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Research Paper: Association of Sleep Spindles, Sleep Apnea, and Other Polysomnography Parameters; a Single Center Preliminarily Report

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is associated with arousals due to the cessation of breathing during sleep. On the other hand, sleep spindles, an EEG wave mainly seen in stage 2 of non-REM sleep (N2), are responsible for many functions including the maintenance of sleep. We aimed to investigate the association between sleep spindles and OSA and compare the additional polysomnography (PSG) metrics in a group of patients with OSA.

Materials and Method: Fifty consecutive patients with moderate and severe OSA were recruited. Association of apnea-hypopnea index (AHI) with spindles in N2 and arousals were evaluated. Other PSG metrics were compared in the moderate versus severe group.

Results: Body mass and snore indices were significantly more in the severe group (p=0.002 and p<0.001, respectively). Arousals were more frequently seen in severe OSA cases (p=0.064). Sleep spindle index did not have any relationship with AHI and the number of arousals. However, arousals were weakly correlated with AHI (Spearman's rho= 0.293, p=0.039) and snore index (Spearman's rho= 0.365, p=0.010).

Conclusion: Severity of OSA did not show a clear correlation with spindle density in N2. Further studies with larger samples and a control group are needed to prove a relationship between sleep spindles and OSA.

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1. Background

Sleep spindles are characteristic electroencephalographic (EEG) findings of non-rapid eye movement (NREM) sleep and are more prevalently seen in stage 2 of sleep (N2) (1). Studies have shown that among many other brain functions, spindles are key elements in sensory shutdown during sleep (2). Spindle activity contributes to neuronal development, memory consolidation, and maintenance of sleep (3). Spindle-rich periods of sleep are known to be more protected from arousals (4).

Some factors are known to change the pattern of sleep spindles. Schizophrenia is widely known to decrease the density of spindle (5). Also, the density and amplitude of sleep spindles are reduced in Parkinson's disease (6). On the other hand, many drugs, most notably sedative-hypnotic drugs, can increase the density of spindles (7).

Obstructive sleep apnea (OSA) is characterized by bouts of cessation or reduction of breathing while sleeping (8). It is historically believed that loss of airflow following airway obstruction in patients with OSA triggers cortical arousal which in turn allows pharyngeal muscles to dilate and open the airway again (9). It is expected that this fragmentation of sleep may cause changes in sleep spindles. Few studies investigated the relationship between sleep apnea and spindles. Himanen et al. compared 12 OSA patients with a control group and found slower spindle frequencies in apnea patients deducing that sleep spindles indicate disturbed sleep and altered neural mechanisms in these cases (10). A study with a large population conducted by Parker et al. found that increased apnea-hypopnea index (AHI) was associated with lower spindle density in N2 and N3, and higher arousal index was associated with greater spindle amplitude. Carvalho et al. found that OSA slows down sleep spindle frequency. (11). A 2021 study by Mohammadi et al. showed that density of spindles in N2 of OSA patients does not differ from healthy individuals. However, the spindle density in N3 in moderate and severe OSA is significantly less than mild OSA and the control group (12). Our study aims to evaluate the association of sleep spindle density and OSA, along with the comparison of other polysomnography (PSG) parameters among OSA patients with different severity.

2. Materials and Methods

We evaluated PSGs of fifty consecutive patients referred to the sleep lab at the School of Advanced Medical Sciences and Technologies, Shiraz, Iran. This human study was performed in accordance with the ethical standards of the institutional/national research committee and with the Declaration of Helsinki 1964.

Inclusion criteria were having at least one of the typical symptoms of OSA according to the American Academy of Sleep Medicine (13), age 18 to 70, and AHI equal or more than 15. Exclusion criteria were the presence of current psychiatric disorder, history of any neurological disease, pregnancy, and consumption of narcotics, sedative-hypnotics, and antihistamines in recent two weeks. Demographic indices, body mass index (BMI), and all PSG data including spindles in 8 EEG electrodes, body position, electrocardiogram, oro-nasal airflow by thermistor, thoracoabdominal respiratory movements, and blood oxygen saturation were collected. PSG parameters were recorded by DOMINO software (SOMNOmedics GmbH, Randersacker, Germany). Two neuroscientists evaluated the EEGs, identified and recorded the sleep spindles. $15 \leq AHI < 30$ was considered as moderate OSA and $AHI \geq 30$ was considered as severe OSA (14). Wherever the term "index" is used in this text, it describes the number of that entity's occurrences per hour.

