Szilvia Puskás*, Norbert Kozák, Dóra Sulina, László Csiba and Mária Tünde Magyar

Quantitative EEG in obstructive sleep apnea syndrome: a review of the literature

DOI 10.1515/revneuro-2016-0064
Received September 29, 2016; accepted November 30, 2016

Abstract: Obstructive sleep apnea syndrome (OSAS) is characterized by the recurrent cessation (apnea) or reduction (hypopnea) of airflow due to the partial or complete upper airway collapse during sleep. Respiratory disturbances causing sleep fragmentation and repetitive nocturnal hypoxia are responsible for a variety of nocturnal and daytime complaints of sleep apnea patients, such as snoring, daytime sleepiness, fatigue, or impaired cognitive functions. Different techniques, such as magnetic resonance imaging, magnetic resonance spectroscopy, and positron emission tomography, are used to evaluate the structural and functional changes in OSAS patients. With quantitative electroencephalographic (qEEG) analysis, the possible existence of alterations in the brain electrical activity of OSAS patients can be investigated. We review the articles on qEEG results of sleep apnea patients and summarize the possible explanations of these qEEG measures. Finally, we review the impact of continuous positive airway pressure (CPAP) treatment on these alterations to assess whether CPAP use can eliminate alterations in the brain activity of OSAS patients.

Keywords: continuous positive airway pressure; nocturnal hypoxemia; sleep fragmentation; slowing ratio; spectral analysis.

Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS)

Obstructive sleep apnea syndrome (OSAS) is the most common type of sleep-related breathing disorders. OSAHS is characterized by the recurrent episodes of the partial or complete upper airway collapse during sleep. The collapse leads to a reduction (hypopnea) or complete (apnea) cessation of airflow despite ongoing inspiratory efforts (De Baker, 2006). Reduced or absent airflow is accompanied by oxygen desaturation and terminated by brief microarousals, which result in sleep fragmentation and diminished amount of slow-wave and rapid eye movement (REM) sleep (Deegan and McNicholas, 1995). Hypercapnia, swings in intrathoracic pressure, and increased sympathetic activity are also the results of repetitive upper airway collapse. Clinically, OSAS is characterized by the occurrence of excessive daytime sleepiness, loud snoring, breathing interruptions, and frequent awakenings due to gasping (Epstein et al., 2009). OSAS affects approximately 2%–14% of adults (Young et al., 2002) and older adults aged 65 years and above have an increased prevalence of sleep apnea (Shochat and Pillar, 2003).

Increased body mass index, neck circumference, and waist-to-hip ratio are common risk factors for OSAS (Young et al., 2004). Craniofacial and upper airway morphology also plays an important role in the occurrence of sleep apnea (Dempsey et al., 2002). Patients with maxillomandibular malformations, adenotonsillar enlargement, increased uvula size, long soft palate, or other upper airway abnormalities often suffer from OSAS.

Untreated sleep apnea can increase the risk of hypertension, diabetes, or heart disease and heart failure (Ho and Brass, 2011) and there is emerging evidence that the risk of stroke is also higher in OSAS patients independently of traditional risk factors (Mohsenin, 2015). Excessive daytime sleepiness is a major consequence of OSAS; reduced wakefulness and vigilance and abnormal daytime tiredness contribute to higher frequency of traffic and occupational accidents among OSAS patients, but impaired cognition, mood disorders, poor social functioning, and reduced quality of life are also common complaints of OSAS patients (Findley et al., 1986; Greenberg et al., 1987; Lloberes et al., 2000; Akashiba et al., 2002; Melamed and Oksenberg, 2002).

Diagnosis and treatment of OSAHS

The diagnosis of OSAS is based on the evaluation of clinical symptoms and objective sleep study findings. Patients

***Corresponding author: Szilvia Puskás,** Department of Neurology, University of Debrecen Medical Center, Móricz Zsigmond krt. 22, H-4032 Debrecen, Hungary, e-mail: szilvia.puskas@yahoo.com. http://orcid.org/0000-0001-8471-1288
Norbert Kozák, Dóra Sulina, László Csiba and Mária Tünde Magyar: Department of Neurology, University of Debrecen Medical Center, Móricz Zsigmond krt. 22, H-4032 Debrecen, Hungary

and bedpartners should be asked about nocturnal sleep and daytime complaints. The most widely used test to screen subjective daytime sleepiness is the Epworth Sleepiness Scale (ESS). The Maintenance of Wakefulness Test (MWT) and the Multiple Sleep Latency Test (MSLT) objectively measure sleepiness and alertness (Mannarino et al., 2012).

