



Short communication

Effect of CPAP on sleep spindles in patients with OSA

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ABSTRACT

Objective: Consequences of OSAS include excessive daytime sleepiness, divided sleep architecture, impaired neurocognitive performance, and significant psychosocial disruption. In this study we aimed to evaluate sleep spindles changes before and after PAP treatment in patient with OSA.

Methods: Seventy-three consecutive patients (M/F:61/12) who applied to Sleep Disorders Center of Inonu University Hospital and met the inclusion criteria were enrolled to this study. Full-night polysomnography and CPAP titration were performed.

Results: Mean AHI were detected as 43.8 ± 24.4 and mean oxygen saturation was 79% in patients under full-night PSG. Significant increasing were observed on spindle count under CPAP titration (192 ± 98 vs 347 ± 165 per hour $p < 0.001$)) and also significant increasing was recorded on oxygen saturation (79 ± 15 vs $94 \pm 4\%$ $p < 0.001$).

Conclusion: Both spindle count and oxygen saturation were recorded to be significantly increased under CPAP titration while there was a significant decrease in apnea-hypopnea. We have shown that significant increase in number of spindles can be achieved with CPAP treatment, those to be decreased in patient with OSA. Number of spindles may play a role as an indicator of better outcome in OSA patients.

1. Introduction

Sleep disorders are common health problem on worldwide. Obstructive sleep apnea (OSA) is one of the most popular sleep disorder characterized by repeated cessations of breathing during sleep. Consequences of OSA include excessive daytime sleepiness, divided sleep architecture, impaired neurocognitive performance, and significant psychosocial disruption (Sanders, 2005; Masood and Phillips, 2000). Patients with OSAS have increased morbidity from cardiovascular events and work accidents (Sanders, 2005; He et al., 1988). The treatment modalities for OSA are nasal continuous positive airway pressure (CPAP) and surgery for some certain conditions. CPAP has been shown to reduce daytime sleepiness, oxyhemoglobin desaturations, heart rate, and pulmonary pressure, improve cognitive performance, and increase quality of life (Sanders, 2005; Kakkar, 2007; Davies and Harrington, 2016).

CPAP treatment is the first choice for most patients with OSA. Positive airway pressure is gold standart for managing in OSA and this method ameliorates sleep problems and sleep architecture. Physiological sleep stages and normal sleep waves are obtained with CPAP devices (Kakkar, 2007).

Sleep spindles are hallmark in Non-REM sleep stage two (N2), and are determined sleep stages on electroencephalography (EEG) records.

Spindles waves have high frequency (9–15 Hz) and 0.5–3 s duration. They repeat every 3–10 s on EEG light stage of Non-REM sleep (Davies and Harrington, 2016). Sleep spindles are distinctive EEG oscillations emerging during non-REM sleep that have been implicated in multiple brain functions, including sleep quality, sensory gating, learning, and memory (Steriade et al., 1993; Dan and Poo, 2004; Diekelmann and Born, 2010). Previous studies have shown slower frequency and deceleration of spindles in moderate OSA patients compare to mild patients (Himanen et al., 2003; Carvalho and Gerhardt, 2014) and patients who treated with CPAP have increased spindles in one study (Saunamäki et al., 2017). Despite considerable knowledge about the mechanisms underlying these neuronal rhythms, their function remains poorly understood and current views are largely based on correlational evidence (Davies and Harrington, 2016).

We have thought that spindle waves might be affected in OSA and it may play role as healing marker in that clinical condition. In this study we aimed to evaluate sleep spindles changes before and after PAP treatment in patient with OSA.

