, not specified	–		–	–	
	SNR	50	44.9 ± 9.9						
Moore et al. [47]	OSA	39	48.0 ± 9.0	PSG, RDI >20 events/h	–		46.0 ± 26.9	11.0 ± 5.0	
Mulgrew et al. [48]	OSA	428	49.3	PSG	21.4 ± 22.0			10.1 ± 5.4	
Sangal & Sangal [49]	OSA	38	48.7 ± 15.5	PSG, RDI >5 events/h	–		–	12.9 ± 5.1	
	ADHD	18	31.9 ± 12.2					8.3 ± 5.6	
Stoohs et al. [50]	OSA	1610	51.5 ± 11.7	PSG, RDI >5 events/h	–		25.6 ± 20.9	9.9 ± 4.9	
	SNR	157	48.7 ± 11.8				2.2 ± 1.3	5.6 ± 3.4	
	OSA–	562	53.0 ± 12.3				23.1 ± 18.0	5.9 ± 3.3	
Ulfberg et al. [51]	OSA	62	49.7	PG, ODI >6 events/h	–		–	–	
	SNR	289	47.1						
					CPAP–	CPAP+		CPAP–	CPAP+
Vernet et al. [52]	OSA+	20	61.1 ± 9.9	PSG, AHI >15 events/h	40.7 ± 17.3	2.4 ± 2.3	–	15.9 ± 5.5	16.4 ± 3.0
	OSA–	20	61.8 ± 9.0		48.9 ± 19.0	2.7 ± 3.9		13.2 ± 3.4	6.2 ± 9.2
	HC	20	55.6 ± 10.0			7.6 ± 5.8			5.7 ± 2.7

AHI = apnea/hypopnea index; COM = community population without OSA; CPAP– = before CPAP treatment; CPAP+ = after CPAP treatment; ESS = Epworth sleepiness scale; HC = healthy controls; NC = narcolepsy; ODI = oxygen desaturation index; OSA– = OSA without residual sleepiness after CPAP; OSA+ = OSA with residual sleepiness after CPAP; PG = polygraphy; PSG = polysomnography; RDI = respiratory disturbance index; SNR = primary snorer.

Cognitive complaints after CPAP treatment

Only two studies reported on the effect of CPAP on cognitive complaints. Mulgrew et al. [47] approached 100 patients, who were prescribed CPAP, from their initial 428 OSA patients included at baseline for a two year follow-up survey. Thirty-eight of the patients completed the follow-up. After two years, 33 patients were

Table 4
Quality assessment of the included studies.

Study	Criterion											
	A	B	C	D	E	F	G	H	I	J	K	Total
Chen et al. (2012) [6]	1	1	1	1	NA	1	1	0	1	1	1	9
Daurat et al. (2010) [7]	1	1	1	1	NA	1	1	1	1	1	1	10
Flemons & Reimer (1998) [44]	1	0	0	1	NA	1	1	0	0	0	0	4
Hood & Bruck (1997) [45]	1	0	0	1	NA	1	1	1	1	0	1	7
Jennum & Sjol (1994) [8]	1	0	0	0	NA	1	1	0	1	0	1	5
Moore et al. (2001) [46]	1	1	1	1	NA	1	1	0	0	1	1	8
Mulgrew et al. (2007) [47]	1	1	1	1	1	1	1	0	0	1	1	9
Sangal & Sangal (2004) [48]	1	1	1	0	NA	1	1	1	1	1	1	9
Sforza et al. (2010) [43]	1	0	0	1	NA	1	1	1	1	1	1	8
Stoohs et al. (2008) [49]	1	1	1	1	NA	1	1	1	1	1	1	10
Ulfberg et al. (1996) [50]	1	1	1	0	NA	1	1	0	1	0	1	7
Vernet et al. (2011) [51]	1	1	1	1	NA	1	1	1	1	1	1	10
Total	12	8	8	9	1	12	12	6	9	8	11	

NA = not applicable.

Table 5
Cognitive complaints in OSA patients compared to healthy controls.

