El-Mekkawy *et al.*
Egypt J Neurol Psychiatry Neurosurg (2022) 58:11
https://doi.org/10.1186/s41983-022-00446-0

The Egyptian Journal of Neurology, Psychiatry and Neurosurgery

RESEARCH Open Access

Screening of non-restorative sleep by quantitative EEG

Leqaa El-Mekkawy, Dina El Salmawy*, Mye A. Basheer, Eman Maher and Mona M. Nada

Abstract

Background: Non-restorative sleep is the major cause of excessive daytime sleepiness and causes injures of the central nervous system. The most common cause of Excessive day sleepiness in a clinical setting is obstructive sleep apnea. Sleepiness scales can assess multiple aspects of the sleep and include subjective and objective measures. The present study aim to disclose the capability of quantitative electroencephalography to screen, as well as to know the pathogenesis of non-restorative sleep in patients with excessive day time sleepiness.

Results: Twenty obstructive sleep apnea patients and 20 healthy control subjects were recruited. All patients were subjected to Epworth sleepiness scale and polysomnography. Quantitative electroencephalography and Karolinska sleepiness scale were done before and after sleep for patients as well as controls. The patients group revealed a significant power reduction in delta and alpha bands, comparing before and after sleep records. Interestingly, there was a significant change in delta power in the temporal delta waves power. Yet, the changes were opposite among cases (significant decrease) versus controls (significant increase). In addition, there were significant correlations between sleepiness scales; Epworth sleepiness scale and Karolinska Sleepiness Scale scores, and alpha band results in quantitative electroencephalography.

Conclusion: Quantitative electroencephalography with further research, could provide us with clues to the pathogenesis of EDS and non-restorative sleep accompanying OSA and an objective screening tool.

Keywords: Non-restorative sleep, Quantitative EEG, Polysomnogram, Karolinska sleepiness scale, Epworth sleepiness scale

Background

Non-restorative sleep and fragmented sleep can produce functional and structural injuries of the central nervous system mainly the prefrontal cortex (PFC) [1]. Neuroimaging indicated functional brain alterations in the inferior parietal cortex and superior parietal lobule, following acute sleep deprivation [2]. Lower prefrontal gray matter volume has been associated with greater sleep fragmentation in older individuals [3]. Fragmentation of sleep decreases the efficacy of its homeostasis in the central nervous system (CNS) and alteration of neuronal, synaptic and glial viability in certain regions responsible for memory, concentration and sleep areas in the brain as prefrontal cortex, hippocampus, insula and amygdala [4].

Non-restorative sleep is the major cause of excessive daytime sleepiness (EDS), defined by the International Classification of Sleep Disorders, Second Edition as "the inability to stay awake and alert during the major waking episodes of the day, leading to unintended lapses into drowsiness or sleep" [5]. Its prevalence was 20% of the population [6]. The patients of EDS are at risk of motor vehicle and work-related accidents [6, 7].

The Sleep Apnea Hypopnea Syndrome SAHS, and other forms of sleep disordered breathing (SDB), leads to sleep fragmentation and excessive day sleepiness. In a clinical setting obstructive sleep apnea (OSA) is the most common cause of EDS [8]. Other causes of EDS are narcolepsy and primary hypersomnia.

*Correspondence: Deena.salmawy@gmail.com
Clinical Neurophysiology Unit, KasrAlaini Hospital, Faculty of Medicine, Cairo University, Manyal 11562, Cairo, Egypt

In SAHS, there are momentary cessations in breathing rhythm (apneas) or momentary or sustained reductions in the air flow (hypopneas), sufficient to cause significant arterial hypoxemia and hypercapnia [9].

