

RESEARCH ARTICLE

## Relationship of symptoms with sleep-stage abnormalities in obstructive sleep apnea-hypopnea syndrome

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**Background:** Patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) present with a variety of sleep-related symptoms. In polysomnography, sleep architecture is almost always abnormal, but it is not known which of the sleep-stage abnormalities are related to symptoms. Finding key sleep-stage abnormality that cause symptoms may be of therapeutic importance to alleviate symptoms. So far the mainstay of treatment is continuous positive airway pressure (CPAP)/bi-level positive airway pressure (BIPAP) therapy, but many patients are non-compliant to it. Correcting the sleep-stage abnormality that cause symptoms by pharmacotherapy may become an important adjunct to CPAP/BIPAP therapy.

**Methods:** A cross-sectional study. Adult subjects who attended a sleep laboratory for diagnostic polysomnography for a period of 1 month were recruited consecutively. OSAHS was diagnosed using American Academy of Sleep Medicine criteria. Subjects filled a questionnaire for symptoms prior to polysomnography.

**Results:** Thirty subjects, of whom 83.3% were obese, met diagnostic criteria, with males constituting 46.7% and females constituting 53%. Mean age was  $53.40 \pm 11.60$  years. Sleep architecture comprised N1 19.50  $\pm$  19.00%, N2 53.93  $\pm$  13.39%, N3 3.90  $\pm$  19.50%, and rapid eye movement 8.92  $\pm$  6.21%. Excessive fatigue or sleepiness, waking up tired, falling asleep during the day, trouble paying attention, snoring and insomnia were significantly related to decreased N3 sleep.

**Conclusions:** Most of the symptoms in OSAHS in adults are related to decreased stage N3 sleep. If confirmed by larger controlled studies, correcting N3 sleep deficiency by pharmacotherapy may become an important adjunct to CPAP/BIPAP therapy to alleviate symptoms.

Keywords: *obstructive sleep apnea-hypopnea syndrome; sleep architecture; stage; symptom*

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Received: 6 May 2016; Accepted: 1 July 2016; Published: 7 September 2016

Sleep architecture refers to the basic structural organization of normal sleep (1). There are two types of sleep, non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. NREM sleep is further divided into three sub-stages: stage N1, stage N2, and stage N3, according to current sleep scoring rules by American Academy of Sleep Medicine (AASM) (2). To note that, older sleep scoring rules had four stages of NREM sleep, but in the current scoring system, stage N3 and stage N4 combined as stage N3 (3). Each stage has its unique characteristics including variations in brain wave patterns, eye movements, and muscle tone. A sleep episode normally begins with a short period of NREM stage 1 progressing through stage 2, followed by stage 3 and finally to REM (1). Over the course of the sleep period,

NREM sleep and REM sleep alternate cyclically every 90–120 min. Normal sleep architecture comprises stage N1 2–5%, stage N2 45–55%, stage N3 15–25%, and REM 20–25% of total sleep time (TST) (4–7).

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common disorder affecting at least 2 to 4% of the adult population in the United States (8, 9). Sleep is fragmented by frequent arousals with increase in stage N1 sleep and decrease in stage N3 sleep and REM sleep (10–18). Patients with OSAHS experience many sleep-related symptoms, including poor cognitive performance, and are subject to various complications. Positive airway pressure in the form of continuous positive airway pressure (CPAP)/bi-level positive airway pressure (BIPAP) is the mainstay of treatment to prevent airway collapse

during sleep, which is the fundamental abnormality in OSAHS. Unfortunately, many patients are non-compliant to CPAP/BIPAP mainly due to discomfort of using the machine. If the symptoms can be attributed to a particular sleep-stage abnormality, therapeutic modality to correct that abnormality may become an important adjunct to CPAP/BIPAP therapy to alleviate symptoms and or complications.