Study	Cognitive complaints		*p*	Comment
Concentration problems				
Chen et al. [6]	Attention & vigilance	↑	.01	
Ulfberg et al. [50]	Concentrating on new tasks	↑	<.05	Odds ratio 7.5
	Performing monotonous tasks	↑	<.05	Odds ratio 20
Memory complaints				
Chen et al. [6]	Memory & learning	↑	.02	
Daurat et al. [7]	Memory capacity		.10	
Hood & Bruck [45]			ns	
Daurat et al. [7]	Memory stability	↑	.012	Cohen's *d* = .75
Hood & Bruck [45]			ns	
Daurat et al. [7]	Anxious about memory	↑	.009	Cohen's *d* = .85
Hood & Bruck [45]			ns	
Ulfberg et al. [50]	Learning new tasks	↑	<.05	Odds ratio 9.1
Executive function complaints				
Chen et al. [6]	Emotional control & motivation	↑	.01	
	Abstract thinking & problem solving		.07	

↑ = more severe cognitive complaints compared to healthy controls; ns = non-significant with no exact *p*-values provided in the paper.

Table 6
Cognitive complaints in untreated OSA from sleep centers compared to other disorders.

Study	Comparison group	Cognitive complaints		p
Hood & Bruck [45]	Narcolepsy	Memory capacity	↓	<.05
		Memory stability	↓	<.05
		Anxious about memory		ns
Sangal & Sangal [48]	ADHD	Inattention	↓	<.001
Stoohs et al. [49]	Primary snorers	Concentration	↑	<.001
Ulfberg et al. [50]	Primary snorers	Concentrating on new tasks	↑	<.05
		Learning new tasks	↑	<.05
		Performing monotonous tasks	↑	<.05

ADHD = attention deficit hyperactivity disorder; ↑ = more severe cognitive complaints compared to comparison group; ↓ = less severe cognitive complaints compared to comparison group; ns = non-significant with no exact *p*-values provided in the paper.

still using CPAP (age = 49 y, AHI = 28 ± 20 events/h, ESS = 9.3) and reported less complaints with time-management ($p < .001$) and cognitive work tasks ($p < .05$). No information on OSA severity or CPAP usage was available at follow-up, nor was a control group included. However, five of the 38 patients that completed follow-up had discontinued CPAP and did not report improvements on time-management ($p = .54$) and cognitive work tasks ($p = .46$). These findings suggest a possible positive effect of CPAP on cognitive complaints.

In contrast, a study by Vernet et al. [51] showed that cognitive complaints may remain after CPAP treatment. They compared OSA patients with residual sleepiness after CPAP ($n = 20$, age = 61 ± 10 y, AHI = 4 ± 2 events/h, ESS = 16 ± 3) to patients without residual sleepiness ($n = 20$, age = 62 ± 9 y, AHI = 4 ± 2 events/h, ESS = 6 ± 3) and healthy controls ($n = 20$, age = 66 ± 10 y, ESS = 6 ± 3). In both OSA groups, memory complaints were significantly more frequent than in healthy controls (prevalence of 95% with residual sleepiness, and 65% without residual sleepiness). Both OSA groups also reported more inattention complaints compared to healthy controls. These data show that cognitive complaints may persist even after successful CPAP treatment.

Factors associated with cognitive complaints

Although cognitive complaints are common among OSA patients, clearly not every patient is affected to the same degree and reports the same type of cognitive dysfunction. Next, we will review possible determinants of cognitive complaints, focusing on the relation with objective cognitive functioning, daytime sleepiness and mood problems.

Cognitive complaints versus objective cognitive functioning

Research in healthy subjects as well as non-sleep disorder patient populations (such as cerebrovascular disease) has shown that the relation between cognitive complaints and objective cognitive functioning is often rather weak or even absent [24,26,52]. Studies in OSA patients support this finding [6,7,51]. Daurat et al. [7] did not find significant correlations between the performance on an episodic memory test and subjective ratings for memory capacity ($r = .09$, $p = .68$), subjective memory stability ($r = .08$, $p = .68$) or anxiety about memory ($r = .06$, $p = .77$). Chen et al. studied possible correlations between cognitive tests for attention, memory, and executive function and subjective ratings for attention, vigilance, memory, learning, abstract thinking, problem solving, emotional control and motivation [6]. Of the resulting 252 Pearson correlation coefficients, none were significant. As reported earlier Vernet et al. [51] found that even after successful CPAP treatment, patients still often reported memory and inattention complaints. Interestingly, this was in the absence of objective impairments on tests for memory, attention and executive function. No correlations were calculated between subjective and objective measures of cognition in this study.