Sleepiness can be assessed subjectively by sleepiness scales as Epworth sleepiness scale (ESS) and Karolinska Sleepiness Scale (KSS) [10]. Objectively using actigraphy that provides useful measures of sleep patterns**.** In addition, there are neurophysiological tools for its assessment but time consuming as the patient must spend a night sleeping in the lab as polysomnography (PSG), multiple sleep latency test (MSLT), maintenance of wakefulness test (MWT) and Pupillometry [11]. Other methods for assessment of hypo vigilance are heart rate variability (HRV) and Combined EEG-fMRI which could be expensive. Driver drowsiness could be detected using the Eyelid closure degree (ECD) either video-based or by EEG sensors [12]. Brain-Machine Interface (BMI) system and Near Infrared Spectroscopy (NIRS). Such measures are sophisticated in comparison to QEEG. Traffic problems could be cut down especially if QEEG is integrated with professional driving licensing and professions whom hypo-vigilance causes major dangers to themselves or their surrounding environment.

The study aims to stand on the capability of QEEG to screen, as well as to know the pathogenesis of non-restorative sleep in patients with excessive day time sleepiness.

Methods

This is an observational case control study, carried out on 20 OSA patients as well as 20 healthy sex- and age matching volunteers. Subjects were recruited in the period from January 2015 to January 2017. The experimental method was approved by the Research Ethics Committee, a written consent was signed by the subjects, and a clinical trial registration number was issued. This study included subjects who were more than 18 years, patients were normal neurologically with Apnea Hypopnea Index (AHI) of more than 5 and having an ESS score of more than 10 [13].

AHI is the number of times you have apnea or hypopnea during one night, divided by the hours of sleep [13].

Normal sleep	An AHI of fewer than five events, on average, per hour.
Mild sleep apnea	An AHI of five to 14 events per hour.
Moderate sleep apnea	An AHI of 15 to 29 events per hour.
Severe sleep apnea	An AHI of 30 or more events per hour.

Patients with AHI of more than 5 were included in the study. However, patients with fragmented sleep and EDS secondary to any other sleep disorder; chronic debilitating disease or encephalopathy causing EEG slowing or on medications that could affect EEG and affects sleep structure as benzodiazepines, anti-psychotics, or stimulants; were excluded.

Patients were clinically assessed; history taking including complaint analysis, history of drug intake, body mass index calculation as well as general and neurological examination. The ESS was performed before sleep [14].

All patients were subjected to sleep study PSG to diagnose any sleep disordered breathing and to exclude any other causes of EDS as parasomnias. The used machine was a digital package (Somnologica, USA) with serial number (F131036-SL) and version 3.2 (Build 1451) on a personal computer, using Microsoft windows XP® platform. Night PSG was done with 6–8 h average duration of recording. All traces were manually scored in 30-s epochs according to the recommendations of the American Academy of Sleep Medicine (AASM) Manual for the scoring of sleep and associated events version 2.6 [15]. Sleep efficiency and AHI were measured by the PSG.

KSS was done before and after sleep for patients as well as controls. It assesses the momentary sleepiness of the patients; by asking them to describe their vigilance state from between the 10 points of the scale 1 (very alert) to 9 (very sleepy). It was done just before sleep and 45 min after wakefulness [16].

QEEG was carried out, for patients and controls. In a separate control room, the video EEG was continuously monitored by a technologist, utilizing a video EEG with an EB-Neuro Galileo NT, PMS, USA machine (its serial number is DAUNL7HQ4NUSFG with model Mizar. B8351037899-Version 3.61). A cap was used for recording. The high frequency filter was 70 Hz, and time constant was 0.3 s. The impedance was kept below 5 KΩ. EEG was done for 30 min duration before and after sleep recording.

Artifact-free epoch of 10-s duration in a common average reference montage was selected for QEEG analysis, during wakefulness resting state with closed eyes. These epochs were selected from EEG record, which was done twice, before and after sleep. The absolute power of 5 electrodes (CZ, T3, T4, T5, T6,) were studied in the following frequency bands: delta (0.5–3 Hz), theta (4–7 Hz). The absolute power of (O1, O2) was studied in the alpha (8–12 Hz) band as well. Power bands for each frequency were calculated automatically by EB-Neuro QEEG with the following equations [17], Alpha Power = 10^(mean (spectra(alphaIdx))/10); Delta Power = 10^(mean(spectra(deltaIdx))/10); where alphaIdx = find(freqs > 8 and freqs < 13); and deltaIdx = find(freqs > 1 and freqs < 4).

