Sleep Stage Determines the Expression Pattern of Sleep Apneas

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Abstract

We report on an obese man with sleep stage-dependent apnea. His type of apnea was predominantly central during non-rapid eye movement (NREM) sleep, while it was obstructive during rapid eye movement (REM) sleep. We found significantly more and more severe apneas during REM sleep compared to NREM sleep. His apneas were remarkably reduced by position adjustment, suggesting that upper airway collapse played a key role in the induction of both types of apnea. As his apneic patterns were dependent on the sleep stages, we assumed that the balance between upper airway obstruction and instability of central respiratory control might be important in determining the expression types.

Key words: central sleep apnea, obstructive sleep apnea, prone position, rapid eye movement

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Introduction

Central sleep apnea (CSA), mixed sleep apnea (MSA), and obstructive sleep apnea (OSA), are the terms that classify apneic types polysomnographically according to their air flow and respiratory movement patterns. It is widely accepted that an upper airway obstruction plays an important role in inducing OSA, while the etiology of CSA still remains unclear. CSA is not a homogeneous disease but has a number of underlying mechanisms responsible for the instability of the central respiratory control (1). For example, primary alveolar hypoventilation, metabolic dysfunction, congestive heart failure, and neurological disorders can be associated with CSA. The upper airway obstruction is another mechanism known to reduce central respiratory drive and lead to central apneas. Several previous reports have suggested that there is a group of patients with CSA whose compliance of the upper airway is increased (2, 3), and that the treatment by nasal continuous positive airway pressure (CPAP) is effective in eliminating CSA as well as OSA (4, 5). This implies that the etiologies responsible for CSA and OSA may overlap, and, as a result, a single pathogenesis may cause different types of apneas. In fact, when we look

into the numerous case reports regarding SAS, the majority of patients have been described to have heterogeneous types of apneic events. Since the process of determining the expression type of apneas has not yet been fully discussed, we focused on the effects of sleep stages on the expression type of apneas in a single case.

Case Report

A 44-year-old obese male patient was admitted to the hospital with a history of loud nocturnal snoring, frequent apneic spells during sleep, and excessive daytime sleepiness, which leads to a poor performance at work. His physical examination revealed a markedly obese (body mass index, 35.3 kg/m²), and normotensive male with a short fat neck. No signs of cor pulmonale were observed. His ECG showed sinus rhythm without any abnormality and his respiratory function was within normal limits. The arterial blood gas values in supine position at rest under air breathing were as follows: pH, 7.4; PaO₂, 79 mmHg; PaCO₂, 50 mmHg. The normalized ventilatory response to carbon dioxide by body surface was below normal (0.35 L min⁻¹ mm Hg⁻¹ mm²). There was no visible lesion in his MRI brain study.

An overnight polysomnography was performed monitor-

Figure 1. Recording of polysomnography, showing typical waveforms of CSA (A) and OSA (B). CSA occurred mostly in NREM sleep, while OSA occurred in REM sleep (C).

Figure 2. Recording of SaO₂ in the supine position, and in the prone position. O₂ desaturation was markedly improved in the prone position.

ing electroencephalogram (EEG), electrooculogram (EOG), electrocardiogram (ECG), submental electromyogram (EMG), and SaO₂. Airflow was monitored at the nose and mouth by thermistors, and chest and abdominal wall movement were monitored by an impedance plethysmography. The patient took a supine position while he was sleeping. His total sleep time

was 411 minutes, and the sleep efficiency was 87.3%. His sleep architecture was perturbed by repeated apneas followed by arousal evidence, and it was predominantly composed of NREM sleep stage, the amount of which was 89.8% of the total sleep time. The proportion of REM sleep stage was 10.2%, which was markedly decreased. The

analysis of the overnight polysomnography showed 375 episodes of apneas (apnea index 54.7), of which 203 were central (Fig. 1A), 84 obstructive (Fig. 1B), and 88 mixed. During NREM sleep, 308 apneas were recorded (apnea index 50.1): 202 episodes of CSA, 27 episodes of OSA; and 79 episodes of MSA. On the other hand, 67 apneas were recorded during REM sleep (apnea index 95.7): 1 episode of CSA, 57 episodes of OSA; and 9 episodes of MSA. Figure 1C depicts the distribution of apneas due to sleep stages, which reveals that CSA occurred mostly during NREM sleep, while OSA occurred during REM sleep. No statistical difference was found between the minimum values of SaO_2 followed by CSA and those by OSA during NREM sleep ($88.9 \pm 0.19\%$ versus $86.3 \pm 1.03\%$); however, the minimum values of SaO_2 followed by apneas were significantly decreased during REM sleep compared to those during NREM sleep ($88 \pm 0.3\%$ versus $78 \pm 0.9\%$; $p < 0.0001$). In addition, the episodes of transitional Wenckebach type second-degree atrioventricular block were associated with obstructive apneas only during REM sleep.