Table 7
Relation between cognitive complaints and sleepiness.

Study	Cognition complaints	ESS	
		r	Slope
Chen et al. [6]	Attention & vigilance problems	.414**	
	Memory & learning problems	.332**	
	Emotional control & motivation problems	.363**	
	Abstract thinking & problem solving problems	.350**	
Daurat et al. [7]	Memory capacity	ns	
	Memory stability	ns	
	Anxious about memory	ns	
Mulgrew et al. [47]	Time management difficulties		1.22***
	Difficulties cognitive work tasks		1.09***
Sangal & Sangal [48]	Attentional deficits	.49***	
Sforza [43]	Subjective cognitive difficulties	.51***	

r = Pearson correlation coefficient; slope = multivariable logistic regression; ** = $p < .01$; *** = $p < .001$; ESS = Epworth sleepiness scale; ns = non-significant with no exact *p*-values provided in the paper.

Cognitive complaints and sleepiness

Findings on correlations between cognitive complaints and sleepiness scores are summarized in Table 7. Both Chen et al. [6] and Sangal and Sangal [48] found complaints on attention to correlate with subjective sleepiness (with *r*-values above .41). Findings for memory complaints were less consistent. Chen et al. [6] found memory complaints and learning problems to correlate with subjective sleepiness ($r = .33$). In contrast, Daurat et al. [7] failed to find correlations between memory complaint ratings and subjective sleepiness. Regarding executive function, correlations were found for emotional control, motivation problems, abstract thinking and problem solving ($r > .35$). Mulgrew et al. [47] used multivariable logistic regression analyses and found that subjective sleepiness predicted complaints of time management difficulties in OSA patients. Unfortunately, none of the studies explored the association between cognitive complaints and objective measures of sleepiness.

Findings comparing cognitive complaints between OSA patients with and without daytime sleepiness are summarized in Table 8.

Table 8
Cognitive complaints in OSA with sleepiness compared to OSA without sleepiness.

Study	Group	ESS	Cognitive complaints		p
Mulgrew et al. [47]	OSA with sleepiness	18–24[a]	Time management	↑	<.001
	OSA without sleepiness	0–5[a]	Cognitive work tasks	↑	<.001
Stoohs et al. [49]	OSA with sleepiness	9.9 ± 4.9	Concentration	↑	<.001
	OSA without sleepiness	5.9 ± 3.3			
Vernet et al. [51]	OSA with residual sleepiness after CPAP	16.4 ± 3.0	Memory	↑	<.10
	OSA without residual sleepiness after CPAP	6.2 ± 2.9	Inattention	↑	<.10

ESS = Epworth sleepiness scale; ↑ = more severe cognitive complaints in OSA with sleepiness compared to OSA without sleepiness.
[a] Only ranges were provided, no means.

Subjects in the reported studies were matched for AHI or RDI. Patients with sleepiness were more likely to report complaints about concentration [49] and difficulties with time management and cognitive work tasks [47]. After successful CPAP treatment, memory and inattention complaints were elevated in patients with residual sleepiness, compared to non-sleepy patients [51].

Cognitive complaints and mood problems

Cognitive complaints, particularly memory complaints, have often been associated with mood problems in the general population and in non-sleep disorder patients [24,25]. In these groups mood problems were shown to be an even stronger predictor for memory complaints than actual impairments in objective memory function [26,53–55]. It is therefore surprising that no study to date has reported on possible associations between cognitive complaints and mood problems in OSA. As more than a quarter of OSA patients report significant depressive symptoms and 20% are estimated to suffer from a depressive syndrome [56], it is not unlikely that mood problems may be a mediator of cognitive complaints in OSA as well.

Discussion

Cognitive complaints have repeatedly been linked to quality of life, work productivity and health care utilization in the general population [32–34] and medical populations such as cancer patients [24,35,36]. In addition to indicators of objective cognitive functioning, cognitive complaints are therefore an important patient outcome measure in OSA. In this paper, we reviewed the current knowledge on cognitive complaints in OSA. Several studies showed an increased prevalence of concentration complaints in OSA patients. The same may be true for memory and executive function problems, but firm conclusions are not possible due to methodological limitations of the (few) available studies. OSA patients with higher level of subjective sleepiness seem to report cognitive complaints more often. Importantly, cognitive complaints are not necessarily a sign of objective cognitive impairment.

