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How do people with drug-resistant mesial temporal lobe epilepsy sleep? A clinical and video-EEG with EOG and submental EMG for sleep staging study

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ABSTRACT

This study aimed to assess subjective and objective sleep parameters in a homogeneous group of drug-resistant mesial temporal lobe epilepsy (MTLE)[1] patients through internationally validated clinical questionnaires, video-electroencephalographic (VEEG)[2] and polysomnographic (PSG)[3] studies. Fifty-six patients with definite diagnosis of MTLE who were candidates for epilepsy surgery underwent a detailed clinical history, the Pittsburgh Sleep Quality Index (PSQI),[4] Epworth Sleepiness Scale (ESS),[5] Stanford Sleepiness Scale (SSS),[6] neurological examination, 1.5 T brain magnetic resonance imaging, VEEG and PSG. Sixteen percent of patients reported significant daytime sleepiness as measured by ESS and 27% reported low levels of sleep quality as measured by PSQI. Patients with medically resistant epilepsy by MTLE showed increased wakefulness after sleep onset (WASO) with mean ± standard deviation of 17.4 ± 15.6, longer non-rapid eye movement (NREM)[7] 1 (7.5 ± 4.6%) and NREM3 sleep (26.6 ± 11.8%), abnormal rapid eye movement (REM)[8] latency in 30/56 patients, shorter REM sleep (16.7 ± 6.6%), and abnormal alpha delta patterns were observed in 41/56 patients. The analysis of interictal epileptic discharges (IEDs)[9] evidenced highest spiking rate during NREM3 sleep and higher concordance with imaging data when IEDs were recorded in sleep, mainly during REM sleep. We concluded that patients with MTLE showed disrupted sleep architecture that may result in daytime dysfunction and sleep complaints. Furthermore, NREM sleep activated focal IEDs and them - when recorded during sleep - had higher localizing value.

1. Introduction

There is a reciprocal interaction between sleep and epilepsy: while seizures tend to occur during sleep in some epileptic syndromes, epilepsy may disrupt the organization and microarchitecture of sleep [1]. Generalized seizures that occur during sleep may delay sleep onset, fragment sleep, increase non-rapid eye movement (NREM) 1 stage sleep, decrease the percentage of NREM2, NREM 3, rapid-eye movement (REM) and increase drowsiness on the day after seizures [2,3].

Patients living with epilepsy (PWE)[10] have a higher prevalence of sleep complaints and sleep disorders than healthy subjects [4]. Pizzatto et al. observed that PWE presented higher levels of daytime sleepiness measured by Epworth sleepiness scale (ESS) than healthy controls, and they demonstrated that factors responsible for disruption of sleep architecture may be beyond those found in the general population [5]. Polysomnographic (PSG) studies performed in patients with temporal lobe epilepsy (TLE)[11] showed that epilepsy itself disturbed sleep architecture, caused poorer sleep efficiency, a higher number of arousals and awakenings, longer NREM1 and NREM2, and shorter slow-wave-sleep (SWS)[12] [6]. In contrast, other authors reported increased SWS, shorter total sleep time and REM sleep [7]. Most of these studies recruited patients with diverse epileptic syndromes or included patients with

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[1] MTLE: mesial temporal lobe epilepsy;
[2] VEEG: video-electroencephalographic;
[3] PSG: polysomnographic;
[4] PSQI: Pittsburgh Sleep Quality Index;
[5] ESS: Epworth Sleepiness Scale;
[6] SSS: Stanford Sleepiness Scale;
[7] NREM: non-rapid eye movement;
[8] REM: rapid eye movement;
[9] IEDs: interictal epileptic discharges.
[10] PWE: Patients living with epilepsy;
[11] TLE: temporal lobe epilepsy;
[12] SWS: slow-wave-sleep;

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temporal lobe epilepsy by different etiologies altogether, which might have undermined their results.

Sleep-related activation of interictal epileptiform discharges (IEDs) may be found and provide lateralizing information about the epileptogenic zone in patients with TLE [8]. It is believed that this activation may occur due to the synchronous synaptic effects related to NREM sleep [9,10] and may be influenced by factors such as: epileptic syndrome, vigilance state, age at epilepsy onset, duration of epilepsy, presence of secondarily generalized tonic-clonic seizures (GTCS),[13] presence of hippocampal sclerosis and timing of the last seizure [10]. Even though most studies demonstrated highest spike rates during SWS compared to other stages of sleep or wakefulness [9,10]; other ones observed maximal spiking during wakefulness, light NREM or REM. There is a significant interindividual variability regarding spiking rate which emphasizes the need for further studies [11].

In this article, we evaluated subjective and objective sleep parameters in a homogeneous group of patients with drug-resistant mesial temporal lobe epilepsy (MTLE) through video-electroencephalographic (VEEG) and PSG studies. We also investigated which clinical data may modulate the IEDs during the sleep-wake cycle and how this modulation could affect the IEDs.

