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Poor sleep is associated with deficits of attention in COPD patients

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ABSTRACT

Background: Poor sleep and attention deficits are common in COPD.
Objectives: To assess the relationship between self-reported poor sleep and attention deficits in COPD. We also studied the association between self-reported sleep and the attention tests with the objective characteristics of sleep.
Methods: Fifty-nine COPD patients were prospectively studied. Self-reported sleep quality was assessed using the Pittsburgh sleep quality index (PSQI). Objective characteristics of sleep were assessed by actigraphy and polysomnography. Attention was evaluated with the Oxford sleep resistance test (OSLER) and the Psychomotor vigilance test (PVT).
Results: 28 (47 %) patients referred poor sleep (PSQI >5). In the OSLER test they showed earlier sleep onset than patients with good sleep, median (Interquartil range): 31.2 min (25.4–40) vs 40 min (28.5–40), p: 0.048. They also spent more time making errors: 4.5 % (0.6–7.6) of total test time vs 0.7 % (0.2–5.3), p: 0.048. In PVT, patients with poor sleep presented a greater dispersion of the reaction time values with a higher value in the slowest 10 % of the reactions, 828 (609–1667) msec. vs 708 (601–993) msec, p: 0.028. No association was found between self-reported poor sleep and objective sleep variables. We found no correlation between OSLER and PVT results and polysomnographic variables except between sleep efficiency and PVT response speed (β: 0.309, p: 0.018).
Conclusion: Self-reported poor sleep in COPD is associated with attention deficits. Sleep quality should be included in future studies of this facet of cognition in COPD, as well as to assess its potential usefulness as a therapeutic target.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a highly prevalent disorder and an important cause of mortality, morbidity and healthcare costs [1]. It has been shown that patients with COPD have cognitive impairments [2,3]. Few studies have evaluated the impact of these impairments in COPD outcomes, suggesting their association with poor adherence to medications, impairment of instrumental activities of daily living and mortality [3]. The cause of this cognitive deterioration is not well known and various factors have been pointed out. Some factors are directly related to COPD, such as its severity or smoking, while others are shared with the general population of a similar age, as the coexistence of some comorbidities such as hypertension, diabetes, or depression. Among the different cognitive domains, multiple studies that have evaluated cognitive function in COPD have systematically detected deficits in attention [2,3], namely the capacity to direct perception, orientation and concentration on selected stimuli, and to inhibit processing of unwanted stimuli [2].

Poor sleep, including short sleep duration and sleep disruption, has been related to deficits in attention in healthy subjects. These deficits are associated with reduced performance, errors, inability to stay awake and accidents [4,5]. Sleep disturbance is one of the most common symptoms reported by COPD patients [6,7]. Poor sleep in these patients has been

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Abbreviations

AHI	Apnea-hypopnea index
BMI	Body mass index
BODEx	Body mass index, airflow Obstruction, Dyspnea and Exacerbations index
CAT	COPD assessment test
COPD	Chronic obstructive pulmonary disease
CT90	Cumulative percentage of time spent with SaO_2 below 90 %
EP	Error profile
ESS	Epworth sleepiness scale
FEV_1	Forced expiratory volume in the first second
FEV_1%	FEV_1 percentage of predicted
FVC	Forced vital capacity
HADS	Hospital anxiety and depression scale
ICS	Inhaled corticosteroids
LABA	Long-acting β2-agonist
LAMA	Long-acting anticholinergic
mMRC	Modified medical research council
OSLER	Oxford Sleep Resistance test
$PaCO_2$	Partial pressure of carbon dioxide in arterial blood
PaO_2	Partial pressure of oxygen in arterial blood
PSG	Polysomnography
PSQI	Pittsburgh sleep quality index
PVT	Psychomotor vigilance test
REM	Rapid eye movement sleep
6MWT	6-minute walking test
1/RT	Response speed
RT	Reaction time
SaO_2	Oxygen saturation by finger pulse oximeter
SD	Standard deviation
TST	Total sleep time
WASO	Wake after sleep onset

associated with the presence of impaired lung function and night hypoxemia, nocturnal respiratory symptoms, comorbidities, psychological distress, medications, and advanced age [6,7]. It has also been associated with a poor quality of life and adverse COPD outcomes including exacerbations and mortality [6–8]. Patients with COPD frequently complain of difficulty initiating or maintaining sleep, and polysomnographic studies in patients with mild or moderate [9] or severe [10] COPD have shown decreased sleep efficiency and decreased length of rapid eye movement (REM) sleep. These findings suggest that COPD patients with poor sleep have chronic partial sleep restriction, which is known to lead to cumulative adverse effects on neurobehavioral functions, especially deficits in attention [5,11]. However, the impact of poor sleep on attention in this population has not been assessed.