The results of the review stress the importance of differentiating between objective cognitive functioning and cognitive complaints. In accordance with findings in other medical populations, no evidence was found for a relation between objective cognitive functioning and cognitive complaints in OSA. In fact, cognitive complaints in OSA may be reported in the absence of objective cognitive impairments. There are several possible explanations for this lack of relation. Firstly, current validated objective tests for cognition are designed to detect cognitive impairments in brain-injured patients and not to specifically assess cognitive impairments in OSA. For example, alertness may fluctuate across different environmental circumstances in OSA patients, while most objective cognitive tests only assess cognitive performance under maximum levels of alertness, potentially masking everyday cognitive failures in sleep apnea. Secondly, cognitive complaints are typically rated over a longer time period, including different circumstances, whereas objective measures only assess cognition at one point in time and under conditions often not comparable to everyday life. Finally, cognitive complaints may be secondary to other daytime symptoms in OSA and not purely related to objective impairments in cognitive performance. So far, only the relation between subjective sleepiness and cognitive complaints has been studied. In other medical populations it has been proposed cognitive complaints are a sign of psychological distress rather than objective cognitive impairments [39]. This hypothesis certainly warrants further exploration in OSA, for it could potentially guide treatment strategies for persisting cognitive complaints.

Meta-analyses have shown that CPAP improves objective cognitive functioning [19], and reduces sleepiness complaints [57,58] and mood problems [58]. No randomized controlled trial on CPAP has used cognitive complaints as an outcome measure. Only one of the reviewed studies [47] performed follow-up after CPAP therapy, showing a positive effect of the intervention on cognitive complaints. A large dropout rate and lack of a control group made it however unclear whether CPAP was the primary cause of this improvement. A study by Vernett et al. [51] showed that even after successful CPAP cognitive complaints may persist, underscoring the importance of improving our understanding of the effect of CPAP on cognitive complaints.

The number of studies on cognitive complaints in OSA is still limited. Moreover, methodological limitations of the available studies limit the extent to which firm conclusions can be drawn. Only concentration complaints were consistently found to be more severe in untreated OSA patients as compared to primary snorers and healthy controls. Findings on OSA and memory complaints were inconsistent, most likely due to the various types of outcome parameters used for memory complaints, small sample sizes and different types of control groups. Subjective measures for executive function were used in only two studies, yielding inconsistent findings on its relation with OSA.

Given the clinical importance of cognitive complaints, there is a clear need for future studies on this topic in OSA. It will be important that severity measures are included, both for the number of nocturnal respiratory events and daytime symptoms, especially sleepiness. As cognitive complaints are prevalent in other medical populations and even the general population, the inclusion of well-specified control groups is of paramount importance. Most important however would be the use of more unified measures for cognitive complaints, that cover domains typically affected in OSA. Validated questionnaires covering various types of cognitive complaints are available, with cut-off scores that distinguish normal levels of cognitive complaints from clinically significant complaints based on general population norms. Examples include the multifactorial memory questionnaire (MMQ) [59,60] for memory complaints, and the behavior rating inventory of executive function (BRIEF) [61] for complaints related to executive function.

We have shown that the literature on cognitive complaints in OSA is far less extensive than studies on objective cognitive functioning. Because of methodological limitations, only firm conclusions can be drawn regarding an increase in concentration problems in OSA, although memory complaints and complaints related to executive function may also be affected. Cognitive complaints appear to be at least partially related to subjective sleepiness and may not necessarily be a sign of objective cognitive impairment.

Practice points

- OSA patients often report complaints with regard to concentration, memory and executive function.
- Concentration problems are worse in OSA compared to primary snorers and healthy controls.
- OSA patients with high levels of subjective sleepiness are more likely to report cognitive complaints.
- Cognitive complaints are not necessarily a sign of objective cognitive impairments in OSA.
- There are data indicating that cognitive complaints may persist even after successful CPAP treatment.