Data were coded and entered using the statistical package Statistical Package for the Social Sciences (SPSS; IBM SPSS Statistics for Windows, Version 24.0, 2016; Armonk, NY: IBM Corp.). Data were summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and frequency (count) and relative frequency (percentage) for categorical data. Quantitative variables comparisons were done using the non-parametric Mann–Whitney test. The non-parametric Wilcoxon signed rank test was used for serial measurements within each patient [18]. For comparing categorical data, chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 [19]. Spearman correlation coefficient was used for quantitative variable correlations [20].

Results

The study group included 20 cases (4 females and 16 males) with mean age of 45.45 ± 7.6 years and the BMI mean was 31.97 ± 4.26 kg/m^2. While the control group included 20 subjects (5 females and 15 males), with a mean age of 41.95 ± 7.29 years and their body mass index (BMI) mean of 29.58 ± 5.64 kg/m^2. There was no statistically significant difference regarding age, BMI, and gender, with *P* value = 0.151, 0.076 and 1.0, respectively.

The ESS was significantly higher in cases than the control groups with high statistically significant difference ($P < 0.001$), 14.5 ± 4.98 in cases compared to 2.20 ± 2.07 in controls.

The PSG of all cases showed OSA syndrome with Apnea–hypopnea index (AHI) mean value 20.26 ± 9.26/h and sleep efficiency mean value 88.01 ± 11.80%, while the control group had AHI mean value of 1.52 ± 1.66/h, while sleep efficiency (%) showed no significant difference between both groups. A baseline digital EEG was analyzed using QEEG and compared between cases and control. It revealed no significant difference.

There was significant reduction of KSS mean results after sleep than before it; from 3.90 to 2.70 ($P = 0.021$) in the cases group and 3.35 to 1.60 in the control group ($P = 0.001$). No significant difference regarding the KSS between cases and controls ($P = 0.076$) (Table 1).

Table 1 KSS comparison from before to after sleep in both groups

	Control group		Cases group		*P* value
	Before sleep	After sleep	Before sleep	After Sleep	
KSS	3.35	1.6	3.90	2.70	0.076
P value	0.001*		0.021*		

*Statistically significant

For the control group, comparison of QEEG showed that the average power (μV2) of temporal delta waves in the baseline EEG record increased in its value after sleep (median = 89.96 μV2) in comparison to its value before sleep (median = 44.69 μV2) with statistically significant differences ($P = 0.04$) (Table 2). The rest of QEEG power analysis showed no significant difference between before and after sleep. These data include average temporal theta, central (theta and delta) and average occipital (theta, delta and alpha) during baseline EEG (Table 2).

In cases group, comparing QEEG from before to after sleep revealed that the power of the central (Cz) delta value was of reduced value after sleep (median = 35.9 μV2) than before (median = 65.3 μV2) with statistically significant difference ($P = 0.044$). In addition, the average power (μV2) of temporal delta waves in the baseline EEG record showed reduction of its value after sleep (median = 26.58 μV2) in comparison to its value before sleep (median = 69.10μV2) with statistically significant differences ($P = 0.025$). The average power (μV2) of occipital alpha waves reduced after sleep than its value before sleep with statistically significant differences ($P = 0.03$). After sleep average power of the occipital alpha waves (median = 12.68 μV2) was reduced in comparison to its value before sleep (median = 18.07 μV2) (Table 3). The rest of QEEG power analysis data showed no significant difference between before and after sleep. These data include average power of temporal theta, central theta and average occipital (theta and delta) during baseline EEG.

Correlations of electrophysiological tools with PSG and sleep scales (ESS, KSS and AHI) showed that occipital alpha difference (before and after sleep) has a significant positive correlation in cases with ESS ($P = 0.022$, $r = 0.509$) (Fig. 1). Positive correlation with KSS before sleep with ($P = 0.005$) (Fig. 2).