Sleep quality can be evaluated using objective techniques such as actigraphy and polysomnography (PSG) or, more frequently in daily clinical practice, it is self-reported by the patient using validated and reliable questionnaires. Although the objective sleep data provided by PSG is considered the gold standard for studying sleep, we know that there are marked interindividual differences in how these objective data are correlated with subjectively perceived sleep quality or with cognitive performance. Studies in normal population have shown that similar physiologically measured sleep can be associated with different subjective sleep quality or cognitive performance measures [12].

In this study we hypothesized that COPD patients with self-reported poor sleep quality have associated deficits in attention. The main objective was to assess the relationship between poor sleep quality in COPD patients, assessed using the Pittsburgh sleep quality index (PSQI) [13], the most commonly used questionnaire of sleep quality in clinical and research settings, and the presence of attention deficits assessed using objective techniques. As secondary objectives we studied the association between the results of the sleep questionnaire and the attention tests with the objective characteristics of sleep assessed by actigraphy and polysomnography.

2. Methods

This was an observational cross-sectional study. All subjects were prospectively recruited from the COPD outpatient clinic of the Respiratory Service of the Vall d'Hebron University Hospital in Barcelona. The study protocol was approved by the institutional review board and informed written consent was obtained from all participants. We included consecutive patients aged 40–80 years, smokers or ex-smokers of at least 10 pack-years, diagnosed with moderate-to-severe COPD (post bronchodilator $FEV_1/FVC < 70$ % and $FEV_1 \geq 30$ but <80 % of predicted in a spirometry performed within six months prior to inclusion into the study). Exclusion criteria were: a) non-stable COPD. Stability was defined as being exacerbation free and without treatment changes for at least four weeks prior to baseline evaluation (three months if hospitalization was required); d) chronic respiratory failure ($PaO_2 < 60$ mmHg and/or $PaCO_2 > 45$ mmHg); b) unstable cardiac or other medical conditions, within the previous three months; c) asthma or other major pulmonary diagnoses; d) known obstructive sleep apnea, other sleep disorder (narcolepsy, periodic limb movements) or shift work; e) treatment with sedative drugs or history of alcohol abuse; f) inability to understand the questionnaires administered in the study or to perform the attention tests due to visual or cognitive impairment.

At the inclusion visit, the following sociodemographic and clinical data were recorded: a) information on comorbidity according to the Charlson Index; b) body mass index (BMI); c) spirometry; d) number of exacerbations with or without hospital admission in the last year; e) degree of dyspnea according to the modified Medical Research Council (mMRC) scale. COPD severity was evaluated using the BODEx (Body mass index, airflow Obstruction, Dyspnea and Exacerbations) index [14]; f) health status, determined using the COPD assessment test (CAT) [15]; g) somnolence, assessed using the Epworth sleepiness scale; h) depression and anxiety, assessed using the Hospital Anxiety and Depression Scale (HADS) questionnaire [16]; i) self-reported sleep quality, measured using the Pittsburgh Sleep Quality Index (PSQI), an 18-item questionnaire that assesses overall sleep quality. Scale items include subjective sleep quality, sleep duration, use of sleep aids, self-estimated sleep efficiency, disturbances, and daytime dysfunction. Scores range from 0 to 21, with higher scores reflecting poorer sleep quality. Sleep was defined as "good" with a PSQI ≤ 5 and "poor" with a PSQI >5 [13].

2.1. Procedures

2.1.1. Actigraphy

After the inclusion visit, the usual sleep pattern of the patients was studied using actigraphy. Patients were asked to wear the actigraph watches (Motionwatch-8, Camntech Ltd, UK) on their non-dominant wrist, removed only for water-based activities, and to maintain sleep diaries for seven consecutive days preceding polysomnography. They were asked not to deliberately change their daily habits for the duration of the study. The actigraphs were returned at the end of the 7-day period and were automatically downloaded and analyzed using dedicated software. One-minute actigraphy epochs were automatically classified into wake and sleep. Before generating sleep statistics, an expert in sleep medicine blinded to the identity of the patient inspected the data and with the help of the sleep diary manually set or altered rest intervals that

seemed to have been missed by the automatic analysis and total sleep time (TST) and sleep efficiency were estimated.