The normality of the data was assessed by the Shapiro-Wilk test. AHI, N2 spindle index, and arousal index proved to be abnormally distributed hence, Spearman's rank correlation coefficient was used to assess the relationship of these continuous variables, and the Mann-Whitney U test was used to compare different indices among moderate and severe OSA groups. A p-value of less than 0.5 was considered statistically significant. Analyses were conducted in Stata (16.1, StataCorp LLC, College Station, TX).

3. Results

A total of fifty cases with moderate to severe OSA were enrolled. The mean age of the participants was 47.78±13.12 years. 27 subjects (54%) were male and 23 (46%) were female. 22 patients (44%) belonged to the moderate and 28 (56%) to the severe OSA group.

Arousal in the severe OSA was significantly more compared to the moderate OSA (84.90 vs. 72.10, p=0.064). The mean of spindle index in moderate OSA was less than severe but the difference was not statistically significant (166.83 vs. 182.75, p-value=0.564). Differences in PSG parameters between mild and moderate OSA are shown in table 1.

Figures 1 and 2 show the scatterplot of AHI with spindle and arousal indices, respectively. Spindle index was not associated with arousals, desaturations, and AHI. With increasing AHI, more arousals and snores were observed. however, these relationships were weak (Spearman's rho= 0.293 and 0.365, p=0.039 and 0.010, respectively) (Table 2).

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Table 1. General characteristics of moderate and severe OSA groups

Patient characteristcs and PSG indices	Moderate OSA (n=22)	Severe OSA (n=28)	p-value
Age	46.14±13.57 (20-70)	49.07±12.85 (18-68)	0.406
Sex Male	11 (50%)	16 (57.14%)	0.828*
Female	11 (50%)	12 (42.86%)	
BMI	25.90±0.61 (24.63- 27.17)	29.54±1.09 (27.30-31.78)	0.002
AHI	22.79±5.64 (15-29.8)	49.24±1811 (30-88.3)	<0.001
Apnea index	1.79±1.47 (0.4-5.1)	9.88±12.32 (02-58.1)	<0.001
Hypopnea index	21.06±5.73 (11.9-29.4)	37.45±16.04 (5.9-76.1)	<0.001
Desaturation below 90 index	13.62±5.88 (4.4-28.1)	44.69±24.30 (5.1-90)	<0.001
Minimal 02	86.36±3.32 (78-92)	77.68±8.81 (57-90)	<0.001
N2 Spindles index	182.75±84.69 (55.8-327.7)	166.83±64.96 (79.9-339.3)	0.564
Arousal index	72.10±18.87 (35.7-111.9)	84.90±27 (31.5-190.6)	0.064
LM index	20.91±12.75 (4.7-54.4)	26.36±17.87 (3.5-81.6)	0.354
PLM index	13.14±11.53 (0-42.3)	15.77±16.39 (0.8-74.4)	0.709
Snore index	171.14±132.56 (0.5-494.1)	345.06±173.04 (66.4-727.4)	<0.001

*calculated with Pearson's chi square test

Abbreviations: AHI: apnea-hypopnea index, BMI: body mass index, LM: leg movement, OSA: obstructive sleep apnea, PLM: periodic leg movement