Table 2 Comparing QEEG before and after sleep in the control group

	Before sleep Median	After sleep Median	*P* value
Delta CZ (baseline μV2)	25.66	13.4	0.218
Theta CZ (baseline μV 2)	2.42	2.66	0.39
Average temporal delta (baseline μV2)	44.69	89.9	0.04*
Average temporal theta (baseline μV2)	5.12	5.81	0.126
Average delta O (baseline μV2)	33.0	54.5	0.37
Average theta O (baseline μV2)	6.43	7.49	0.57
Average alpha O (baseline μV2)	6.76	18.37	0.97

*Statistically significant

Table 3 Comparing QEE G before and after sleep in the cases group

	Before sleep Median	After sleep Median	*P* value
Delta CZ (baseline μV2)	65.36	35.92	0.044*
Theta CZ (baseline μV 2	2.42	2.66	0.39
Average temporal delta (baseline μV2	69.10	26.58	0.025*
Average temporal theta (baseline μV 2	3.71	3.48	0.126
Average delta O (baseline μV2)	66.56	40.19	0.296
Average theta O (baseline μV 2)	5.76	5.37	0.654
Average alpha O (baseline μV2)	18.07	12.68	0.03*

*Statistically significant

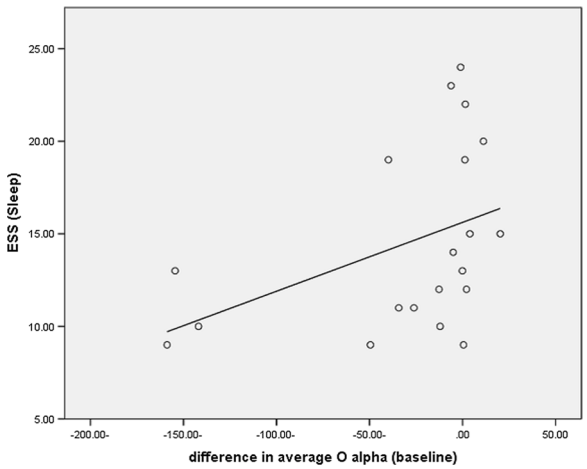

Fig. 1 Positive significant correlation between the difference of EEG (Average Occipital O alpha) before and after sleep with ESS in the cases. ($P=0.022$)

No significant correlation with AHI ($P=0.167$) ($r=0.321$) and KSS after sleep ($P=0.077$, $r=0.405$).

Discussion

In the study, we found that the main EDS cause was OSA and almost all recruited patients were discovered retrospectively by PSG to be suffering from OSA, this is agreement with the literature that the most common cause of EDS in a clinical setting is obstructive sleep apnea (OSA) [7]. Almost all our study demonstrations will be about EDS due to OSA.

Our cases group included 20 cases (4 females and 16 males). This higher male percentage is in, historical, agreement with Chan et al. (2003) study that reported the prevalence (which is the proportion of the whole affected

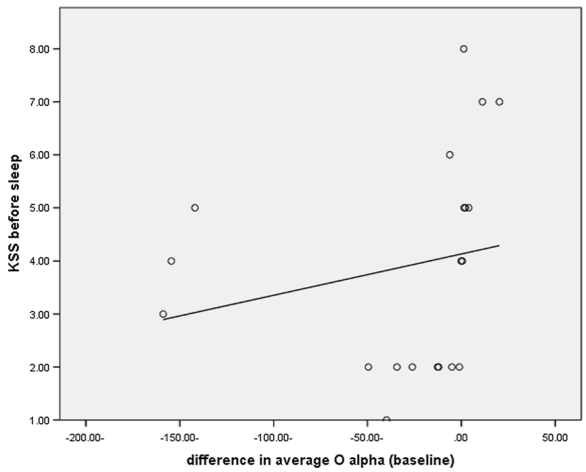

Fig. 2 Positive significant correlation between the difference of EEG (Average Occipital O alpha) before and after sleep with KSS before sleep in the cases. ($P=0.005$)

subjects) of OSA according to gender was two to three-folds major risk for men compared with women in most of the population-based studies [19]. Also found higher prevalence of OSA in men than women until after the age of 50 years, when both genders became at equal risk for the disease. Regarding OSA incidence, Strohl et al. (1996) reported that the overall incidence of moderate-to-severe OSA over a 5-year period was 11.1% in men and 4.9% in women [21].