To confirm the suspicion of OSAS, nocturnal, laboratory-based polysomnography (PSG) remains the gold standard. While the patient sleeps, several parameters (i.e. electrocardiogram, blood oxygen saturation, electroencephalogram, electro-oculogram, nasal and oral airflow, chest and abdominal wall movements, and electromyogram) are recorded and measured. The diagnosis and severity of OSAS is based on the apnea-hypopnea index (AHI), which is the number of obstructed breathing events per hour of sleep. OSAS is defined as an AHI of 5 or greater with associated clinical symptoms (e.g. excessive daytime sleepiness, fatigue, or impaired cognition) or as an AHI of 15 or greater regardless of associated symptoms (Park et al., 2011). According to the third edition of the International Classification of Sleep Disorders, OSAS can be diagnosed in the presence of selected risk factors and comorbidities (i.e. high blood pressure or coronary heart disease, type II diabetes, and mood disorders) even for otherwise asymptomatic patients with an AHI of 5–15 (Stuck and Maurer, 2016). An AHI of 5–14 is classified as mild sleep apnea; for moderate severity, AHI should be between 15 and 29; in severe OSAS, AHI is above 30 (McNicholas, 2008).

Continuous positive airway pressure (CPAP) is the primary treatment modality in patients with severe OSAS (Lévy et al., 2015). CPAP prevents upper airway collapses, improves oxygen saturation, and reduces sleep fragmentation. In the mild to moderate form of OSAS, the use of mandibular advancement devices is recommended (Randerath et al., 2011). Oral appliance can be an alternative approach in CPAP intolerance or CPAP failure. Surgical procedures, such as maxillomandibular osteotomy, are also efficient in patients who refuse conservative treatment. Weight loss, postural treatments, and sleep hygiene can be also recommended in selected cases.

Quantitative electroencephalography (qEEG) analysis in OSAS patients

The effects of OSAS on brain structure and function were investigated in several previous studies using different techniques, i.e. structural and functional magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), positron emission tomography (PET), and event-related potentials (Mohsenifar et al., 1994; Kamba et al., 1997; Macey et al., 2002; Morrell et al., 2003; Raggi and Ferri, 2012; Park et al., 2016).

EEG is an indispensable tool in both research and clinical practice, because the electromagnetic oscillations of the brain cannot be detected by any other investigating methods, except for magnetoencephalography. In addition, EEG has excellent temporal resolution in millisecond scale. Conventional visual EEG analysis is not eligible to assess those subtle details of the electrical activity of the brain, which might be relevant in research or clinical practice. qEEG techniques can provide additional information for the detection of subtle brain abnormalities associated with OSAS.

In recent years, research groups performed a quantitative analysis of both wake and sleep EEG of OSAS patients. qEEG techniques were used to characterize the changes in brain electrical activity, which accompany sleep fragmentation, daytime sleepiness, repetitive nocturnal hypoxemia, or neurocognitive deficits. Studies were also conducted to explore whether qEEG parameters change after CPAP treatment of sleep apnea patients.

qEEG analysis of background EEG activity in untreated OSAS patients

Morisson et al. (1998) hypothesized that the deficit in executive functions, which was often reported in OSAS patients, may be associated with frontal lobe dysfunction. EEG recordings of sleep apnea patients and normal controls were compared to calculate the slowing ratio (ratio of slow frequencies to fast frequencies). Changes in this ratio could reflect EEG slowing due to an increase in slow frequencies, a decrease in fast frequencies, or both. During wakefulness, EEG slowing was observed over all cortical regions, not only over frontal cortex. In another study of Morisson et al. (2001), a higher slow activity to fast activity ratio was described during both wakefulness and REM sleep for all cortical regions pooled in untreated OSAS patients. Consistent with the previous findings of Morisson et al. (1998, 2001), Mathieu et al. (2007) reported slowing of the EEG across all cortical regions in OSAS patients compared to healthy controls with EEG spectral analysis. They also investigated if age interacted with the severity of cortical slowing in OSAS as increased slow activity was described in normal subjects with advancing age using qEEG analysis (Breslau et al., 1989). Comparing