As the patient's family mentioned that his snoring was much better in the prone position compared with that in the supine position, a repeat polysomnography was performed in the prone position. It demonstrated that there were only 8 episodes of apneas (apnea index 1.2), of which 2 were central, 5 obstructive, and 1 mixed during the total sleep of 417 minutes. In the prone position, the patient had better sleep quality, more III-IV sleep stages, and more REM sleep; however, the reduction of apneas did not correlate with the change of sleep architecture. Moreover, oxygen desaturation was markedly improved (Fig. 2), and there were no episodes of arrhythmia when he slept in the prone position. Although nasal CPAP had an equivalent effect for diminishing his apneas, he complained of discomfort from the device and preferred to be treated with sleep position adjustment.

Discussion

Here, we report a case that shows a strong correlation between apneic patterns and sleep stages. In this case, the apneic pattern was predominantly central; however, CSA occurred mainly during NREM sleep, while OSA occurred during REM. It is difficult to determine whether the primary cause of apneas of the present patient is related to upper airway obstruction, disability of central respiratory drive, or both. Since all types of his apneas were dramatically improved with either nasal CPAP or the prone position, we speculated that his apneas were primarily caused by upper airway collapse. His anatomical airway narrowing may have caused OSA, and the pharyngeal collapse may have inhibited the central respiratory drive by stimulating mechanoreceptors in the upper airway, thus yielding CSA. In addition, decreased respiratory drive due to less severe oxygen desaturation during NREM sleep compared to that during REM sleep may have possibly affected the pathogenesis of CSA in this case. It is interesting to note that upper airway col-

lapse triggered different types of apneas through different pathways and that the sleep stages modified the expression type of apneas.

Both NREM and REM are two distinct sleep stages that have a different physiologic influence on producing breathing disturbance (6). In REM sleep, it is well recognized that OSA tends to be more accentuated (7, 8). The factors which emphasize OSA during REM sleep are not well understood; however, an increased pharyngeal collapsibility has been described to be one such factor (9, 10). Moreover, the respiratory effort in response to upper airway occlusion and the ventilatory response to hypoxia and hypercapnia have been found to decrease more in REM sleep than in NREM sleep, and they are considered to contribute to the prolongation of OSA (11-13). In contrast, CSA was demonstrated to occur mostly in NREM sleep. Medullary respiratory rhythms were found to be more unstable during sleep onset, which might explain the increased number of CSA in NREM sleep (14, 15). The absence of posthyperventilation-induced apneic threshold in REM sleep could be another predisposing factor for the diminishing CSA during REM sleep (16). There are several reports demonstrating Cheyne-Stokes respiration which had a selective association with NREM sleep in patients with neurological problems (17-19); however, there is no report focusing on the selective association of CSA with NREM sleep and that of OSA with REM sleep in the same individual without any specific neurological disorder.

Although numerous therapeutic approaches have been used for the treatment of CSA syndrome (1), there is yet no established approach due to its complicated etiology. The effectiveness of sleep position adjustment has been commonly reported in OSA syndrome patients, and it has been suggested that changing positions prevents the upper airway from narrowing and collapsing (20, 21). As well as OSA, several investigators observed that, in some cases with CSA relating to upper airway reflexes, apneas were less frequent when the patients lay on the side (4, 22). In the present case, after changing the patient's sleep position from supine to prone, we experienced a dramatic improvement in his symptoms, the prevalence and severity of his apneas, the sleep architecture, and the arrhythmia. As changing the sleeping posture is a simple, noninvasive, and inexpensive procedure, we suggest that it has a clinically therapeutic value in some patients with CSA syndrome.

In conclusion, we characterized the close relationship between sleep apneic patterns and sleep stages in the present report. The associations of CSA with NREM sleep and OSA with REM sleep in this case implies that the representing type of apnea can be determined by the balance between upper airway collapse and central respiratory control, contributed by sleep stages. In addition, in those cases with positional CSA, the adjustment of sleep positions may be an effective intervention.