### Materials and methods

This is a cross-sectional study. Subjects aged 18 years or older who attended a hospital sleep laboratory for diagnostic polysomnography during a 1-month period were recruited consecutively. A diagnosis of OSAHS was made if apnea-hypopnea index (AHI) score was 5 or more, according to AASM criteria (8). Those who met the diagnostic criteria for OSAHS were included for analysis. Mild, moderate, and severe OSAHS were defined as AHI of 5 to <15, 15 to 30, and >30, respectively (8).

Subjects filled a questionnaire for symptoms before the overnight polysomnography. Following symptoms were assessed in the questionnaire: excessive fatigue or sleepiness, falling asleep during the day, waking up tired, inattention (trouble paying attention due to sleepiness), snoring, stopped breathing during sleep, insomnia and leg jerks during sleep. Symptoms were graded as 0 if absent, 1 if sometimes, 2 if usually, and 3 if almost always present. This ranking of severity of symptoms was used in Spearman's correlation test.

Subjects who attended for positive airway pressure (PAP) titration studies were excluded from the study. This is because polysomnographic abnormalities during titration studies do not reflect the baseline abnormalities.

Polysomnograms were scored manually following AASM scoring manual (2). Data were analyzed using SPSS version 20. Sleep stages were presented as percentages of TST. Mean and standard deviation were used for normally distributed data and median and interquartile ranges were used for non-normally distributed data.

Shapiro–Wilk test was used for normality of data distribution. Spearman's test was used to see any significant correlation.  $P < 0.05$  was considered significant.

### Results

Thirty subjects met diagnostic criteria for OSAHS, of which males constituted 46.7% and females constituted 53.3%. Mean age was  $53.87 \pm 10.73$  years. Mean BMI was  $39.10 \pm 9.10$ . Majority (83.3%) were obese with BMI  $\geq 30$ . Mild, moderate, and severe OSAHS were present in 30.0, 23.3, and 46.7%, respectively. Symptoms reported by patients or observed by partners are presented in Table 1.

Sleep architecture and AHI are presented in Table 2.

We did Spearman's rank correlation between symptoms and sleep architecture. Results are presented in Table 3.

### Discussion

Most of the patients were obese older adults with slight female predominance. Sleep onset was normal but TST and sleep efficiency were low. There were frequent arousals with increased stage N1 and high normal stage N2 sleep. Stage N3 and REM sleep were low. Most patients were symptomatic and snoring was present in almost all of them. In Spearman's rank correlation, the more the subjects were deprived of N3 sleep, the more they complained of snoring, excessive fatigue, sleepiness, falling asleep during the day, trouble paying attention, and insomnia. None of the symptoms were related to other sleep-stage abnormalities. Frequent arousal during sleep correlated with frequent complaints of insomnia. Median sleep efficiency was low, but those who had relatively better sleep efficiency, they complained more of waking up tired. Although AHI correlated with most of the sleep architecture abnormalities, it had no relationship with any of the symptoms. AHI also did not correlate with Epworth sleepiness scale, which is on par with findings described in other studies (19, 20). If the

Table 1. Frequency of symptoms

Symptoms	Absent (%)	Present			Total present (%)	Total
		Sometimes (%)	Usually (%)	Almost always (%)		
Snoring	3.7	14.8	7.4	74	96.3	27
Falling asleep during the day	15.4	53.8	15.4	15.4	84.6	26
Waking up tired	19.2	34.6	26.9	19.2	80.8	26
Excessive fatigue or sleepiness	20.0	28.0	24.0	28.0	80	25
Stopped breathing during sleep	32.0	32.0	24.0	12.0	68	25
Insomnia	34.6	38.5	19.2	7.7	65.4	26
Trouble paying attention	34.6	42.3	15.4	7.7	65.4	26
Leg jerks during sleep	59.1	36.4	4.5	0	40.9	22