younger (25–50 years) to older (51–72 years) OSAS patients, no age-related changes could be identified in EEG activity. Xiromeritis et al. (2011) could detect a significant increase in relative θ and δ power in the parietal, temporal, and occipital regions in severe OSAS patients compared to normal subjects, but no significant differences were observed in the relative power of the frequency bands in patients with mild and moderate OSAS compared to healthy controls.

Because waking EEG patterns of sleep apnea patients have many similarities with EEG changes in normal subjects under hypobaric hypoxia (Kraaier et al., 1988), i.e. increased slow activity and decreased α and β activities, nocturnal hypoxia was suggested as a possible explanation for EEG slowing in OSAS patients. Morisson et al. (1998) found a weak positive correlation between wake EEG slowing and the degree of oxygen desaturation during sleep. Morisson et al. (2001) could not reproduce the previous findings, as EEG slowing of untreated sleep apnea patients and the severity of nocturnal hypoxemia were independent. Xiromeritis et al. (2011) could confirm the relationship between nocturnal hypoxia and brain dysfunction with consequent EEG slowing. In their analysis, the desaturation index of OSAS patients positively correlated with the θ relative power in frontal, central, parietal, temporal, and occipital areas and also with the δ relative power in central, parietal, temporal, and occipital areas. In contrast to the possible role of hypoxia in EEG slowing, Wang et al. (2015) demonstrated that hypercapnia but not hypoxia might play a key role in slowing of the EEG (increased δ/α ratio) in healthy individuals. In OSAS patients, a correlation between hypercapnia and qEEG changes was not examined.

Another possible explanation of slowing in awake EEG could be sleep fragmentation that may affect the restorative functions of sleep. As a consequence, OSAS patients have excessive daytime sleepiness or reduced vigilance. In healthy individuals, increased θ activity and decreased α activity were reported when drowsiness was manifested (Broughton and Hasan, 1995). Sforza et al. (2002) compared the absolute EEG power values of sleepy and non-sleepy OSAS patients and found that sleepy patients had greater θ and slow α powers than patients without excessive daytime sleepiness, but the differences did not reach statistical significance. The authors could not disclose any significant relationship between waking EEG powers and any markers of sleep fragmentation, confirming that these indices play little, if any, role in the occurrence of slowing of the EEG. Similarly, Morisson et al. (1998) also failed to demonstrate a correlation between diffused EEG slowing and objective sleepiness.

In contrast, the results of Mathieu et al. (2007) support the hypothesis that diffused cortical slowing is a manifestation of sleep fragmentation, as they found a relationship between EEG slowing ratio in all investigated cortical regions and sleep fragmentation (indexed by microarousal).

The previously mentioned studies all could confirm slowing in awake EEG of OSAS patients, but Lee et al. (2008) could not detect any changes in slow waves in sleep apnea patients. The explanation of this finding might be that this study group compared patients with mild OSAS to severe OSAS patients, not to normal subjects.

To investigate the changes in brain electrical activity in 3D space, an EEG source localization method, low-resolution electromagnetic tomography (LORETA), was also applied by research groups. Lee et al. (2008) demonstrated a decreased α activity at the right posterior cingulate gyrus in cases with severe OSAS compared to mild OSAS. The authors concluded that the α reduction is a sign of brain dysfunction from hypoxic damage caused by repeated chronic hypoxia and the dysfunction of the identified brain region may play a role in cognitive deficits. In contrast to the previous findings, Toth et al. (2009) observed a significantly increased α2 (10.5–12 Hz) frequency activity bilaterally in the precuneus and posterior cingulate cortex with LORETA by comparing OSAS patients to normal subjects. These alterations were also thought to reflect the effect of intermittent chronic hypoxia in regions associated with influencing emotional regulation, long-term memory, and the default mode network. Significantly overlapping with the regions where abnormalities were identified by Lee et al. (2008) and Toth et al. (2009), Jones et al. (2014) found circumscribed broadband reduction in EEG power in OSAS subjects relative to controls using high-density sleep EEG recordings. According to the authors, regional deficits may be a useful clinical marker for neural disruption in OSAS and high-density EEG is sensitive enough to detect early pathological cortical changes.

