ACTA SCIENTIFIC NEUROLOGY (ISSN: 2582-1121)

Volume 7 Issue 6 June 2024

Review Article

Neurophysiology Of Obstructive Sleep Apnea

Kalpana AP[1]*, Kannabiran B[2], Nagarani R[2] and Sivakumar S[3]

[1]Ph.D. Scholar, RVS College of Physiotherapy /Professor, KMCH College of Physiotherapy, Coimbatore Affiliated to the Tamil Nadu Dr. MGR Medical University, Chennai, India

[2]Professor/Ph.D. Guide, RVS College of Physiotherapy, Coimbatore Affiliated to the Tamil Nadu Dr. MGR Medical University, Chennai, India

[3]Professor KMCH College of Physiotherapy, Coimbatore, The Tamil Nadu Dr. M. G. R. Medical University, Chennai, India

***Corresponding Author:** Kalpana AP, Ph.D. Scholar, RVS College of Physiotherapy / Professor, KMCH College of Physiotherapy, Coimbatore Affiliated to the Tamil Nadu Dr. MGR Medical University, Chennai, India.

DOI: 10.31080/ASNE.2024.07.0739

Received: March 15, 2024

Published: May 20, 2024

Abstract

Obstructive sleep apnea is often an undiagnosed condition worldwide. Untreated sleep apnea may lead to many adverse consequences such as cardiovascular events, road traffic accidents, and fatigue. Hence there is a need to address the neurophysiological changes associated with obstructive sleep apnea. This review of evidence on the neurophysiology of OSA showed the changes in neuronal activity during the sleep-wake cycle. Snoring, a common symptom of OSA induces vibratory trauma to the upper airway muscles. Various imaging techniques showed the significance of genioglossus muscle in maintaining airway stability during sleep and reduced muscle activation increases the pharyngeal resistance and predisposes to collapse. Ultrasound measurement of the diaphragm of OSA patients noticed the increased thickness of the diaphragm compared with the age-matched subjects. Increased sympathetic activity was observed in OSA patients. A high level of evidence is needed in the area of neuro-physiological changes in obstructive sleep apnea patients.

Keywords: Neurophysiology; Obstructive Sleep; Apnea

Introduction

Sleep is the fundamental need of an individual. Sound sleep is mandatory for the physical and mental well-being of human beings. The quality of sleep is affected by sleep-related disorders. One of those disorders is Obstructive sleep apnea. The prevalence rate of obstructive sleep apnea is found to be 32.5% as per a recent study in India [1].

The rate is very high when compared to the previous study result which was around 3.76% of the South Indian population [2]. Increase in prevalence is primarily due to the obesity. Most obstructive sleep apnea is undiagnosed as snoring is perceived by many people as a normal happening during sleep. The complications of sleep apnea are cardiovascular diseases including hypertension, motor vehicle accidents, decreased quality of sleep, etc.., [3].

As the sleep disorder affects the quality of life, attention must be given to the management of obstructive sleep apnea. Understanding the neurophysiology of the condition always helps to manage the disorder. Waters pointed out the significance of

critical closing pressure of the upper airway, reduced recruitment of muscles and increased loop gain on sleep apnea in the handbook of clinical neurology [4,5].

So this study aims to review the recent evidence on neurophysiological changes in individuals with obstructive sleep apnea.

Method

A literature review was carried out to know the neuro physiological changes in obstructive sleep apnea.

Results

Physiology of sleep

Figure 1: Stages of sleep cycle.

Aserinsky., *et al.* described the various stages of sleep and recurring cycles of stages of sleep. Delta wave power ratios may be considered biomarkers for their characteristics of attenuation in Non-rapid eye movement sleep and subsequent increase in rapid eye movement sleep [6]. Sulaman., *et al.* proposed a de-arousal model which stresses the significance of pre-sleep behavior on the neuromodulatory background necessary for sleep initiation [7].

A study on the sleep-wake cycle emphasized how hypothalamic circuitry integrates time cues of photic and nonphotic environmental on the architecture and circadian rhythm of sleep [8].

Updated information on the biology of sleep stated how the rapid eye movement phase of sleep affects processes such as sensory motor function [9]. New technology such as optogenetics, and chemo genetics helps to understand the sleep-wake cycle [10].

Neurophysiology of sleep

Suprachiasmatic nuclei present in the hypothalamus control the circadian rhythm sleep-wake cycle. The preoptic nucleus present at the ventro lateral aspect of the hypothalamus has the neuroanatomical substrates of Non-Rapid eye movement and Pons has substrates of Rapid eye movement [11].

Neural mechanism for paradoxical sleep

Neuronal activity increases in pons, amygdala, and cingulate gyrus during rapid eye movement sleep. It is triggered by pontine potentials in the form of ponto-geniculo-occipital spikes and Acetylcholine seems to have a role on sleep [12].