Research agenda

- Studies on cognition in OSA should include both measures of objective cognitive functioning and measures of cognitive complaints, as these are related to different aspects of daytime functioning.
- Cognitive complaints in OSA patients should be studied using validated and norm-referenced questionnaires covering cognitive domains typically affected in this population (memory, concentration and executive function).
- The relation between cognitive complaints and sleepiness and mood problems warrants further study, as both are potential determinants of cognitive complaints in OSA.

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References

[1] Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc 2008;5:136–43.
[2] Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002;165:1217–39.
[3] Lee W, Nagubadi S, Kryger MH, Mokhlesi B. Epidemiology of obstructive sleep apnea: a population-based perspective. Expert Rev Respir Med 2008;2:349–64.
[4] Sleep apnea: what is sleep apnea? NHLBI: Health Information for the Public. U.S. Department of Health and Human Services; 2009. Accessed 01.06.11, 2011, at: http://www.nhlbi.nih.gov/health/dci/Diseases/SleepApnea/SleepApnea_WhatIs.html.
[5] Aloia MS, Arnedt JT, Davis JD, Riggs RL, Byrd D. Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: a critical review. J Int Neuropsychol Soc 2004;10:772–85.
*[6] Chen CW, Yang CM, Chen NH. Objective versus subjective cognitive functioning in patients with obstructive sleep apnea. Open Sleep J 2012;5:33–42.
[7] Daurat A, Huet N, Tiberge M. Metamemory beliefs and episodic memory in obstructive sleep apnea syndrome. Psychol Rep 2010;107:289–302.
[8] Jennum P, Sjol A. Self-assessed cognitive function in snorers and sleep apneics. An epidemiological study of 1,504 females and males aged 30–60 years: the Dan-MONICA II Study. Eur Neurol 1994;34:204–8.
[9] Diagnosis and treatment of sleep breathing disorders. Proceedings of a symposium. Grenoble, France, December 1998. Sleep 2000;23:S91–227.
*[10] Beebe DW, Groesz L, Wells C, Nichols A, McGee K. The neuropsychological effects of obstructive sleep apnea: a meta-analysis of norm-referenced and case-controlled data. Sleep 2003;26:298–307.
[11] Naegele B, Launois SH, Mazza S, Feuerstein C, Pepin JL, Levy P. Which memory processes are affected in patients with obstructive sleep apnea? An evaluation of 3 types of memory. Sleep 2006;29:533–44.
[12] Spruyt K, Capdevila OS, Kheirandish-Gozal L, Gozal D. Inefficient or insufficient encoding as potential primary deficit in neurodevelopmental performance among children with OSA. Dev Neuropsychol 2009;34:601–14.
[13] El-Ad B, Lavie P. Effect of sleep apnea on cognition and mood. Int Rev Psychiatry 2005;17:277–82.
[14] Jackson ML, Howard ME, Barnes M. Cognition and daytime functioning in sleep-related breathing disorders. Prog Brain Res 2011;190:53–68.
[15] Nowak M, Kornhuber J, Meyrer R. Daytime impairment and neurodegeneration in OSAS. Sleep 2006;29:1521–30.
[16] Salorio CF, White DA, Piccirillo J, Duntley SP, Uhles ML. Learning, memory, and executive control in individuals with obstructive sleep apnea syndrome. J Clin Exp Neuropsychol 2002;24:93–100.
[17] Verstraeten E, Cluydts R, Pevernagie D, Hoffmann G. Executive function in sleep apnea: controlling for attentional capacity in assessing executive attention. Sleep 2004;27:685–93.
[18] Engleman HM, Douglas NJ. Sleep. 4: sleepiness, cognitive function, and quality of life in obstructive sleep apnoea/hypopnoea syndrome. Thorax 2004;59:618–22.
*[19] Kylstra WA, Aaronson JA, Hofman WF, Schmand BA. Neuropsychological functioning after CPAP treatment in obstructive sleep apnea: a meta-analysis. Sleep Med Rev 2013;17:341–7.
[20] Matthews EE, Aloia MS. Cognitive recovery following positive airway pressure (PAP) in sleep apnea. Prog Brain Res 2011;190:71–88.
[21] Burgess PW, Alderman N, Evans J, Emslie H, Wilson BA. The ecological validity of tests of executive function. J Int Neuropsychol Soc 1998;4:547–58.
[22] Chaytor N, Schmitter-Edgecombe M. The ecological validity of neuropsychological tests: a review of the literature on everyday cognitive skills. Neuropsychol Rev 2003;13:181–97.
[23] Schagen SB, van Dam FS, Muller MJ, Boogerd W, Lindeboom J, Bruning PF. Cognitive deficits after postoperative adjuvant chemotherapy for breast carcinoma. Cancer 1999;85:640–50.
[24] Shilling V, Jenkins V. Self-reported cognitive problems in women receiving adjuvant therapy for breast cancer. Eur J Oncol Nurs 2007;11:6–15.