qEEG analysis of apnea and arousal

qEEG was also used to investigate the changes that occur during transient hypoxic events that are induced by apnea episodes. Svanborg and Guilleminault (1996) studied 16-channel EEG during periods of sleep apneas in REM and non-REM (NREM) sleep. The δ-band activity increased progressively and was generalized over the scalp during NREM apneas, and δ amplitudes tended to have a maximum in the posterior frontal, central, and parietal regions. Also, during REM apneas, increased δ

activity was present, but it was much less marked than during NREM apneas and occurred without progression. Morisson et al. (1998) investigated samples from REM sleep EEG of OSAS patients in the middle of the apnea episodes. Compared to normal controls, they also described EEG slowing in REM sleep during apneic pauses over the frontal, central, and parietal regions. Walsleben et al. (1993) reported decreased total brain activity in association with apneic events.

A relationship between EEG changes during apnea episodes and accompanying oxygen desaturations was investigated by Svanborg and Guilleminault (1996). The authors concluded that there were no significant correlations between increases in δ activity during REM and NREM apneas and degree of desaturation, which indicates that the δ increases in REM and NREM apneas might not be caused by hypoxemia. This finding is in agreement with the results of Morisson et al. (1998) who also did not find a correlation between EEG slowing of REM apneic pauses and degree of oxygen desaturation. Apnea and hypopnea-induced cortical arousals cause sleep fragmentation, hence daytime sleepiness, but a subset of apneas and hypopneas are not terminated by visible cortical arousals. Dingli et al. (2002) tested whether qEEG would be a useful tool for detecting nonvisible signal changes in brain activity related to apnea/hypopnea termination.

During NREM sleep when arousals were visible, a decrease in normalized θ power was detected, which was derived from the increase in α and σ power. When arousals were not visible in NREM sleep, the θ fraction decreased as a result of δ power increase. During REM sleep arousal, terminating apneas/hypopneas were associated with a decrease in θ power fraction alone. REM-related apneas/hypopneas, which were not terminated by visible arousals, were not associated with any significant spectral power changes.

qEEG in OSAS patients with CPAP treatment

CPAP is currently the most effective treatment for OSAS. Studies were conducted to investigate whether EEG abnormalities observed before treatment are reversible by comparing the results of qEEG analysis before and after CPAP use. If the EEG slowing is reversible, it might be the consequence of hypoxic brain dysfunction, and with the correction of hypoxia, the brain activity normalizes. Permanent EEG slowing can be a sign of possible brain damage.

Morisson et al. (2001) confirmed that after 6 months of CPAP treatment the slowing ratio and the absolute activity in the δ band returned to normal values for both wakefulness and REM. Although the brain activity of sleep apnea patients normalized, patients' daytime sleepiness was not completely recovered after CPAP treatment. Similar results were reported by Lee et al. (2012). Assessing the qEEG changes after at least 3 months of CPAP therapy, EEG slowing was significantly improved across the cerebral regions investigated and these improvements were associated with reductions in daytime sleepiness. In contrast to the results of Morisson et al. (2001) and Lee et al. (2012), Xiromeritis et al. (2011) could demonstrate an increase of EEG slowing after 6 months of CPAP treatment. The authors could not give a clear explanation for the results. Six months of CPAP use improved daytime sleepiness and EEG demonstrated a decrease in the α (frontal, central, and temporal areas) and θ (frontal areas) relative power. The β relative power was increased mainly in central brain areas and the δ relative power was increased in all brain areas. The authors concluded that hypoxia in patients with severe OSAS might be responsible for brain dysfunction, which could not be restored after 6 months of treatment.

After the initiation of CPAP use, rapid changes in brain electrical activity were described by Toth et al. (2012). They performed LORETA analysis of sleep apnea patients after one night of CPAP therapy. The significant difference observed without CPAP treatment in the α2 frequency range bilaterally in the precuneus, paracentral, and posterior cingulate cortex vanished after CPAP initiation. According to the authors, this change might be considered as a first sign of elimination of chronic intermittent hypoxia.