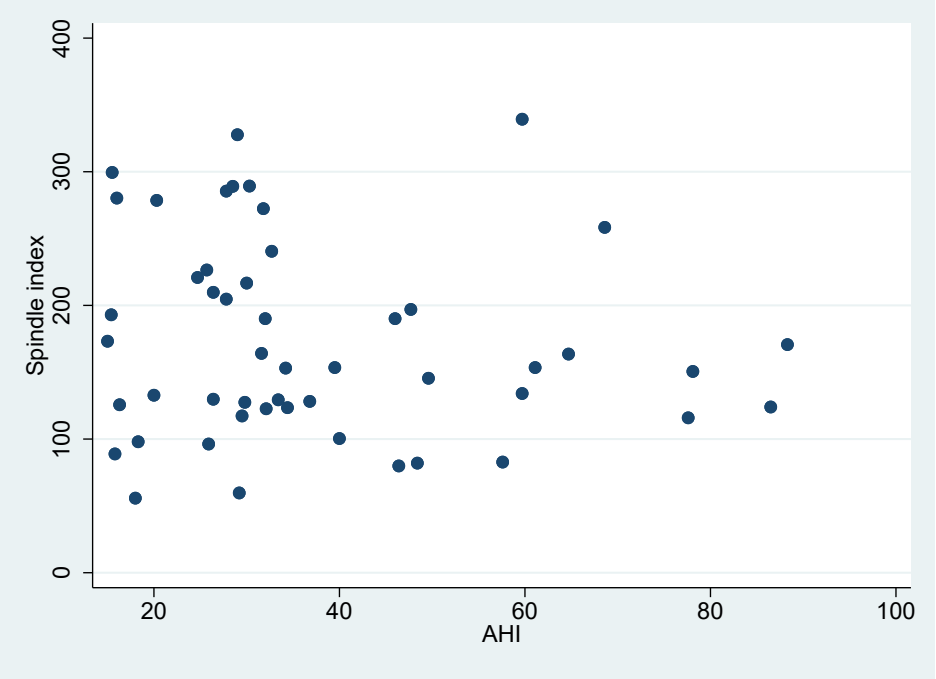

Figure 1. Scatterplot of spindle index and AHI

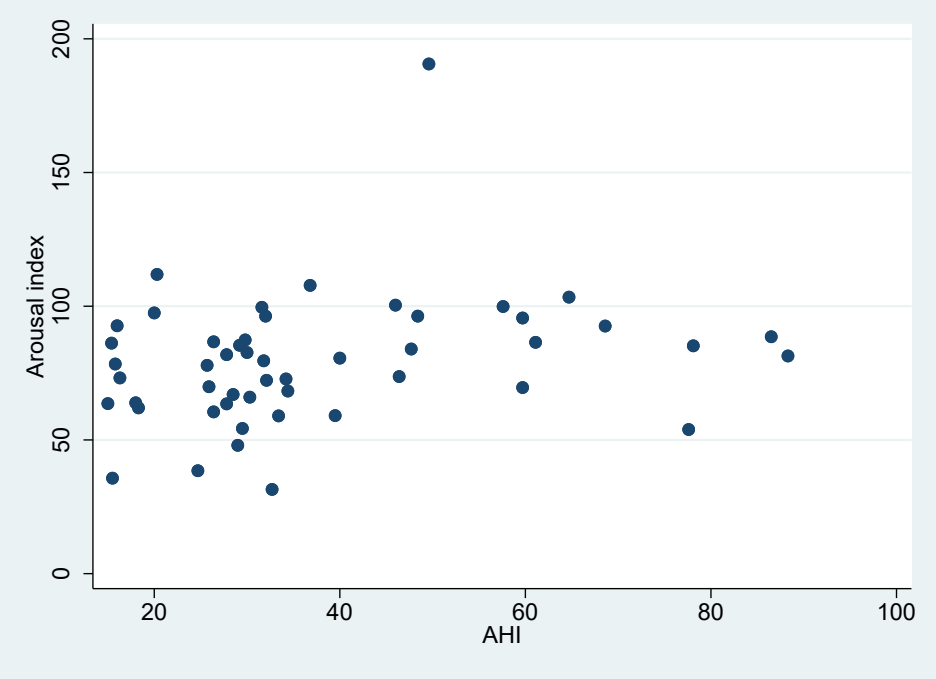

Figure 2. Scatterplot of arousal index and AHI

Table 2. Correlation between apnea-hypopnea index and desaturations below 90%, spindle, and arousal indices

	Spearman's rho	p-value
AHI & spindle index	-0.143	0.321
AHI & arousal index	0.293	0.039
Desaturations below 90% & spindle index	-0.266	0.062
Arousal index & spindle index	-0.012	0.931
AHI & snore index	0.365	0.010

4. Discussion

In this study, the different PSG metrics among moderate and severe OSA were evaluated. Our main findings were that frequency of spindles in N2 does not decrease with increased severity of OSA, and there is a weak positive relationship between severity of OSA in AHIs above 15 and the number of arousals.

Our findings were in line with Mohammadi et al. who also found no association between AHI and densities of spindles in N2. However, our findings contrast those of Parker et al. who demonstrated such association (11, 15). Although we did not evaluate N3, there is evidence of a negative association between spindles and AHI in N3 (16). This suggests that the impact of sleep apnea on spindles is probably more prominent in N3.

The positive relationship between snores and AHI indicates that the snores can be used as crude signs of severity of the disease when put together with symptoms of OSA in a clinical setting.

5. Limitations

A major shortcoming of our study is the lack of a control group. To better study the relationship between sleep spindles and the severity of OSA, a healthy group is required. Another limitation was the relatively low number of cases which attributed to insignificant p-values in some models. For future researches, other features of sleep spindles like amplitude and duration in N3 as well as N2 should be recorded.

6. Conclusion

Although the role of sleep spindles in sleep maintenance is well-established, their role in the context of OSA is yet to be determined. There is contradictory evidence about the association between OSA and sleep spindles. Larger case-control studies using a reliable spindle detection algorithm are required for a decisive verdict.

Conflict of interests

The authors declare no conflict of interest that is relevant to the content of this article.

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