2.1.2. Polysomnography

The same day that the patients returned the actigraphs an overnight sleep study was conducted at the Sleep Unit using a computerized polysomnography device (Profusion E Series, Compumedics, Abbotsford, Victoria, Australia). Polysomnography included recordings of frontal, central and occipital electroencephalographic channels, bilateral electro-oculograms, chin and tibial electromyogram, electrocardiogram, airflow by nasal pressure transducer and oronasal thermocouples, thoracic and abdominal movements, snoring, oxygen saturation by finger pulse oximeter (SaO_2), body position and simultaneous video recording. An expert scorer blinded to the study reviewed all sleep studies. Sleep stages, arousals and respiratory events were scored according to standard criteria. Briefly, sleep quality was objectively assessed in all study patients by obtaining the following measurements: sleep efficiency (time asleep/time in bed), sleep architecture, sleep latency, wake after sleep onset time and the arousal index. An apnea was defined as the cessation of airflow with duration of at least 10 seconds. Differentiation was made between obstructive and central apneas according to the respiratory effort channels (presence or absence of thoracoabdominal movements). Hypopnea was defined as a >30 % reduction in nasal cannula tracing with a duration of at least 10 seconds associated with a cyclical dip in SaO2 ≥ 3 % or an arousal. The apnea-hypopnea index (AHI) was defined as the sum of apneas plus hypopneas divided by the total hours of sleep. Three SaO_2 measures were assessed: the cumulative percentage of time spent below 90 % (CT90), and the basal and average SaO_2.

2.1.3. Attention tests

The morning after the polysomnography, the patients remained in the sleep unit to perform the Oxford Sleep Resistance test (OSLER) and the Psychomotor vigilance test (PVT). Both behavioral tests were performed with an Osler-2 unit (Stowood, Oxford, UK). Prior to the first OSLER and PVT trials a preliminary 1-min test was performed in order to familiarize the patients with the procedures. Meals were provided at regular times throughout the protocol, caffeinated foods and drinks were not allowed. Between neurobehavioral test bouts, patients were allowed to read or consult the mobile phone and interact with sleep unit staff to help them stay awake, but no naps/sleep or vigorous activities were allowed.

The OSLER test is a behavioral alternative to the maintenance of wakefulness test. It measures the ability to stay awake and to maintain a constant level of vigilance in a monotonous boring situation that requires sustained attention. Patients were placed semirecumbent in a dark and quiet video-monitored room and asked to remain awake and to react to a flashing light, which appeared on a screen for 1 second every 3 seconds, by hitting a button. Each subject underwent the OSLER test three times (at 9 a.m., 11:30 a.m. and 2 p.m.). Prior to each test patients were asked if they needed to go to the bathroom. The capacity to maintain wakefulness and a constant level of vigilance was evaluated by analyzing consecutive errors occurring during the test. As previously described, sleep latency was defined as the time between the onset of the test and the moment corresponding to seven consecutive flashes (i.e., 21 seconds) without response [17]. The test was stopped after sleep onset, and the patient was awakened immediately, or after a maximum of 40 minutes. Subjects were asked to leave the room and walk around for 10 minutes to restore alertness. In addition, the error profiles (EP) during the test were also analyzed. The percentage of time corresponding to the presence of errors during the test ([3 seconds x number of omissions/-sleep latency duration in seconds]/100) was also calculated. In accordance with previously published data [18,19] it was considered that one period of 9 to 18 second misses (EP3–6) or > 4 episodes of 3 to 6 second misses (EP1–2) represent fluctuations in vigilance during the test.

The PVT measures the reaction time to a relatively high stimulus rate to avoid boredom and task fatigue effects [20]. It is widely used to assess vigilant attention and it is considered highly reliable and sensitive to the effect of sleep deprivation on cognitive performance, and it reflects the cumulative worsening of performance during the task when an individual is unable to sustain attention [21]. Three 10-minute PVTs were performed at 10 a.m., 12:30 a.m. and 3 p.m. The patient was seated in an isolated normally lighted and video-monitored room and instructed to press a response button as quickly as possible as soon as a yellow light appeared on a screen and the reaction time (RT) in milliseconds was registered. The inter-stimulus interval, defined as the period between the last response and the appearance of the next stimulus, varied randomly from 2 to 10 seconds. Standard PVT outcomes were recorded: median reaction time (RT), the standard deviation of RTs, mean reciprocal reaction time or response speed (1/RT), mean of the slowest 10 % RT, mean of the fastest 10 % RT, the number of lapses (RT > 500 ms) and false starts defined as responses that occurred before the visual stimulus was presented or with a RT < 100 ms.

2.2. Statistical analysis

Based on previous studies [22], we assumed a prevalence of poor sleep quality assessed by the PSQI of 50 % in COPD patients. Mean OSLER sleep latency and 1/RT were considered the primary outcomes. The expected difference in these variables and the pooled standard deviation were specified on the basis of previously published studies comparing normal subjects and patients with insufficient sleep syndrome [21] or obstructive sleep apnea [19]. The required sample size to detect a difference of 5 min in OSLER sleep latency and 0.5 in 1/RT with 90 % power at the 5 % significance level was 23 patients in each group.