Neurophysiology in OSA

As sleep apnea occurs only during sleep, the impact of sleep stages on respiration is of critical importance. Oscillation in ventilation during sleep occurs due to alteration in feedback control of breathing [4,13].

Dysfunctional mesencephalic trigeminal nucleus may be incapable of activating neurons in the ascending reticular activating system that controls vegetative functions and electroencephalographic findings associated with both sleep apnea and normal sleep [14].

Clinical predictors

Apnea hypopnea index of more than 47 and lowest oxygen saturation of less than 77% are identified as clinical predictors of central and obstructive apnea in patients with OSA [15]. When compared with pure obstructive sleep apnea, mixed apnea patients have a significant problem in non-rapid eye movement stage of sleep, increased percentage of sleep at first stage, a reduced percentage of second stage of NREM sleep, and an almost complete loss of third stage of NREM sleep [15].

The compliance rate of CPAP use in few OSA patients is poor which could result in reduced stability of respiratory regulation [16].

Neuroimaging in obstructive sleep apnea

Atrophy of the hippocampus was noticed in patients with OSA. White matter impairment especially in frontal lobes, neural differences in motor, sensory, and autonomic brain regions were noticed. Depending on the cognitive task, increased or decreased frontal lobe activation was found in functional neuroimaging [17].

The navigated Trans cranial magnetic stimulation study concluded that resting motor threshold was increased; duration of cortical silent period is prolonged, short latency afferent inhibition is reduced and reduced cortical afferent inhibition in OSAS patients [18].

Genioglossus muscle activation is positively correlated with cricoid pressure during stable sleep [19]. Pierce R., *et al.* documented the relationship between activation of muscles and airway collapsibility at sleep onset in patients with OSA. Wakeful Genioglossus electromyography, early sleep Tensor palatine electromyography, and the sleep deprivation were directly correlated to cricoid pressure. Tensor palatine muscle activation was negatively correlated with pharyngeal resistance during awake fullness and genioglossus electromyography at the onset of sleep [20].

Tonic EMG responses of genioglossus were greater in sleep apnea subjects than age-matched subjects, whereas the phasic component of the response showed no difference between them [21].

Increased output from the brainstem respiratory centres could have contributed to the change in tonic responses [21].

Studies using Computed tomography scan, acoustic reflection, and, magnetic resonance imaging have identified small diameter airways in patients with apnea [22].

Repeated vibratory trauma during snoring is another potential source of injury or changes in the upper airway muscles [23].

Parameters such as cross-sectional area of airway, thickness of pharyngeal wall, width of mandible and pharyngeal fat thickness and distance from mandible to verterbra were assessed using MRI. The result showed that size of parapharyngeal fat pads significantly increased with age and it is independent of body mass index. Older women who have increased pharyngeal airway length are predisposed to develop width of pharyngeal collapse [24].

Activity of the sympathetic system is increased in OSA patients which increases inflammatory mediators such as cytokines and leptin, cellular oxidation and renin angiotensin activity [25]. Parasympathetic activity is reduced in OSA which could trigger systemic inflammation and predisposes cardiac diseases [26].

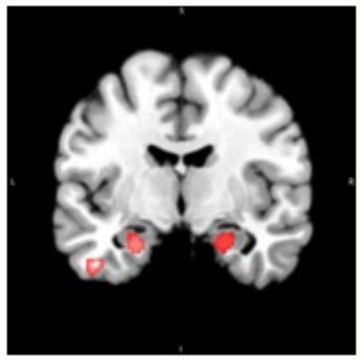

Figure 2: Neuro imaging of OSA: Thickness of grey matter is reduced in OSA.

Thickness of grey matter at paracentral and pre central anterior lobule of cortex is reduced in OSA patients [27]. Diaphragm has a greater thickness in patients with OSA, through ultrasound measurements [28].

Change in the synergy between phrenic nerve and vagus nerve attribute to difficulty in swallowing and reflux [29].

Conclusion

This study concluded that many neuro-physiological changes occur with obstructive sleep apnea. The pronounced changes are in the neuronal activity of the brain, electromyographic changes in the genioglossus muscle, changes in the respiratory muscles, and increased sympathetic stimulation. Future studies with a large number of participants and using advanced imaging techniques to identify changes in various systems of obstructive sleep apnea patients are recommended.

Special Note

This work is done as a part of the Ph.D. thesis of the Tamil Nadu Dr. M. G. R. Medical University, Chennai, India.

Funding

This research received no external funding.

Conflict of Interest

We declare that there is no conflict of Interest.

Bibliography

1. Abhishek Goyal., *et al*. "Prevalence of OSA in Indian population and diagnostic accuracy of different tools for OSA". *ERJ Open Research* 9.11 (2023): 58.

2. Pinto AM., *et al*. "Obstructive Sleep Apnea in a rural population in South India: Feasibility of health care workers to administer level III sleep study". *Lung India* 35.4 (2018): 301-306.