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2. Methods

2.1. Patients

Seventy-three consecutive patients (M/F:61/12) who applied to Sleep Disorders Center of Inonu University Hospital and met the inclusion criteria were enrolled to this study. All patients had nocturnal snoring, excessive daytime sleepiness, and witnessed apnea. Epworth Sleepiness Scale ESS (Johns, 1991) was applied to all patients, and cases with high scores (ESS > 10) were accepted into the full-night sleep study. Full-night polysomnography was performed using conventional instrumentation and analysis according to the recommendations on syndrome definition and measurement techniques published by the American Academy of Sleep Medicine (American Academy Of Sleep Medicine., 1999). Sleep stages were detailed by Standard electroencephalographic, electro-oculographic, and electromyographic (EMG) criteria. Apneas and hypopneas were recorded by oronasal flow cannulae attached to a pneumotachograph. Arterial oxygen saturation was measured by pulse oximetry using a finger probe. Thoracic and abdominal movements were recorded by using inductive plethysmography to document respiratory effort. Periodical limb movements were recorded from surface EMG electrode on tibialis anterior muscle of the lower extremity. Obstructive apneas were defined as absence of airflow for longer than 10 s, obstructive hypopneas described as a 50% decrease in airflow or a clear but lesser decrease in airflow if coupled with either a desaturation of > 3% or an arousal in the context of ongoing respiratory effort. All records were scored manually for sleep stage, arousals, apneas, and hypopneas. Sleep spindles were counted during fifteen minutes first N2 stage and arranged to one hour.

After full-night polysomnography, CPAP titration were performed to patients with moderate-to severe OSAS (AHI > 15) Sleep spindles were counted again first N2 stage during fifteen minutes and arranged to one hours. Because, uninterrupted sixty minutes N-REM light sleep is not possible due to alteration N-REM light to REM or N-REM light to N-REM deep sleep

2.2. Statistical analysis

Paired-t test was applied to compare before and after values. Spearman correlation test was used to evaluate the correlation between sleep spindle, age. A p value of < 0.05 was considered statistically significant.

3. Results

Mean age of patient was $50,3 \pm 12,2$ (M/F: 61/12, range:28-90 years, Table 1). Mean AHI were detected $43,8 \pm 24,4$ and mean oxygen saturation was 79% of patients under full-night PSG. Statistically significant increase was observed on spindle count under CPAP titration compare to pretreatment values (192 ± 98 .vs 347 ± 165 per hour $p < 0.001$) and also significant increase was recorded on oxygen saturation (79 ± 15 vs $94 \pm 4\%$ $p < 0.001$) and mean AHI was lower than 5/h during titration (Table 2). Significant negative correlation was detected between spindles and age ($r:0.74$ $p < 0.001$) and positive correlation was observed between spindles and oxygen

Table 1
Patients Demographics

M/F	61/12
Mean age year	$50,3 \pm 12,2$
BMI	$32.2 \pm 5,1$
ESS	11.7 ± 1.8

ESS Epworth Sleepiness Scale.
BMI body mass index.

Table 2

Comparisons of parameters before and after treatment.

	before CPAP	CPAP titration	p value
Oxygen%.	79 ± 15	94 ± 4	$p < 0.001$
AHI	$43,8 \pm 24,4$	$4,1 \pm 3$	$p < 0.001$
Spindles per hour	192 ± 98	347 ± 165	$p < 0.001$

AHI apnea-hypopnea index.

saturation ($r = 0.257, p = 0.012$).

4. Discussion

Recurrent apnea and hypopnea episodes cause intermittent hypoxia in OSA. It is reported that Intermittent hypoxia is potential factor causing neuronal damage and neurocognitive impairments in sleep apnea patients (Xie, 2012; Feng et al., 2012; Werli et al., 2016). Sleep spindles are generated by neuronal circuits reside in the intrathalamic cells and thalamocortical cells (Astori et al., 2013). Spindles play role on sleep quality, cellular plasticity and memory consolidation (Steriade et al., 1993; Dan and Poo, 2004; Diekelmann and Born, 2010). We have shown that spindles decrease in OSA patients and after CPAP treatment number of spindles significantly increase in this study (Table 2). We have observed the existence of the positive correlation between oxygen saturation and number of spindles and existence of the negative correlation between spindles and patient ages as well. Apnea and hypopneas were shown to be recovered in CPAP treatment and patients have stated that all neurological symptoms are ameliorated (Sanders, 2005; Masood and Phillips, 2000; Davies and Harrington, 2016). Under CPAP device, higher oxygen levels are obtained on central nervous system and intrathalamic cells without apnea-hypopneas, thereby those cells might have more ability to generate sleep spindles. Decreased respiratory events and increased number of spindles in patients with OSA while sleeping may be responsible for the recovery of the clinical symptoms and neurocognitive functions. In the other words, high number of spindle count and decreased number of apnea-hypopnea may be a good prognostic factor in OSA. In this study, we have shown the significantly increased number of spindles after CPAP treatment which were shown to be decreased in untreated OSA patients. The impact of OSA on cardiovascular and endocrine system were already shown in literature, however neurocognitive disorders caused by OSA still needs to be investigated.