Our cases age ranged from 32 to 58 years with a mean age of 45.45 ± 7.6 years. This age range of our study group was near to the age group of Tishler et al. (2003) in their study of 1190 patients suffering from increased sleepiness during daily normal activities which was 36–50 years [22]. This age group was also near to many studies as Newman et al. (2005) [23].

The risk of having OSA increases with age [24]. This may be due to increased length of the soft palate, fat deposition in the parapharyngeal region and changes in body structures that surround the pharyngeal tissue, yet its still observational and needs more research [25]. As for the BMI, its mean in our cases was 31.97 ± 4.26 (kg/m^2) and ranged from (32.0 to 58.0 kg/m^2) which is in agreement with Punjabi et al. (2008) study that found that the prevalence of OSA is higher in overweight people ($BMI > 25$ kg/m^2). This comes in agreement with the worldwide epidemiologic studies about body weight, which was considered as the strongest risk factor for obstructive sleep apnea [26]. In addition, it was stated by Martikainen et al. (1992) that every 10% increase in the body weight leaded to an increase of the AHI by 32% and a sixfold increase in the risk of developing moderate to severe OSA [24].

Regarding QEEG results, our QEEG analysis it surprisingly showed statistically significant reduction of delta waves in the central (Cz) as well as the temporal electrodes in the cases, while controls did not show this reduction it showed only increase in the delta waves in the temporal electrodes. Therefore, likely, patients experiencing EDS due to their fragmented night sleep and non-restorative sleep which was presented in the form of reduction of the centro-temporal delta power and occipital alpha power in Eikermann et al. (2007) [27].

The suggested mechanism that demonstrated the reduction of delta power in EDS patients secondary to OSA after sleep could be attributed to hypoxemia and/or hypercapnia during OSA as detected by Tufik et al. (2010) who found a correlation between the severity of hypoxemia and hypercapnia during the OSA and changes in delta power [28].

The reduction in the central and temporal delta power of the EEG in our cases after sleep supported the idea of non-restorative sleep in EDS patients secondary to OSA. According to the synaptic homeostasis hypothesis theory of sleep function which stated that learning activities and synaptic plasticity acquired during wakefulness state as a result, to an increase in the duration of slow wave activity in the following night sleep. This theory makes restorative sleep which is reflected in the form of increased duration of the central slow waves is important for the synaptic strength and its nutrient supply, important for grey matter consumption and preservation of learning and memory [1].

In OSA patients, because of night sleep deprivation and fragmentation, they lost this sleep regulation function leading to "cerebral overloading" and in turn impairment of their memory and learning abilities. So that these changes in delta power in our cases were suggested to be a contributor to daytime symptoms of non-alertness and non-attentiveness in OSA patients [29].

Our control group showed increase in the absolute delta power in the temporal electrodes in comparing EEG after with before sleep. This finding agreed also with synaptic homeostasis hypothesis; being had a normal restorative night sleep [1], the control group had normal synaptic homeostasis, preventing cerebral overloading and so that they had normal day neurobehavioral functions.

In contrast to our study results regarding delta power spectral analysis in EDS patients—secondary to OSA—during wakefulness, was Morisson et al. (1998) study that investigated changes of waking EEG in OSA patients over 24 h of sustained wakefulness in comparison to healthy controls and found that the absolute delta power was higher in OSA patients than controls [30], the same was found also by Tononi et al. (2003) in OSA patients but after 40 h of extended wakefulness in comparison to controls [31]. This increase in delta power could be demonstrated by a theory stating that disturbance of the restorative power of sleep in OSA patients leading to increase in the low frequency bands activity during wakefulness, inducing drowsiness and EDS, especially at the end of the 24-h period of sustained wakefulness. This QEEG finding may be due to the presence of combined effects of both acute and chronic sleep deprivation in OSA patients in such study with augmentation of sleepiness effects in those patients [30]. This is not the case in our study that investigated the chronic night sleep deprivation and fragmentation effects in EDS patients secondary to OSA.