Conclusion

In this review, we summarized the results of studies that were conducted to quantitatively analyze EEG changes in adult OSAS patients before and after CPAP therapy. qEEG techniques have been particularly helpful in the detection of subtle alterations in brain electrical activity, which cannot be discovered with conventional visual analysis.

The most consistent finding in the evaluation of brain activity in untreated OSAS patients was diffused EEG slowing during wakefulness, and only a limited number of studies reported circumscribed changes in brain activity. It was hypothesized that the slowing in awake EEG is a consequence of sleep fragmentation, but the majority of studies could not prove any significant relationship

between waking EEG measures and any markers of sleep fragmentation. Increased awake slow EEG frequency in OSAS may represent drowsiness or reduced vigilance, which is a common complaint of sleep apnea patients, but studies have shown that neither objectively nor subjectively measured sleepiness is associated with EEG slowing during wakefulness. As researchers suggested, an alternative possibility is that hypoxemia and recurrence of apneas would contribute to cerebral impairment and altered or damaged brain functions are reflected in the slowing of the EEG activity. CPAP treatment is proven to be effective in reversing respiratory impairments during the night, but CPAP therapy seems to be useful in correcting pretreatment qEEG abnormalities as well.

Further studies with the routine use of high-density EEG and advanced qEEG techniques on large groups of patients of similar age, disease severity, and comorbidity are needed to better understand the relationship between OSAS and changes in brain activity.

Acknowledgments: The preparation of this manuscript was supported by the Hungarian Brain Research Program (Grant No. KTIA_13_NAP-A-II/6). The authors thank Edit Imre Badarné, Katalin Oláh, and Andrea Dobó Pállné for their help in preparing the manuscript.

References

Akashiba, T., Kawahara, S., Akahoshi, T., Omori, C., Saito, O., Majima, T., and Horie, T. (2002). Relationship between quality of life and mood or depression in patients with severe obstructive sleep apnea syndrome. Chest *122*, 861–865.

Breslau, J., Starr, A., Sicotte, N., Higa, J., and Buchsbaum, M.S. (1989). Topographic EEG changes with normal aging and SDAT. Electroencephalogr. Clin. Neurophysiol. *72*, 281–289.

Broughton, R. and Hasan, J. (1995). Quantitative topographic electroencephalographic mapping during drowsiness and sleep onset. J. Clin. Neurophysiol. *12*, 372–386.

De Baker, W. (2006). Obstructive apnea-hypopnea syndrome. Definitions and pathophysiology. Sleep Apnea: Current Diagnosis and Treatment (Progress in Respiratory Research. Vol. 35). W.J. Randerath, B.M. Sanner, and V.K. Somers, eds. (Basel, Switzerland: Karger), p. 90.

Deegan, P.C. and McNicholas, W.T. (1995). Pathophysiology of obstructive sleep apnoea. Eur. Respir. J. *8*, 1161–1178.

Dempsey, J.A., Skatrud, J.B., Jacques, A.J., Ewanowski, S.J., Woodson, B.T., Hanson, P.R., and Goodman, B. (2002). Anatomic determinants of sleep-disordered breathing across the spectrum of clinical and nonclinical male subjects. Chest *122*, 840–851.

Dingli, K., Assimakopoulos, T., Fietze, I., Witt, C., Wraith, P.K., and Douglas, N.J. (2002). Electroencephalographic spectral analysis: detection of cortical activity changes in sleep apnoea patients. Eur. Respir. J. *20*, 1246–1253.

Epstein, L.J., Kristo, D., Strollo, P.J., Jr., Friedman, N., Malhotra, A., Patil, S.P., Ramar, K., Rogers, R., Schwab, R.J., Weaver, E.M., et al. (2009). Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J. Clin. Sleep Med. *5*, 263–276.

Findley, L.J., Barth, J.T., Powers, D.C., Wilhoit, S.C., Boyd, D.G., and Suratt, P.M. (1986). Cognitive impairment in patients with obstructive sleep apnea and associated hypoxemia. Chest *90*, 686–690.