[25] Grafman J, Schwartz V, Dale JK, Scheffers M, Houser C, Straus SE. Analysis of neuropsychological functioning in patients with chronic fatigue syndrome. J Neurol Neurosurg Psychiatry 1993;56:684–9.
[26] Reid LM, Maclullich AM. Subjective memory complaints and cognitive impairment in older people. Dement Geriatr Cogn Disord 2006;22:471–85.
[27] Bolla KI, Lindgren KN, Bonaccorsy C, Bleecker ML. Memory complaints in older adults. Fact or fiction? Arch Neurol 1991;48:61–4.
[28] Jungwirth S, Fischer P, Weissgram S, Kirchmeyr W, Bauer P, Tragl KH. Subjective memory complaints and objective memory impairment in the Vienna-Transdanube aging community. J Am Geriatr Soc 2004;52:263–8.
[29] Kahn RL, Zarit SH, Hilbert NM, Niederehe G. Memory complaint and impairment in the aged. The effect of depression and altered brain function. Arch Gen Psychiatry 1975;32:1569–73.
[30] Antonelli-Incalzi R, Corsonello A, Trojano L, Acanfora D, Spada A, Izzo O, et al. Correlation between cognitive impairment and dependence in hypoxemic COPD. J Clin Exp Neuropsychol 2008;30:141–50.
[31] Hopkins RO, Weaver LK, Chan KJ, Orme Jr JF. Quality of life, emotional, and cognitive function following acute respiratory distress syndrome. J Int Neuropsychol Soc 2004;10:1005–17.
[32] Stenfors CU, Marklund P, Magnusson Hanson LL, Theorell T, Nilsson LG. Subjective cognitive complaints and the role of executive cognitive functioning in the working population: a case-control study. PLoS One 2013;8:e83351.
[33] Waldorff FB, Siersma V, Waldemar G. Association between subjective memory complaints and health care utilisation: a three-follow up. BMC Geriatr 2009;9:43.
[34] Montejo P, Montenegro M, Fernandez MA, Maestu F. Memory complaints in the elderly: quality of life and daily living activities. A population based study. Arch Gerontol Geriatr 2012;54:298–304.
[35] Correa DD, Hess LM. Cognitive function and quality of life in ovarian cancer. Gynecol Oncol 2012;124:404–9.
[36] Wu LM, Austin J, Hamilton JG, Valdimarsdottir H, Isola L, Rowley S, et al. Self-efficacy beliefs mediate the relationship between subjective cognitive functioning and physical and mental well-being after hematopoietic stem cell transplant. Psychooncology 2012;21:1175–84.
[37] Wells RD, Freedland KE, Carney RM, Duntley SP, Stepanski EJ. Adherence, reports of benefits, and depression among patients treated with continuous positive airway pressure. Psychosom Med 2007;69:449–54.
[38] Greenberg-Dotan S, Reuveni H, Simon-Tuval T, Oksenberg A, Tarasiuk A. Gender differences in morbidity and health care utilization among adult obstructive sleep apnea patients. Sleep 2007;30:1173–80.
[39] Pullens MJ, De Vries J, Roukema JA. Subjective cognitive dysfunction in breast cancer patients: a systematic review. Psychooncology 2010;19:1127–38.
[40] van Rijsbergen MW, Mark RE, de Kort PL, Sitskoorn MM. Subjective cognitive complaints after stroke: a systematic review. J Stroke Cerebrovasc Dis 2014;23:408–20.
[41] Kronholm E, Sallinen M, Suutama T, Sulkava R, Era P, Partonen T. Self-reported sleep duration and cognitive functioning in the general population. J Sleep Res 2009;18:436–46.
[42] Ohayon MM, Vecchierini MF. Daytime sleepiness and cognitive impairment in the elderly population. Arch Intern Med 2002;162:201–8.
[43] Sforza E, Roche F, Thomas-Anterion C, Kerleroux J, Beauchet O, Celle S, et al. Cognitive function and sleep related breathing disorders in a healthy elderly population: the SYNAPSE study. Sleep 2010;33:515–21.
[44] Flemons WW, Reimer MA. Development of a disease-specific health-related quality of life questionnaire for sleep apnea. Am J Respir Crit Care Med 1998;158:494–503.
[45] Hood B, Bruck D. Metamemory in narcolepsy. J Sleep Res 1997;6:205–10.
[46] Moore P, Bardwell WA, Ancoli-Israel S, Dimsdale JE. Association between polysomnographic sleep measures and health-related quality of life in obstructive sleep apnea. J Sleep Res 2001;10:303–8.
*[47] Mulgrew AT, Ryan CF, Fleetham JA, Cheema R, Fox N, Koehoorn M, et al. The impact of obstructive sleep apnea and daytime sleepiness on work limitation. Sleep Med 2007;9:42–53.
[48] Sangal RB, Sangal JM. Rating scales for inattention and sleepiness are correlated in adults with symptoms of sleep disordered breathing syndrome, but not in adults with symptoms of attention-deficit/hyperactivity disorder. Sleep Med 2004;5:133–5.
*[49] Stoohs RA, Knaack L, Blum HC, Janicki J, Hohenhorst W. Differences in clinical features of upper airway resistance syndrome, primary snoring, and obstructive sleep apnea/hypopnea syndrome. Sleep Med 2008;9:121–8.