References

1. De Backer WA. Central sleep apnoea, pathogenesis and treatment: an overview and perspective. *Eur Respir J* **8**: 1372-1383, 1995.
2. Bradley TD, Brown IG, Zamel N, Phillipson EA, Hoffstein V. Differences in pharyngeal properties between snorers with predominantly central sleep apnea and those without sleep apnea. *Am Rev Respir Dis* **135**: 387-391, 1987.
3. Pepin JL, Pajon A, Veale D, Ferretti G, Levy P. Central sleep apnoea syndrome with upper airway collapse. *Eur Respir J* **6**: 592-595, 1993.
4. Issa FG, Sullivan CE. Reversal of central sleep apnea using nasal CPAP. *Chest* **90**: 165-171, 1986.
5. Hoffstein V, Slutsky AS. Central sleep apnea reversed by continuous positive airway pressure. *Am Rev Respir Dis* **135**: 1210-1212, 1987.
6. Roth T, Roehrs T. Sleep organization and regulation. *Neurology* **54**(Suppl 2): S2-7, 2000.
7. Series F, Cormier Y, La Forge J. Influence of apnea type and sleep stage on nocturnal postapneic desaturation. *Am Rev Respir Dis* **141**: 1522-1526, 1990.
8. Goh DY, Galster P, Marcus CL. Sleep architecture and respiratory disturbances in children with obstructive sleep apnea. *Am J Respir Crit Care Med* **162**(2 pt 1): 682-686, 2000.
9. Wiegand L, Zwillich CW, Wiegand D, White DP. Changes in upper airway muscle activation and ventilation during phasic REM sleep in normal men. *J Appl Physiol* **71**: 488-497, 1991.
10. Issa FG, Sullivan CE. Upper airway closing pressures in obstructive sleep apnea. *J Appl Physiol* **57**: 520-527, 1984.
11. Krieger J, Sforza E, Boudewijns A, Zamagni M, Petiau C. Respiratory effort during obstructive sleep apnea: role of age and sleep state. *Chest* **112**: 875-884, 1987.
12. Douglas NJ, White DP, Weil JV, et al. Hypoxic ventilatory response decreases during sleep in normal men. *Am Rev Respir Dis* **125**: 286-289, 1982.
13. Douglas NJ, White DP, Weil JV, Pickett CK, Zwillich CW. Hypercapnic ventilatory response in sleeping adults. *Am Rev Respir Dis* **126**: 758-762, 1982.
14. Perez-Padilla J, West P, Kryger M. Snoring in normal young adults: prevalence in sleep stages and associated changes in oxygen saturation, heart rate and breathing pattern. *Sleep* **10**: 249-253, 1987.
15. Horner RL, Kozar LF, Kimoff RJ, Phillipson EA. Effects of sleep on the tonic drive to respiratory muscle and the threshold for rhythm generation in the dog. *J Physiol* **474**: 525-537, 1994.
16. Xi L, Smith CA, Saupe KW, Henderson KS, Dempsey JA. Effects of rapid-eye-movement sleep on the apneic threshold in dogs. *J Appl Physiol* **75**: 1129-1139, 1993.
17. Power WR, Mosko SS, Sassin JF. Sleep-stage-dependent Cheyne-Stokes respiration after cerebral infarct: a case study. *Neurology* **32**: 763-766, 1982.
18. Dean AC, Graham BA, Dalakas M, Sato S. Sleep apnea in patients with postpolio syndrome. *Ann Neurol* **43**: 661-664, 1998.
19. Oksenberg A, Arons E, Snir D, Radwan H, Soroker N. Cheyne-Stokes respiration during sleep: a possible effect of body position. *Med Sci Monit* **8**: CS61-CS65, 2002.
20. McEvoy RD, Sharp DJ, Thornton AT. The effects of posture on obstructive sleep apnea. *Am Rev Respir Dis* **133**: 662-666, 1986.
21. Neill AM, Angus SM, Sajkov D, McEvoy RD. Effects of sleep posture on upper airway stability in patients with obstructive sleep apnea. *Am J Respir Crit Care Med* **155**: 199-204, 1997.
22. Bradley TD, McNicholas WT, Rutherford R, Popkin J, Zamel N, Phillipson E. Clinical and physiologic heterogeneity of the central sleep apnea syndrome. *Am Rev Respir Dis* **134**: 217-221, 1986.