Greenberg, G.D., Watson, R.K., and Deptula, D. (1987). Neuropsychological dysfunction in sleep apnea. Sleep *10*, 254–262.

Ho, M.L. and Brass, S.D. (2011). Obstructive sleep apnea. Neurol. Int. *3*, e15.

Jones, S.G., Riedner, B.A., Smith, R.F., Ferrarelli, F., Tononi, G., Davidson, R.J., and Benca, R.M. (2014). Regional reductions in sleep electroencephalography power in obstructive sleep apnea: a high-density EEG study. Sleep *37*, 399–407.

Kraaier, V., Van Huffelen, A.C., and Wieneke, G.H. (1988). Quantitative EEG changes due to hypobaric hypoxia in normal subjects. Electroencephalogr. Clin. Neurophysiol. *69*, 303–312.

Kamba, M., Suto, Y., Ohta, Y., Inoue, Y., and Matsuda, E. (1997). Cerebral metabolism in sleep apnea. Evaluation by magnetic resonance spectroscopy. Am. J. Respir. Crit. Care Med. *156*, 296–298.

Lee, H.K., Park, D.H., Shin, H.S., and Hong, S.C. (2008). Comparison of low resolution electromagnetic tomography imaging between subjects with mild and severe obstructive sleep apnea syndrome: a preliminary study. Psychiatry Invest. *5*, 45–51.

Lee, S.D., Ju, G., Kim, J.W., and Yoon, I.Y. (2012). Improvement of EEG slowing in OSAS after CPAP treatment. J. Psychosom. Res. *73*, 126–131.

Lévy, P., Kohler, M., McNicholas, W.T., Barbé, F., McEvoy, R.D., Somers, V.K., Lavie, L., and Pépin, J.L. (2015). Obstructive sleep apnoea syndrome. Nat. Rev. Dis. Primers *1*, 15015.

Lloberes, P., Levy, G., Descals, C., Sampol, G., Roca, A., Sagales, T., and de la Calzada, M.D. (2000). Self-reported sleepiness while driving as a risk factor for traffic accidents in patients with obstructive sleep apnoea syndrome and in non-apnoeic snorers. Respir. Med. *94*, 971–976.

Macey, P.M., Henderson, L.A., Macey, K.E., Alger, J.R., Frysinger, R.C., Woo, M.A., Harper, R.K., Yan-Go, F.L., and Harper, R.M. (2002). Brain morphology associated with obstructive sleep apnea. Am. J. Respir. Crit. Care Med. *166*, 1382–1387.

Mannarino, M.R., Di Filippo, F., and Pirro, M. (2012). Obstructive sleep apnea syndrome. Eur. J. Intern. Med. *23*, 586–593.

Mathieu, A., Mazza, S., Petit, D., Décary, A., Massicotte-Marquez, J., Malo, J., and Montplaisir, J. (2007). Does age worsen EEG slowing and attention deficits in obstructive sleep apnea syndrome? Clin. Neurophysiol. *118*, 1538–1544.

McNicholas, W.T. (2008). Diagnosis of obstructive sleep apnea in adults. Proc. Am. Thorac. Soc. *5*, 154–160.

Melamed, S. and Oksenberg, A. (2002). Excessive daytime sleepiness and risk of occupational injuries in non-shift daytime workers. Sleep *25*, 315–322.

Mohsenifar, Z., Stein, M., DeLilly, J., Mahler, M.E., Mandelkern, M., and Williams, A.J. (1994). Regional metabolic dependency in obstructive sleep apnea. Am. J. Med. Sci. *308*, 75–78.

Mohsenin, V. (2015). Obstructive sleep apnea: a new preventive and therapeutic target for stroke: a new kid on the block. Am. J. Med. *128*, 811–816.

Morrell, M.J., McRobbie, D.W., Quest, R.A., Cummin, A.R., Ghiassi, R., and Corfield, D.R. (2003). Changes in brain morphology associated with obstructive sleep apnea. Sleep Med. *4*, 451–454.