Data are presented as mean (SD) or median (interquartile range) for quantitative variables or percentages for qualitative variables. Chi-squared test or Fisher's exact test were used for comparison of qualitative variables. For quantitative variables paired or unpaired Student t tests were used for patient characteristics and actigraphic and PSG results, and Mann-Whitney test was applied to the OSLER and PVT results. Pearson's correlation analysis was used to assess the correlation between the primary outcomes and TST, sleep efficiency, arousal index, AHI and CT90, as polysomnographic markers of sleep quality. To identify potential independent predictors of attention deficits, a stepwise backward linear regression model was used with mean OSLER sleep latency and 1/RT as dependent variables and age, FEV_1 (% of predicted) and polysomnographic parameters as independent variables. Statistical significance was accepted for $p < 0.05$. Data analysis was carried out using Stata software v14.0. (Stata Corporation, College Station, TX, USA).

3. Results

3.1. Characteristics of the study population

Fifty-nine patients were studied, mean age 65.6 (8.7) years, 40 (68 %) male, mean FEV_1 54.8 (17.4) percent of predicted. Twenty-eight patients (47 %) reported poor sleep in the PSQI. Table 1 summarizes their characteristics according to the results of the PSQI. Subjects were predominantly male and there were no differences between the normal and poor sleep groups regarding demographic characteristics, comorbidity, severity of COPD according to the BODEx index, self-reported severity of dyspnea on the mMRC scale, lung function tests, or the treatment received. Both groups showed normal values on the Epworth sleepiness scale. Patients with poor sleep had higher scores on the CAT questionnaire and on the anxiety and depression components of the HADS questionnaire.

3.2. Self reported sleep and attention tests

The results of the OSLER and PVT are shown in Table 2. The poor

Table 1
Baseline characteristics of study population.

	Good sleep (PSQI ≤5) n = 31	Poor sleep (PSQI >5) n = 28	p
Age (yr)	67.4 (7.8)	63.6 (9.2)	0.091
Sex (F/M), n	8/23	11/17	0.269
Packs/yr	52.6 (42.8)	37.5 (25.1)	0.109
Charlson index	2.2 (1.8)	1.6 (1.0)	0.138
- Myocardial infarction/	9 (29)	7 (25)	
CHF, n (%)	4 (12.9)	2 (7.1)	
- Periferal vascular disease,	1 (3.2)	0	
n (%)	2 (6.5)	3 (10.7)	
- CVA/TIA, n (%)	7 (22.6)	3 (10.7)	
- Peptid ulcer disease/liver	3 (9.7)	0	
disease, n (%)			
- Diabetes mellitus, n (%)			
- Solid tumor, n (%)			
BMI (kg/m^2)	27.9 (5.8)	25.8 (5.1)	0.141
BODEx	2.2 (1.8)	2.6 (2.1)	0.397
mMRC	1.4 (0.8)	1.8 (1.0)	0.077
ESS	4.8 (2.7)	6.1 (3.9)	0.133
PSQI	3.2 (1.3)	10.4 (3.4)	0.000
CAT	11.8 (7.2)	20.3 (9.6)	0.000
HAD A	4.0 (3.4)	9.4 (4.4)	0.000
HAD D	3.0 (2.9)	7.0 (4.6)	0.000
FVC (%)	72.2 (13.4)	71.3 (17.0)	0.937
FEV_1 (%)	53.1 (15.0)	56.7 (19.9)	0.517
FEV_1/FVC (%)	55.3 (10.3)	58.5 (11.2)	0.254
6MWD (meters)	394.9 (84.7)	362.1 (104.2)	0.285
LAMA, n (%)	26 (84)	24 (85)	0.844
LABA, n (%)	25 (81)	23 (82)	0.883
ICS, n (%)	20 (64)	17 (61)	0.763

Data are presented as mean (SD) unless otherwise indicated. Definition of abbreviations: CHF, congestive heart failure; CVA, cerebrovascular accident; TIA, transient ischemic attack; BMI, body mass index; BODEx, Body mass index, airflow Obstruction, Dyspnea and Exacerbations index; mMRC, degree of dyspnea according to the modified Medical Research Council; ESS, Epworth sleepiness scale; PSQI, Pittsburgh Sleep Quality Index; CAT, COPD assessment test; HAD A, Hospital Anxiety and Depression Scale, anxiety component; HAD D, Hospital Anxiety and Depression Scale, depression component; FVC (%), Forced vital capacity, percentage of predicted; FEV_1(%), forced expiratory volume in the first second, percentage of predicted; 6MWD, 6 min walking distance; LAMA, long-acting anticholinergic; LABA, long-acting β2-agonist; ICS, inhaled corticosteroids.

Table 2
OSLER and Psychomotor Vigilance tests results.