We also found a significant decrease in the occipital alpha power in cases ($P=0.03$) and positive correlation ($P=0.022$) in the cases between the difference of average occipital (O) alpha power (between before and after sleep) and ESS score explaining un wakefulness of the cases on the other day of non-restorative sleep, while Grenèche et al. (2008), who studied the correlation between ESS score and alpha relative power in OSA patients and recorded the EEG during wakefulness in the morning found that ESS score was negatively correlated with alpha relative power; as the patient's sleepiness level increased, the ESS score also increased and in turn the alpha relative power decreased [32]. This negative correlation of the author's results was different from our positive one. This might be attributed to the use of the relative alpha power in QEEG analysis in his study instead of the absolute alpha power that we used in ours.

Another statistically significant positive correlation was found in the cases group of our study between the difference of average occipital alpha power (between before and after sleep) with KSS before sleep ($P=0.005$). This is aligning with D'Rozario et al. (2013) study; in which QEEG assessment was done for patients with OSA during oral intake of Modafinil with acute withdrawal of continuous positive airway pressure CPAP for 2 days (CPAP was used for the first night and then withdrawn for 2 subsequent nights). It showed significant positive correlation of KSS (subjective alertness assessment) with Alpha/Delta ratio (absolute alpha power/delta power) and fast ratio (Power ratio of (alpha beta)/ (delta theta) but not with any of the individual frequency bands [33]. The significance of our study lies in its predicting of EDS cases that are functioning during the day in critical professions, as example driving and healthcare. During the last decade, lots of literature focused on instantaneous diagnosis of hypo vigilance in such professions using various electrophysiological modalities, For example hypo vigilance could be detected by heart rate variability (HRV) [34], driver drowsiness detector using the Eyelid closure

degree (ECD) as a video-based method or using EEG sensors instead of video based method as ECD exhibits a linear relationship with changes of the occipital EEG [35]. BMI system aimed to detect driver drowsiness at its early stage by enriching the EEG data with the intensity of head-movements [35]. Combined EEG-fMRI studies have suggested a close association of fMRI-defined resting state networks with EEG microstates [36, 37]. As well combination of EEG and NIRS, to detect driver drowsiness. EEG, EOG, ECG and NIRS signals [38].

Limitations and recommendations

Sample size could have been larger, yet the patients had to spend a whole night at the lab for PSG, which made the patients less interested to continue the research.

We are recommending expansion of the study of pre/vs/post sleep QEEG extensive analysis to reach the most valid methodology suggestive of non-restorative sleep.

Conclusion

QEEG can offer a new, easy screening tool in patients with non-restorative sleep and hypo vigilance the day after. It opens the research in non-restorative and EDS pathogenesis. There were significant correlations between ESS and KSS scores from one side, and alpha band results in Q-EEG from another side. This highlight the proximity of these subjective sleepiness scales to the EEG background. This emphasizes that QEEG, with further research, will probably be added to sleepiness screening tools, with the privilege of being an objective test.

Abbreviations

AASM: American academy of sleep medicine; AHI: Apnea Hypopnea Index; BMI: Body mass index; BMI: Brain machine interference; CNS: Central nervous system; CPAP: Continuous positive airway pressure; ECD: Eye lid closure; ECG: Electrocardiogram; EDS: Excessive daytime sleepiness; EEG: Electroencephalogram; EOG: Electrooculography; ESS: Epworth sleepiness scale; HRV: Heart rate variability; KSS: Karolinska sleepiness scale; MRI: Magnetic resonance imaging; MSLT: Multiple sleep latency test; MWT: Maintenance of wakefulness; NIRS: Near infrared spectroscopy; OSA: Obstructive sleep apnea; PFC: Prefrontal cortex; PSG: Polysomnography; PSQI: Pittsburgh Sleep Quality Index; QEEG: Quantitative EEG; SAHS: Sleep apnea hypopnea syndrome; SPSS: Statistical package for social science; SSS: Stanford sleepiness scale.