Morisson, F., Lavigne, G., Petit, D., Nielsen, T., Malo, J., and Montplaisir, J. (1998). Spectral analysis of wakefulness and REM sleep EEG in patients with sleep apnoea syndrome. Eur. Respir. J. *11*, 1135–1140.

Morisson, F., Décary, A., Petit, D., Lavigne, G., Malo, J., and Montplaisir, J. (2001). Daytime sleepiness and EEG spectral analysis in apneic patients before and after treatment with continuous positive airway pressure. Chest *119*, 45–52.

Park, J.G., Ramar, K., and Olson, E.J. (2011). Updates on definition, consequences, and management of obstructive sleep apnea. Mayo Clin. Proc. *86*, 549–554.

Park, B., Palomares, J.A., Woo, M.A., Kang, D.W., Macey, P.M., Yan-Go, F.L., Harper, R.M., and Kumar, R. (2016). Disrupted functional brain network organization in patients with obstructive sleep apnea. Brain Behav. *6*, e00441.

Raggi, A. and Ferri, R. (2012). Cognitive evoked potentials in obstructive sleep apnea syndrome: a review of the literature. Rev. Neurosci. *23*, 311–323.

Randerath, W.J., Verbraecken, J., Andreas, S., Bettega, G., Boudewyns, A., Hamans, E., Jalbert, F., Paoli, J.R., Sanner, B., Smith, I., et al. (2011). European respiratory society task force on non-CPAP therapies in sleep apnoea. Non-CPAP therapies in obstructive sleep apnoea. Eur. Respir. J. *37*, 1000–1028.

Sforza, E., Grandin, S., Jouny, C., Rochat, T., and Ibanez, V. (2002). Is waking electroencephalographic activity a predictor of daytime sleepiness in sleep-related breathing disorders? Eur. Respir. J. *19*, 645–652.

Shochat, T. and Pillar, G. (2003). Sleep apnoea in the older adult: pathophysiology, epidemiology, consequences and management. Drugs Aging *20*, 551–560.

Stuck, B.A. and Maurer, J.T. (2016). Recent developments in the diagnosis and treatment of obstructive sleep apnea. English version. HNO. [Epub ahead of print]. DOI: 10.1007/s00106-016-0176-0.

Svanborg, E. and Guilleminault, C. (1996). EEG frequency changes during sleep apneas. Sleep *19*, 248–254.

Toth, M., Faludi, B., Wackermann, J., Czopf, J., and Kondakor, I. (2009). Characteristic changes in brain electrical activity due to chronic hypoxia in patients with obstructive sleep apnea syndrome (OSAS): a combined EEG study using LORETA and omega complexity. Brain Topogr. *22*, 185–190.

Toth, M., Faludi, B., and Kondakor, I. (2012). Effects of CPAP-therapy on brain electrical activity in obstructive sleep apneic patients: a combined EEG study using LORETA and Omega complexity: reversible alterations of brain activity in OSAS. Brain Topogr. *25*, 450–460.

Walsleben, J.A., O'Malley, E.B., Bonnet, K., Norman, R.G., and Rapoport, D.M. (1993). The utility of topographic EEG mapping in obstructive sleep apnea syndrome. Sleep *16*, S76–S78.

Wang, D., Yee, B.J., Wong, K.K., Kim, J.W., Dijk, D.J., Duffin, J., and Grunstein, R.R. (2015). Comparing the effect of hypercapnia and hypoxia on the electroencephalogram during wakefulness. Clin. Neurophysiol. *126*, 103–109.

Xiromeritis, A.G., Hatziefthimiou, A.A., Hadjigeorgiou, G.M., Gourgoulianis, K.I., Anagnostopoulou, D.N., and Angelopoulos, N.V. (2011). Quantitative spectral analysis of vigilance EEG in patients with obstructive sleep apnoea syndrome: EEG mapping in OSAS patients. Sleep Breath. *15*, 121–128.

Young, T., Peppard, P.E., and Gottlieb, D.J. (2002). Epidemiology of obstructive sleep apnea: a population health perspective. Am. J. Respir. Crit. Care Med. *165*, 1217–1239.

Young, T., Skatrud, J., and Peppard, P.E. (2004). Risk factors for obstructive sleep apnea in adults. J. Am. Med. Assoc. *291*, 2013–2016.