	Good sleep (PSQI ≤5)	Poor sleep (PSQI >5	p
OSLER test			
Mean sleep latency (min.)	40 (28.5–40)	31.2 (25.4–40)	0.048
Time making errors[1] (%)	0.75 (0.2–5.3)	4.5 (0.6–7.6)	0.048
Patients with EP7, n	11/31	19/28	0.019
Patients with vigilance fluctuations[2], n	21/31	24/28	0.133
Psychomotor vigilance test			
RT (msec.)	347 (287–447)	417 (307–578)	0.318
Standard deviation of RT (msec.)	172 (105–254)	300 (137–478)	0.025
1/RT (1/msec.)	3.1 (2.6–3.7)	2.8 (2.4–3.7)	0.576
Slowest 10 % RT (msec.)	708 (601–993)	828 (609–1667)	0.028
Fastest 10 % RT (msec.)	230 (190–258)	251 (195–275)	0.440
Lapses[3], n	8.3 (5.3–18.3)	11.5 (4.7–26.3)	0.537
False starts[4], n	0 (0–0)	0 (0–0)	0.353

Data are presented as median (interquartile range) unless otherwise indicated. Definition of abbreviations: EP7, error profile 7, seven consecutive flashes (i.e., 21 s) without response; RT: reaction time; 1/RT: response speed. [1] Time making errors expressed as percentage of sleep latency.
[2] Vigilance fluctuation: one period of 9–18 s misses (EP3–6) or > 4 episodes of 3- to 6-s misses (EP1–2). [3] Lapses: RT > 500 msec. [4] False starts: responses that occurred before the visual stimulus was presented or with a RT < 100 msec.

sleeper group presented a lower overall sleep latency. In the first test session in the morning there were no differences between the groups; however, in the two subsequent sessions good sleepers maintained a stable sleep latency, while poor sleepers according to the PSQI presented worse results with shorter sleep latency (Fig. 1). Eleven (35 %) good sleepers and 19 (68 %) poor sleepers presented EP7 errors indicative of sleep onset during the test (p: 0.019). Most of the patients presented episodes of fluctuations in vigilance, with no differences between the two groups. However, since the recording time was shorter in the poor sleepers due to their lower sleep latency, when the number of errors was analyzed as the percentage of the recording time, the poor sleepers showed a higher mean time making errors: 4.5 % (0.6–7.6) vs 0.75 % (0.2–5.3) p:0.048. The value was higher in poor sleepers in all sessions but was only statistically significant in the last one (Fig. 2).

In the PVT no differences were detected in the number of lapses or in the response speed between the two groups. However, poor sleepers presented a greater dispersion of the RT values and higher values of the slowest 10 % RT.

3.3. Self reported and objective sleep data

Table 3 shows the actigraphy and PSG results. No differences were found between the two groups in terms of the PSG variables. Both groups had prolonged sleep latency, reduced TST, and low sleep efficiency. Nor did actigraphy reveal differences between these variables; however, compared to PSG, actigraphy identified lower sleep latency (p: 0.132 in good sleepers and p: 0.002 in poor sleepers), longer TST (p: 0.14 and p: 0.006 respectively) and greater sleep efficiency ($p < 0.001$ both groups).

3.4. Polysomnographic variables and attention tests

Univariate analysis showed a weak but significant correlation of the response speed with TST and sleep efficiency ($r = 0.267$, p: 0.043 and $r = 0.290$, p: 0.027 respectively), but not with the arousal index, CT90 or AHI. In the multivariate analysis including age, FEV_1%, TST, sleep efficiency, arousal index, CT90 and AHI, only sleep efficiency showed a significant independent correlation with response speed (β: 0.309, p: 0.018). Neither age, nor FEV_1% nor any of the PSG variables showed a significant correlation with mean sleep latency in the OSLER test.

4. Discussion

In this study, the PSQI results showed poor sleep to be common in stable COPD patients. Poor sleep was associated with objectively assessed attention deficits, especially according to the OSLER test, which identified a large number of poor sleepers with a lower ability to maintain wakefulness and a greater percentage of time making errors. In the PVT no differences were observed in the RT, but poor sleepers presented a greater dispersion of values with higher mean values of the slowest 10 % RT. We found no association between self-reported poor sleep and the sleep variables assessed by polysomnography and actigraphy; nor did we find a correlation between attention deficits and age, COPD severity assessed by FEV_1%, or polysomnographic variables, except for a weak correlation between sleep efficiency and PVT response speed.