3. Harding SM. "Complications and consequences of obstructive sleep apnea". *Current Opinion in Pulmonary Medicine* 6.6 (2000): 485-489.

4. Waters Tina and Reena Mehra. "Clinical neurophysiology of apnea." *Handbook of Clinical Neurology* 161 (2019): 345-352.

5. White David P. "Pathogenesis of obstructive and central sleep apnea". *American Journal of Respiratory and Critical Care Medicine* 172.11 (2005): 1363-1370.

6. Hussain Iqram., *et al*. "Quantitative Evaluation of EEG-Biomarkers for Prediction of Sleep Stages". *Sensors (Basel, Switzerland)* 22.8 (2022): 3079.

7. Sulaman Bibi A., *et al*. "Neuro-orchestration of sleep and wakefulness". *Nature Neuroscience* 26.2 (2023): 196-212.

8. Fuller Patrick M., *et al*. "Neurobiology of the sleep-wake cycle: sleep architecture, circadian regulation, and regulatory feedback". *Journal of Biological Rhythms* 21.6 (2006): 482-493.

9. Peever John and Patrick M Fuller. "The Biology of REM Sleep". *Current Biology: CB* 27.22 (2017): R1237-R1248.

10. Shiromani Priyattam J and John H Peever. "New Neuroscience Tools That Are Identifying the Sleep-Wake Circuit". *Sleep* 40.4 (2017): zsx032.

11. Chokroverty S. "Overview of sleep and sleep disorders". *The Indian Journal of Medical Research* 131 (2010): 126-140.

12. Sembuling K and Sembuling P. "Essential of Medical Physiology. 6th Edition". New Jaypee Brothers Medical Publishers, Delhi, India (2012).

13. Holfinger S., *et al*. "Neurobiology of Obstructive Sleep Apnea". *Oxford Research Encyclopedia of Neuroscience* (2021).

14. Andrisani G and Andrisani G. "Sleep apnea pathophysiology". *Sleep Breath* 27 (2023): 2111-2122 (2023).

15. Liu P., *et al*. "Clinical Predictors of Mixed Apneas in Patients with Obstructive Sleep Apnea (OSA)". *Nature and Science of Sleep* 14 (2022): 373-380.

16. Yamauchi M., *et al*. "Differences in breathing patterning during wakefulness in patients with mixed apnea-dominant vs obstructive-dominant sleep apnea". Chest 140.1 (2011): 54-61.

17. Zimmerman Molly E and Mark S Aloia. "A review of neuroimaging in obstructive sleep apnea". *Journal of Clinical Sleep Medicine: JCSM: Official publication of the American Academy of Sleep Medicine* 2.4 (2006): 461-471.

18. Rogić Vidaković Maja., *et al*. "Obstructive Sleep Apnea Syndrome: A Preliminary Navigated Transcranial Magnetic Stimulation Study". *Nature and Science of Sleep* 12 (2020): 563-574.

19. Philip-Joet F., *et al*. "Effects of genioglossal response to negative airway pressure on upper airway collapsibility during sleep". *Journal of Applied Physiology* 80 (1996): 1466-1474.

20. Pierce R., *et al*. "Upper airway collapsibility, dilator muscle activation and resistance in sleep apnoea". *The European Respiratory Journal* 30.2 (2007): 345-353.

21. Nguyen AT., *et al*. "Laryngeal and velopharyngeal sensory impairment in obstructive sleep apnea". *Sleep* 28 (2005): 585-593.

22. Bradley TD., *et al*. "Pharyngeal size in snorers, non-snorers, and patients with obstructive sleep apnea". *The New England Journal of Medicine* 315 (1986): 1327-1331.

23. Fogel RB., *et al*. "Sleep. 2: pathophysiology of obstructive sleep apnoea/hypopnoea syndrome." *Thorax* 59.2 (2004): 159-163.

24. Malhotra A., *et al*. "Aging influences on pharyngeal anatomy and physiology: the predisposition to pharyngeal collapse". *The American Journal of Medicine* 119.1 (2006): 72.e9-14.

25. Almendros I., *et al*. "Metabolic dysfunction in OSA: is there something new under the sun?" *Journal of Sleep Research* 31 (2022): e13418.

26. Pal A., *et al*. "Insular functional organization during handgrip in females and males with obstructive sleep apnea". *PLoS One* 16 (2021): e0246368.

27. Li H., *et al*. "Abnormal intrinsic functional hubs and connectivity in stable patients with COPD: a resting-state MRI study". *Brain Imaging and Behavior* 14 (2020): 573-585.

28. Molnár V., *et al*. "Examination of the diaphragm in obstructive sleep apnea using ultrasound imaging". *Sleep Breath* 26 (2022): 1333-1339.

29. Marra L., *et al*. "The association between dysphagia and OSA". *ACTA Otorhinolaryngologica Italica* 42 (2002): 82-88.