5. Conclusion

In this study, increased sleep spindles might be played role on neurocognitive behavior in patients with OSA. According to these findings sleep spindles might be evaluated as better outcome for OSA patients. Sleep specialist should be awareness not only counting apnea-hypopnea but also be noticed the density of spindles on EEG records.

Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Authors' contributions

OY and DA wrote the manuscript. All authors have read and approved the manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent: Informed consent was obtained from all individual participants included in the study.

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References

- Sanders, 2005. MH sleep breathing disorders. In: Kryger, M.H., Roth, T., Dement, W.C. (Eds.), *Principles and Practice of Sleep Medicine*, 4th edn. Elsevier, Amsterdam, pp. 969–1121.
- Masood, A., Phillips, B., 2000. Sleep apnea. *Curr. Opin. Pulm. Med.* 6, 479–484.
- He, J., Kryger, M.H., Zorick, F.J., Conway, W., Roth, T., 1988. Mortality and apnea index in obstructive sleep apnea: experience in 385 male patients. *Chest* 94, 9–14.
- Kakkar, R.K., 2007. Berry RB Positive airway pressure treatment for obstructive sleep apnea. *Chest* 132, 1057–1072.
- Davies, C.R., Harrington, J.J., 2016. Impact of obstructive sleep apnea on neurocognitive function and impact of continuous positive air pressure. *Sleep Med Clin.* 113, 287–298.
- Astori, S., Wimmer, R.D., Lüthi, A., 2013. Manipulating sleep spindles ?expanding views on sleep, memory, and disease. *Trends Neurosci.* 36, 738–748.
- Steriade, M., et al., 1993. Thalamocortical oscillations in the sleeping and aroused brain. *Science* 262, 679–685.
- Dan, Y., Poo, M.M., 2004. Spike timing-dependent plasticity of neural circuits. *Neuron* 44, 23–30.
- Diekelmann, S., Born, J., 2010. The memory function of sleep. *Nat. Rev. Neurosci.* 112, 114–126.
- Himanen, S.L., Virkkala, J., Huupponen, E., Hasan, J., 2003. Spindle frequency remains slow in sleep apnea patients throughout the night. *Sleep Med.* 4, 361–366.
- Carvalho, D.Z., Gerhardt, G.J., 2014. Dellagustin G, de santa-Helena EL, lemke N, segal AZ, schönwald SV loss of sleep spindle frequency deceleration in obstructive sleep apnea. *Clin. Neurophysiol.* 125, 306–312.
- Saunamäki, T., Huupponen, E., Lopenon, J., Himanen, S.L., 2017. CPAP treatment partly normalizes sleep spindle features in obstructive sleep apnea. *Sleep Disord* 2017<http://dx.doi.org/10.1155/2017/2962479>. (in press).
- Johns, M.W., 1991. A new method for measuring daytime sleepiness. *Sleep* 14, 540–545.
- American Academy Of Sleep Medicine, 1999. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American Academy of Sleep Medicine task force. *Sleep* 22, 667–689.
- Xie, H., 2012. Yung WH Chronic intermittent hypoxia-induced deficits in synaptic plasticity and neurocognitive functions: a role for brain-derived neurotrophic factor. *Acta Pharmacol. Sin.* 33 (1), 5–10.
- Feng, J., Wu, Q., Zhang, D., 2012. Chen BY Hippocampal impairments are associated with intermittent hypoxia of obstructive sleep apnea. *Chin. Med. J.* 125, 696–701.
- Werli, K.S., Otuyama, L.J., Bertolucci, P.H., Rizzi, C.F., Guilleminault, C., Tufik, S., Poyares, D., 2016. Neurocognitive function in patients with residual excessive sleepiness from obstructive sleep apnea: a prospective, controlled study. *Sleep Med.* 26, 6–11.