4.1. Self-reported sleep quality and attention tests

Studies that have evaluated cognitive function in COPD patients have shown that attention deficits are common [2,3]. The origin of these deficits and other cognitive alterations is not well known and it has been proposed that a key mechanism is neuronal damage secondary to hypoxia, although attention deficits have also been reported in COPD patients either without hypoxia or with the mild hypoxia present in our patients [3]. It has been suggested that the presence of other factors such as the presence of vascular disease and smoking also contributes to this

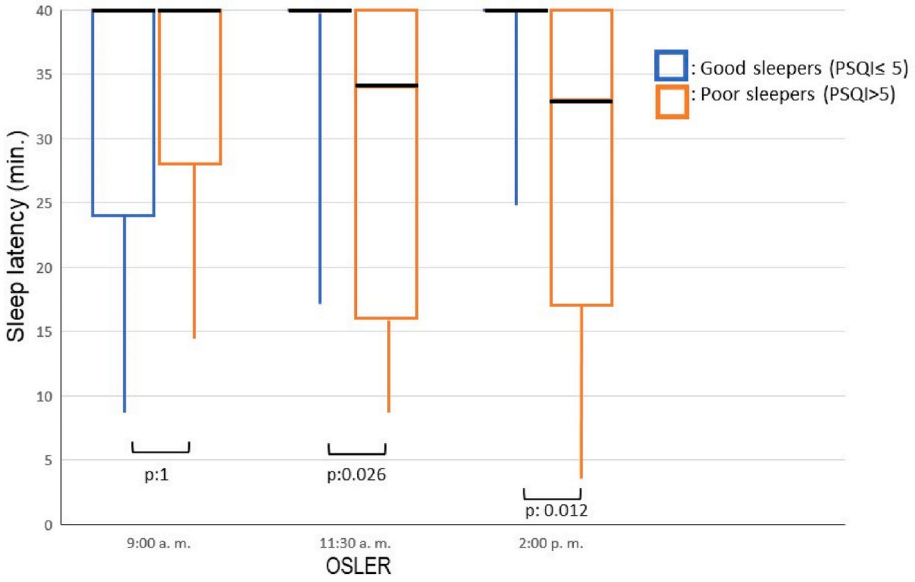

Fig. 1. Sleep latencies in OSLER's sessions. Each box shows the interquartile range and the black horizontal line represents the median; in the 11.30 a.m. and 2 p.m. sessions, the good sleepers presented similar median and 25th and 75th percentile values (40 min). The vertical lines extend from 25th until 10th percentile values. PSQI, Pittsburgh Sleep Quality Index.

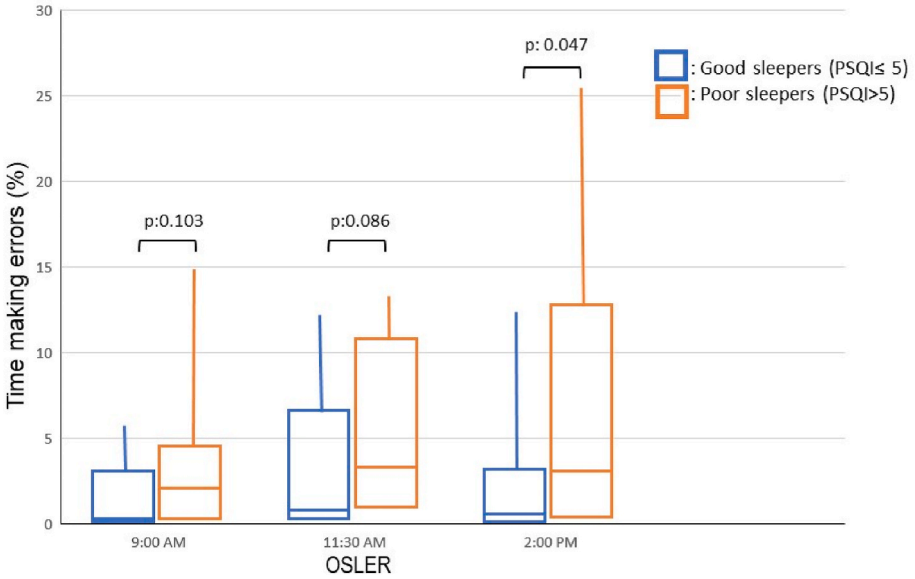

Fig. 2. Percentage of time making errors in OSLER's sessions. Each box shows the interquartile range and the horizontal line inside the box represents the median. The vertical lines extend from 75th until 90th percentile values. PSQI, Pittsburgh Sleep Quality Index.