Table 2. Sleep architecture and AHI

Variable	Mean	SD	95% CI	Median	IQR
Sleep onset (min)				10.00	15.25 (2.50–17.75)
Total sleep time (min)				334.0	83.75 (276.25–360.00)
Sleep efficiency (%)				84.00	21.00 (70.00–91.00)
Arousal index				15.50	41.65 (8.75–50.40)
Stage N1 sleep (% of TST)				19.50	19.00 (13.40–32.40)
Stage N2 sleep (% of TST)	53.93	13.39	48.40–59.46		
Stage N3 sleep (% of TST)				3.90	19.50 (0.00–19.50)
REM sleep (% of TST)	8.92	6.21	6.35–11.48		
AHI				19.40	65.60 (10.60–76.20)

AHI = apnea-hypopnea index; IQR = interquartile range; TST = total sleep time.

findings of this study can be confirmed by larger controlled studies, correcting stage N3 sleep deficiency by PAP or pharmacotherapy may result in symptomatic improvement in patients with obstructive sleep apnea-hypopnea syndrome.

### Conclusions

Most of the symptoms in obstructive sleep apnea-hypopnea syndrome in adults are related to decreased stage N3 sleep. If confirmed by larger controlled studies, correcting stage N3 sleep deficiency by pharmacological

Table 3. Correlations of symptoms with sleep architecture and AHI

		N1	N2	N3	REM	Sleep onset	Sleep time	Sleep efficiency	Arousal index	AHI
Snoring	Correlation coefficient	0.267	0.062	−0.417	−0.089	0.264	0.065	0.091	0.185	0.223
	<i>p</i>	0.178	0.760	<b>0.031</b>	0.660	0.184	0.748	0.650	0.356	0.264
Falling asleep during the day	Correlation coefficient	0.234	0.105	−0.571	0.175	−0.302	0.246	0.236	0.146	0.104
	<i>p</i>	0.249	0.609	<b>0.002</b>	0.393	0.134	0.225	0.246	0.477	0.613
Waking up tired	Correlation coefficient	0.075	0.061	−0.346	0.090	−0.226	0.357	0.423	0.224	0.062
	<i>p</i>	0.716	0.765	0.083	0.662	0.267	0.074	<b>0.031</b>	0.271	0.763
Excessive fatigue or sleepiness	Correlation coefficient	0.355	−0.054	−0.449	−0.161	0.214	−0.045	−0.059	0.170	0.148
	<i>p</i>	0.082	0.798	<b>0.024</b>	0.443	0.305	0.830	0.780	0.416	0.479
Stopped breathing during sleep	Correlation coefficient	0.163	0.070	−0.200	0.083	0.019	0.077	0.161	0.058	0.178
	<i>p</i>	0.436	0.740	0.337	0.693	0.929	0.714	0.442	0.784	0.396
Insomnia	Correlation coefficient	0.281	−0.078	−0.426	−0.264	−0.213	−0.336	−0.264	0.445	0.151
	<i>p</i>	0.164	0.707	<b>0.030</b>	0.192	0.297	0.093	0.193	<b>0.023</b>	0.463
Trouble paying attention	Correlation coefficient	0.245	0.026	−0.479	−0.215	−0.296	0.042	0.104	0.318	0.249
	<i>p</i>	0.227	0.899	<b>0.013</b>	0.291	0.141	0.837	0.612	0.113	0.220
Leg jerks during sleep	Correlation coefficient	−0.161	0.351	0.069	0.294	−0.008	0.250	0.278	−0.145	−0.178
	<i>p</i>	0.475	0.109	0.760	0.183	0.972	0.262	0.211	0.520	0.427
AHI	Correlation coefficient	0.605	−0.364	−0.484	−0.552	−0.012	−0.388	−0.394	0.775	–
	<i>p</i>	<b>0.000</b>	<b>0.048</b>	<b>0.007</b>	<b>0.002</b>	0.949	<b>0.034</b>	<b>0.031</b>	<b>0.000</b>	

AHI = apnea-hypopnea index.

Only statistically significant values are highlighted.

means may become an important adjunct to PAP therapy to alleviate symptoms.

### Conflict of interest and funding

The authors have not received any funding or benefits from industry or elsewhere to conduct this study.

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