* The most important references are denoted by an asterisk.

[50] Ulfberg J, Carter N, Talback M, Edling C. Excessive daytime sleepiness at work and subjective work performance in the general population and among heavy snorers and patients with obstructive sleep apnea. Chest 1996;110:659–63.
*[51] Vernet C, Redolfi S, Attali V, Konofal E, Brion A, Frija-Orvoen E, et al. Residual sleepiness in obstructive sleep apnoea: phenotype and related symptoms. Eur Respir J 2011;38:98–105.
[52] Duits A, Munnecom T, van Heugten C, van Oostenbrugge RJ. Cognitive complaints in the early phase after stroke are not indicative of cognitive impairment. J Neurol Neurosurg Psychiatry 2008;79:143–6.
[53] Comijs HC, Deeg DJ, Dik MG, Twisk JW, Jonker C. Memory complaints; the association with psycho-affective and health problems and the role of personality characteristics. A 6-year follow-up study. J Affect Disord 2002;72:157–65.
[54] Jonker C, Geerlings MI, Schmand B. Are memory complaints predictive for dementia? A review of clinical and population-based studies. Int J Geriatr Psychiatry 2000;15:983–91.
[55] Rohling ML, Green P, Allen 3rd LM, Iverson GL. Depressive symptoms and neurocognitive test scores in patients passing symptom validity tests. Arch Clin Neuropsychol 2002;17:205–22.
[56] Schroder CM, O'Hara R. Depression and obstructive sleep apnea (OSA). Ann Gen Psychiatry 2005;4:13.
[57] Marshall NS, Barnes M, Travier N, Campbell AJ, Pierce RJ, McEvoy RD, et al. Continuous positive airway pressure reduces daytime sleepiness in mild to moderate obstructive sleep apnoea: a meta-analysis. Thorax 2006;61:430–4.
[58] Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnoea in adults. Cochrane Database Syst Rev; 2006:CD001106.
[59] Troyer AK, Rich JB. Psychometric properties of a new metamemory questionnaire for older adults. J Gerontol B Psychol Sci Soc Sci 2002;57:P19–27.
[60] van der Werf SP, Vos SH. Memory worries and self-reported daily forgetfulness: a psychometric evaluation of the Dutch translation of the Multifactorial Memory Questionnaire. Clin Neuropsychol 2011;25:244–68.
[61] Rabin LA, Roth RM, Isquith PK, Wishart HA, Nutter-Upham KE, Pare N, et al. Self- and informant reports of executive function on the BRIEF-A in MCI and older adults with cognitive complaints. Arch Clin Neuropsychol 2006;21:721–32.