neuronal damage [3]. However, although attention deficits are a well-known consequence of sleep disturbance, until now their relationship with subjective poor sleep quality has not been assessed in COPD patients. Among our patients, poor sleep was reported by 47 %, a prevalence similar to that reported in previous studies that have used the PSQI [22,23]. To assess the presence of attention deficits in our patients, we used a protocol that, in an attempt to reproduce potential fatigue conditions in real life, included boring repetitive actions in an environment conducive to the onset of sleep, as well as more demanding activities that required a higher degree of sustained attention. Our patients with self-reported poor sleep in the PSQI did not present a greater tendency to sleep or make errors in the OSLER test in the first morning session; however, in the second and third test sessions there was a progressive decrease in sleep latency and a higher percentage of time making errors, suggesting increased fatigability. Poor sleepers also presented a greater RT and more lapses in the PVT, though the differences with good sleepers were not significant; however, we found in poor sleepers a greater variability in the speed of the responses, with a marked increase in the RT of the slower response reactions. These results, worse than those described in healthy subjects in the OSLER test [19,24] and in the PVT [21,24], suggest an increased risk of errors and accidents in real life among COPD patients with self-reported poor sleep. COPD patients are known to be more predisposed to falls and trauma [25], and decreased driving performance has also been reported [26]. Although other factors associated with COPD, such as musculoskeletal deconditioning and impairment in balance are considered to be the causes of these problems, our results suggest a possible involvement of attention deficits associated with poor quality sleep. It could also be speculated that these attention deficits might be associated with other frequent problems in COPD patients, such as low adherence to treatment

Table 3
Actigraphic and polysomnographic sleep parameters.

	Good sleep (PSQI ≤5) n = 31	Poor sleep (PSQI >5) n = 28	p
Actigraphy			
TST (min)	388.0 (68.0)	385.0 (76.8)	0.883
Sleep efficiency (%)	82.0 (7.0)	81.1 (7.7)	0.946
Sleep latency (min)	17.5 (12.5)	17.4 (19.0)	0.989
Polisomnography			
TST (min)	337.2 (81.2)	319.8 (94.1)	0.449
Sleep efficiency (%)	69.2 (14.9)	64.9 (17.4)	0.318
Sleep latency (min)	27.6 (32.9)	35.3 (26.6)	0.325
Stage 1 (% TST)	18.4 (14.5)	18.0 (16.1)	0.927
Stage 2 (% TST)	52.0 (12.5)	54.0 (13.1)	0.536
Stage 3 (% TST)	15.6 (7.1)	13.6 (7.4)	0.312
REM (% TST)	14.1 (6.1)	14.3 (9.8)	0.933
Arousal index (n/hr)	20.7 (9.2)	22.7 (9.1)	0.417
WASO (min)	118.0 (63.7)	141.9 (80.4)	0.209
AHI (events/hr)	19.4 (18.3)	14.8 (16.5)	0.317
Basal SaO_2	93.6 (2.8)	94.7 (2.6)	0.127
Mean SaO_2	89.5 (4.8)	91.7 (4.0)	0.154
CT90 (%)	44.3 (40.1)	29.1 (40.4)	0.154

Data are presented as mean (SD). Definition of abbreviations: TST, total sleep time; REM, rapid eye movement sleep; WASO, wake after sleep onset; AHI, apnea-hypopnea index; SaO_2, oxygen saturation by finger pulse oximeter; CT90, cumulative percentage of sleep time spent with SaO_2 below 90 %.

or social isolation.

4.2. Self-reported sleep and objective sleep data

In our patients PSG showed reductions in TST and sleep efficiency, with increases in sleep latency and arousal index, similar to those previously described in COPD patients [10] and worse than normative data reported in healthy adults [27]. The AHI, a factor potentially involved in poorer sleep quality, showed values similar to those previously reported in COPD patients [28] and slightly higher than those reported in healthy population of similar age [27], and showed no differences between our good and poor sleepers. Further, in actigraphy our patients presented a similar mean sleep efficiency and a slightly lower mean sleep time with regard to previous reports in COPD [29], below the usually recommended sleep duration of 7–9 h. The shorter sleep time and reduced efficiency recorded in the PSG compared to actigraphy in our patients is consistent with previous reports in patients with chronic diseases [30]. All these objective sleep data point to poor quality sleep in our patients; however, we did not find a relationship between the objective characteristics of sleep and its poor subjective quality as assessed by the PSQI.

The weak correlation between these two types of sleep assessment is well known [12]. Poor sleep quality reported by our patients on the PSQI was associated with higher scores on the anxiety and depression scales, as previously described in COPD patients [8,22]. Our results support the notion that the subjective assessment of sleep depends on individual traits and show that at present we lack validated biomarkers of sleep quality able to inform us whether individual physiological needs have been met.

4.3. Objective sleep data and attention tests

The OSLER test and the PVT are sensitive to sleep restriction, and our patients frequently presented TST within a range usually considered as "short" and associated with attention deficits in healthy individuals [4]. However, when considering the polysomnographic characteristics potentially involved in the attention deficits detected, we found only a weak correlation between sleep efficiency and response speed in the PVT, and none with TST, arousal index, AHI, or CT90. As in the case of the lack of a relationship mentioned above between polysomnographic variables and subjective perception of poor quality, this lack of correlation with objective measures of cognitive performance has been reported in multiple studies [12] and, consistent with our results, large and enduring inter-individual differences have been found in the PVT and in alertness tests in situations of lack of sleep [31].