Acknowledgements

No acknowledgements.

Authors' contributions

All authors have participated in designing of the study, acquisition of data, and data interpretation and revising. *DS* carried out editing of the manuscript. *LM* recruited the patients, carried out clinical evaluation and participated in interpretation of the study results. *MB* participated in interpretation of the study results and editing the manuscript. MN revised data interpretation, study results and manuscript editing. All authors have read and approved the manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of the data and materials

All raw data will be available on the editor request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the research ethical committee, faculty of medicine, Cairo University Egypt with date 30-5-2015, under the code number (N-29-2015). Participation was voluntary and all contributors received detailed information about the aims of this research work and an informed written consent was obtained prior to the commencement of the study.

Consent for publication

Not applicable.

Competing interests

None of the authors have conflicts of interest to be disclosed.

Received: 27 June 2021 Accepted: 4 January 2022
Published online: 21 January 2022

References

1. Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. J Sleep Res. 2002;11(1):1–6.
2. Tahmasian M, Noori K, Samea F, Zarei M, Spiegelhalder K, Eickhoff SB, et al. Lack of consistent brain alterations in insomnia disorder: an activation likelihood estimation meta-analysis. Sleep Med Rev. 2018;1(42):111–8.
3. Takeuchi H, Taki Y, Nouchi R, Yokoyama R, Kotozaki Y, Nakagawa S, et al. Shorter sleep duration and better sleep quality are associated with greater tissue density in the brain. Sci Rep. 2018;8(1):1–8.
4. Tahmasian M, Samea F, Khazaie H, Zarei M, Masouleh SK, Hoffstaedter F, et al. Author Correction: The interrelation of sleep and mental and physical health is anchored in grey-matter neuroanatomy and under genetic control. Commun Biol. 2020;3(1):290.
5. Boulos MI, Murray BJ. Current evaluation and management of excessive daytime sleepiness. Can J Neurol Sci. 2010;37(2):167–76.
6. Pagel JF. Excessive daytime sleepiness. Am Fam Phys. 2009;79(5):391–6.
7. Ronksley PE, Hemmelgarn BR, Heitman SJ, Flemons WW, Ghali WA, Manns B, et al. Excessive daytime sleepiness is associated with increased health care utilization among patients referred for assessment of OSA. Sleep. 2011;34(3):363–70.
8. Slater G, Steier J. Excessive daytime sleepiness in sleep disorders. J Thorac Dis. 2012;4(6):608.
9. Park JG, Ramar K, Olson EJ. Updates on definition, consequences, and management of obstructive sleep apnea. Mayo Clin Proc. 2011;86(6):549–54.
10. Lomeli HA, Pérez-Olmos I, Talero-Gutiérrez C, Moreno CB, González-Reyes R, Muñoz-Delgado J, et al. Sleep evaluation scales and questionaries: a review. Actas Esp Psiquiatr. 2008;36(1):50–9.
11. Mollayeva T, Kendzerska T, Colantonio A. Self-report instruments for assessing sleep dysfunction in an adult traumatic brain injury population: a systematic review. Sleep Med Rev. 2013;17(6):411–23.
12. Li G, Chung WY. Estimation of eye closure degree using EEG sensors and its application in driver drowsiness detection. Sensors (Basel). 2014;14(9):17491–515.
13. https://www.webmd.com/sleep-disorders/sleep-apnea/sleep-apnea-ahi-numbers
14. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14(6):540–5.
15. Anderer P, Moreau A, Woertz M, Ross M, Gruber G, Parapatics S, Loretz E, et al. Computer-assisted sleep classification according to the standard of the American Academy of Sleep Medicine: validation study of