2. Material and methods

2.1. Subjects

Fifty-six consecutive adult patients (over 18 years old) diagnosed with MTLE according to International League Against Epilepsy (ILAE)[14] [12–15] who were candidates for epilepsy surgery, underwent a comprehensive presurgical evaluation at the Epilepsy Center of Santa Catarina (CEPESC),[15] Governador Celso Ramos Hospital (HGCR),[16] Florianópolis, Brazil, between October 2009 and September 2013. It consisted of a detailed clinical history, neurological examination, 1.5 T brain magnetic resonance imaging (MRI),[17] neuropsychological, psychiatric and psychosocial assessments. Exclusion criteria were non-drug-resistant epilepsy, patients with known or suspected sleep disorders, and psychiatric comorbidities.

2.2. Clinical assessment

Subjects completed an extensive survey on the first day of hospitalization, in the afternoon before the PSG started, which included demographic and clinical variables, the Epworth Sleepiness Scale (ESS) [16], Pittsburgh Sleep Quality Index (PSQI) [17], and Stanford Sleepiness Scale (SSS) [18]. Exclusion criteria for completing these questionnaires were the presence of illiteracy or cognitive impairment that precluded the patient from completing them adequately. The ESS consists of 8 self-rated items, each scoring from 0 to 3 that measures an individual's habitual "likelihood of dozing or falling asleep" in common daily situations. The ESS score represents the sum of individual items and ranges from 0 to 24. Scores greater than ten are considered to indicate significant sleepiness. The Portuguese-language version of the ESS validated to be used in Brazil was useful to assess sleepiness in PWE [20]. The PSQI is a 19-item self-rated questionnaire to evaluate sleep quality over the previous month. The 19 questions are combined into seven clinically derived component scores (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep-inducing medication, and daytime dysfunction) that are each weighted equally and scored from 0 to 3. The 7 component scores are added to obtain a global score ranging from 0 to 21, with higher scores indicating worse sleep quality. A global score greater than five is defined as a low sleep quality. The Portuguese-language version of the PSQI validated to Brazil was used to assess sleep quality index [21]. The SSS quantifies subjective sleepiness levels at the time of evaluation. Participants selected one of 7 options to identify their current level of sleepiness. A score equal or greater than three is associated with a decline in performance that is related to sleepiness. Participants also answered ten questions with yes or no alternatives to assess the presence of other common sleep disorders such as insomnia, nonrestorative sleep, restless sleep, sleep talking, sleepwalking, bruxism, abnormal dreams and sleep paralysis.

All patients were receiving maintenance antiepileptic medication (AEM)[18] therapy and pharmacological assessment. To allow comparisons among diverse AEM regimen, either as monotherapy or in combination, a measure of equipotency must be determined. Therefore, all AEM daily doses were standardized as a ratio of prescribed daily dose (PDD)[19] to defined daily dose (DDD)[20] for each patient. While PDD is the prescribed dose for each subject in our population, the DDD is determined by the World Health Organization (WHO)[21] as the average maintenance dose per day for each AEM used for its main indication in adults by analysis of literature and drug registration data; for instance, carbamazepine's DDD is 1000 mg/day. The DDD does not necessarily reflect the PDD and differences between PDD and DDD may reflect the severity of the disease [23,24].

2.3. MRI data

Neuroimaging studies included high-resolution MRI (1.5 T) with special protocols for epilepsy [25]. All patients had clear MRI findings consistent with hippocampal sclerosis (HS),[22] defined by the presence on visual inspection of atrophy, increased T2-weighted signal, decreased T1-weighted signal, and disrupted internal hippocampal structure [26–28]. Based on visual analysis of MRI, the neurologists classified HS as (a) unilateral, when HS was observed on one side; or (b) bilateral, when HS was observed on both sides.

2.4. Polysomnographic evaluation

Overnight (one night) PSG study was performed on the first night of hospital admission. In order to avoid the "first night effect" affecting PSG parameters we encouraged the patients to bring their personal belongings to make the laboratory environment as familiar as possible, all patients were admitted in the morning, started recordings at 7 AM and spent the entire daytime under monitorization and getting acquainted with the VEEG/sleep equipment before the overnight PSG study started. The video-polysomnography included extended 18-channel electroencephalogram (EEG)[23] montage based on the International 10–20 System (IS)[24] [29,30] and analyzed the following parameters: standard electrooculography (EOG),[25] chin electromyogram (EMG),[26] airflow (oronasal thermistor and nasal pressure), snoring, arterial oxygen saturation, body position and electrocardiogram (EKG)[27] [31,32].

Nurses instructed the patients to sleep at 10 PM and awakened them at 6 AM. All patients were recorded in a single room on a hospital ward, and all efforts were made to optimize sleeping conditions - during recordings, the doors of the room remained closed, the lights off and the patients undisturbed unless a seizure occurred. Following seizures, patients were encouraged to return to sleep.

[13] GTCS: generalized tonic-clonic seizures.
[14] ILAE: International League Against Epilepsy;
[15] CEPESC: Epilepsy Center of Santa Catarina;
[16] HGCR: Governador Celso Ramos Hospital;
[17] MRI: magnetic resonance imaging.
[18] AEM: antiepileptic medication.
[19] PDD: prescribed daily dose;
[20] DDD: defined daily dose;
[21] WHO: World Health Organization;
[22] HS: hippocampal sclerosis;
[23] EEG: electroencephalogram;
[24] IS: International 10–20 System;
[25] EOG: electrooculography;
[26] EMG: electromyogram
[27] EKG: electrocardiogram;