Although PSG is the accepted gold-standard for the objective assessment of sleep, it may not capture all sleep deficits. In our patients the effects of poor objective sleep on attention tests were only evidenced in patients with poor subjective perception of sleep quality. The clinical relevance of the subjective perception of sleep compared to the polysomnographic results was already reported by Bennett et al. [32] who, in subjects with objective sleepiness assessed by a multiple sleep latency test, found that only those who were subjectively sleepy presented attention deficits in the PVT. Similarly, in the Sleep Heart Health Study cohort Bertisch et al. [33] found that short polysomnographic sleep was associated with a higher incidence of cardiovascular events only in patients with subjective complaints of poor sleep. These findings and the results of our study allow us to hypothesize that the subjective perception of sleep constitutes a therapeutic target of special interest. Interestingly, an improvement in self-reported sleep quality has been observed in COPD patients with bronchodilator [34] or rehabilitation [35] treatment.

4.4. Limitations

The main strength of the study is that, to our knowledge, it is the first to offer a simultaneous assessment of subjective sleep quality, objective sleep measurements and the presence of attention deficits in patients with COPD. However, its observational design does not allow us to infer causal relationships. COPD is a complex and multicomponent disorder and our patients, consecutively recruited from a COPD outpatient clinic, presented differences in various factors potentially involved in our results. As expected, although the presence of known OSA was an exclusion criterion and the participants did not present sleepiness on the Epworth scale, due to the known high prevalence of OSA in the general population and in COPD, we found some patients with an AHI >5. However, the AHI was lower in patients with self-reported poor sleep and it did not correlate with the results of attention deficits, suggesting that upper airway obstructive events were not related to the perception of poor sleep quality or attention deficits. Likewise, as previously described, patients with poor sleep had a higher score on the anxiety and depression scales [8,22] and reported a greater symptomatic burden of COPD [8] in the CAT questionnaire. New studies focused on these aspects of COPD patients are necessary to assess their potential causal relationship with poor sleep quality and the detected attention deficits.

Other limitations of the study must be recognized. First, we assessed sleep quality using the PSQI, a questionnaire widely used but of a generic nature. We attempted to minimize the influence of non-respiratory comorbidities by excluding non-stable patients and no differences were detected in comorbidity between good and bad sleepers. However, PSQI results do not necessarily reflect respiratory sleep disturbances which should be also assessed using COPD specific sleep questionnaires [36]. Second, we were unable to carry out the attention tests in a longer schedule including the afternoon and early hours of the night; the chance to do so might have revealed greater differences than the ones detected, given the influence of the circadian rhythm on attention [4]. Similarly, performing the attention tests after a second night at home without the discomfort associated with a prior PSG in the sleep unit would have complemented our results. However, our design allowed us to observe that, after a PSG without significant differences between self-reported poor and good sleepers, only poor sleepers presented attention deficits. Third, we performed a standard analysis of polysomnographic variables, but our results indicate the need to explore new approaches to the interpretation of traditional signals [37] or to

incorporate new parameters [38] for discovering new links between objective and subjective sleep quality and the associated consequences.

5. Conclusions

In summary, we found that in COPD patients poor self-reported sleep quality is very frequent and is associated with attention deficits, which may be related with worse outcomes. Patients with poor self-reported sleep had a higher COPD symptom burden and higher values on anxiety and depression scales. However, subjective poor sleep and attention deficits were not related to objective sleep data. Our results point to the need to include sleep quality in future studies on attention in COPD patients, as well as to assess its potential usefulness as a therapeutic target.

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CRediT authorship contribution statement

Júlia Sampol: Conceptualization, Methodology, Formal analysis, participant recruitment, Data curation, Writing – original draft, Writing – review & editing, Supervision, Funding acquisition. **Jaume Ferrer:** Conceptualization, Methodology, Formal analysis, participant recruitment, Writing – review & editing, Supervision, Writing – original draft. **Marc Miravitlles:** Conceptualization, Methodology, Data curation, Writing – review & editing, Supervision, Writing – original draft. **María Sáez:** Methodology, Data curation, Writing – review & editing. **Odile Romero:** Data curation, Writing – original draft, participant recruitment, Writing – review & editing. **Gabriel Sampol:** Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision, Funding acquisition, Writing – original draft, All authors have read and agreed to the current version of the manuscript.

Declaration of competing interest

Júlia Sampol declares to have no conflict of interest.

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