the AASM version of the Somnolyzer 24 × 7. Neuropsychobiology. 2010;62(4):250–64.
16. Shahid A, Shen J, Shapiro CM. Measurements of sleepiness and fatigue. J Psychosom Res. 2010;69(1):819.
17. http://www.researchgate.net/post/How-can-I-calculate-relative-band-powers-delta-theta-alpha-beta.
18. Chan YH. Biostatistics 102: quantitative data–parametric & non-parametric tests. Singapore Med J. 2003;44(8):391–6.
19. Chan YH. Biostatistics 103: qualitative data-tests of independence. Singapore Med J. 2003;44(10):498–503.
20. Chan YH. Biostatistics 104: correlational analysis. Singapore Med J. 2003;44(12):614–9.
21. Strohl KP, Redline S. Recognition of obstructive sleep apnea. Am J Respir Crit Care Med. 1996;154(2 Pt 1):279–89.
22. Tishler PV, Larkin EK, Schluchter MD, Redline S. Incidence of sleep-disordered breathing in an urban adult population: the relative importance of risk factors in the development of sleep-disordered breathing. JAMA. 2003;289(17):2230–7.
23. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, et al. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. Arch Intern Med. 2005;165(20):2408–13.
24. Martikainen K, Hasan J, Urponen H, Vuori I, Partinen M. Daytime sleepiness: a risk factor in community life. Acta Neurol Scand. 1992;86(4):337–41.
25. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med. 2001;163(3 Pt 1):608–13.
26. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):136–43.
27. Eikermann M, Jordan AS, Chamberlin NL, Gautam S, Wellman A, Lo YL, et al. The influence of aging on pharyngeal collapsibility during sleep. Chest. 2007;131(6):1702–9.
28. Tufik S, Santos-Silva R, Taddei JA, Bittencourt LR. Obstructive sleep apnea syndrome in the Sao Paulo epidemiologic sleep study. Sleep Med. 2010;11(5):441–6.
29. Liddell BJ, Paul RH, Arns M, Gordon N, Kukla M, Rowe D, et al. Rates of decline distinguish Alzheimer's disease and mild cognitive impairment relative to normal aging: integrating cognition and brain function. J Integr Neurosci. 2007;6(1):141–74.
30. Morisson F, Lavigne G, Petit D, Nielsen T, Malo J, Montplaisir J. Spectral analysis of wakefulness and REM sleep EEG in patients with sleep apnoea syndrome. Eur Respir J. 1998;11(5):1135–40.
31. Tononi G, Cirelli C. Sleep and synaptic homeostasis: a hypothesis. Brain Res Bull. 2003;62(2):143–50.
32. Grenèche J, Krieger J, Erhardt C, Bonnefond A, Eschenlauer A, Muzet A, et al. EEG spectral power and sleepiness during 24 h of sustained wakefulness in patients with obstructive sleep apnea syndrome. Clin Neurophysiol. 2008;119(2):418–28.
33. D'Rozario AL, Kim JW, Wong KK, Bartlett DJ, Marshall NS, Dijk DJ, et al. A new EEG biomarker of neurobehavioural impairment and sleepiness in sleep apnea patients and controls during extended wakefulness. Clin Neurophysiol. 2013;124(8):1605–14.
34. Xiromeritis AG, Hatziefthimiou AA, Hadjigeorgiou GM, Gourgoulianis KI, Anagnostopoulou DN, Angelopoulos NV. Quantitative spectral analysis of vigilance EEG in patients with obstructive sleep apnoea syndrome: EEG mapping in OSAS patients. Sleep Breath. 2011;15(1):121–8.
35. Wang D, Bai XX, Williams SC, Hua SC, Kim JW, Marshall NS, et al. Modafinil increases awake EEG activation and improves performance in obstructive sleep apnea during continuous positive airway pressure withdrawal. Sleep. 2015;38(8):1297–303.
36. Chua EC, Tan WQ, Yeo SC, Lau P, Lee I, Mien IH, et al. Heart rate variability can be used to estimate sleepiness-related decrements in psychomotor vigilance during total sleep deprivation. Sleep. 2012;35(3):325–34.
37. Mishra A, Marzban N, Cohen MX, Englitz B. Dynamics of neural microstates in the VTA-striatal-prefrontal loop during novelty exploration in the rat. J Neurosci. 2021;28:2256–320.
38. Li G, Chung WY. A context-aware EEG headset system for early detection of driver drowsiness. Sensors (Basel). 2015;15(8):20873–93.

Publisher's Note