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Sleep–wake pattern, chronotype and seizures in patients with epilepsy

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ABSTRACT

Purpose: Although mounting evidence suggests that sleep and epilepsy are reciprocal and seizures influence circadian rhythms, sleep–wake pattern and seizure control have not been widely researched. This study aimed to investigate the association of sleep–wake pattern, sleep quality, and chronotype with seizures in patients with epilepsy (PWE).
Methods: 160 consecutive PWE (aged 20–49 years, focal epilepsy, FE: generalized epilepsy, GE = 127:33) and 130 age–gender matched healthy controls (HC) were enrolled. All subjects completed a sleep diary for more than 2 weeks, Pittsburgh Sleep Quality Index (PSQI), Epworth sleepiness scale (ESS), and the Morningness–Eveningness questionnaire (MEQ). Detailed seizure history was reviewed for the last 1 year.
Key findings: Sleep–wake patterns on workdays were different between PWE and HC ($p < 0.001$), although PSQI, ESS, and MEQ did not differ. Social jetlag (difference of mid-sleep time between workdays and free days) was more evident in PWE (1.4 h) than HC (0.7 h, $p < 0.001$). GE showed lower MEQ, later mid-sleep time on both workdays and free days, and larger social jetlag than FE. Higher seizure frequency was positively correlated with higher PSQI and ESS after adjusting for age, gender, and number of antiepileptic drugs ($p < 0.05$). PWE with lower MEQ presented worse sleep quality.
Significance: Contrary to HC, PWE maintained sleep–wake patterns more regularly during workdays and free days. GE patients reported more eveningness-preference; however, their sleep quality was not worse than FE. Although sleep quality may affect seizure frequency, sleep–wake patterns and chronotype were not related to seizures in PWE.

1. Introduction

Sleep is an important physiologic process that helps in the recovery of brain or physical damage. Maintaining normal sleep is necessary for physical and mental health (Chae, 2007). There is a reciprocal interaction between sleep and epilepsy; epilepsy may disrupt sleep, and sleep disorders can impair seizure control (Bazil, 2003; Hofstra and De Weerd, 2009). The prevalence of sleep disturbance was reportedly two-fold higher in epilepsy, as compared to normal control (38.6 vs. 18.0%) (De Weerd et al., 2004).

The nature of sleep disturbance in epilepsy is diverse, and the etiologies are complex. Sleep disturbance in epilepsy may consist of insufficient sleep, inadequate sleep hygiene, coexisting sleep disorders such as obstructive sleep apnea, and the effects of antiepileptic drugs (AEDs) (Bazil, 2003). Epilepsy is disruptive to sleep. Although sleep disturbance is more common in patients who have a tendency toward nocturnal seizures, the causal relationship between sleep quality and seizures is not clear.

Sleep is regulated by sleep homeostasis and circadian processes. The homeostatic sleep pressure increases with sleep deprivation, and the circadian process provides an endogenously mediated 24-h sleep–wake rhythmic cycle (Chae, 2007). This sleep–wake cycle has considerable inter-individual variation in the preferred timing, widely known as chronotype. Circadian dysregulation between individual chronotype and daily activity are known to cause

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sleep problems. One study showed that individuals with a circadian preference for evening activities (evening-type) showed higher prevalence of sleep disturbance than morningness or intermediated-type (Selvi et al., 2012). Homeostatic changes in sleep deprivation, as well as different individual chronotype can cause sleep disorders.

Previous studies on sleep in patients with epilepsy (PWE) focused on sleep homeostasis and sleep disturbance in terms of sleep duration, and sleep hygiene. However, there is scant research on the influence of sleep–wake pattern and chronotype on sleep and related seizure frequency. This study compares the sleep–wake pattern, sleep quality, and chronotype between PWE and healthy controls (HC). Furthermore, we investigated the relationship between sleep–wake patterns with chronotype and seizures according to epilepsy classification (focal epilepsy, FE vs. generalized epilepsy, GE).

2. Material and methods

2.1. Subjects

The PWE, aged between 20 and 49 years with a history of epilepsy of more than 1 year were recruited from a university affiliated hospital epilepsy center. A diagnosis of epilepsy was according to the criteria of the International League Against Epilepsy, confirmed by the epileptologist based on detailed history and electroencephalography (EEG). Age- and sex-matched HC were also recruited through an advertisement from local community. Exclusion criteria of the study included: (1) inability to read or understand questionnaires; (2) non-Korean speaking foreigners; (3) psychiatric, neurological or relevant internal comorbidities; (4) habitual use of hypnotics (≥3 nights/week); (5) mean daily sleep time ≤5 h; (6) shift-workers; (7) PWE without previous history of taking AEDs; (8) documented or suspected non-epileptic seizures. Subjects with psychiatric and neurological comorbidities were excluded based on the medical records.

Since chronotype may be age- and sex-dependent (Roenneberg et al., 2007), 25 people from each age and sex group were enrolled. Two hundred and eight PWE and 172 HC were consecutively recruited from September 2012 to January 2013. Of these, 48 PWE and 42 controls were excluded (Fig. 1).

For sub-group analyses, PWE were classified into focal epilepsy (FE) and generalized epilepsy (GE) based on epilepsy history, seizure semiology, routine EEG, video-EEG monitoring (if available), and brain MRI.

2.2. Methods

Data obtained from self-reported questionnaires, and medical records were reviewed retrospectively. Clinical information including epilepsy history, classification, seizure frequencies during the past year, and number of antiepileptic drugs (AEDs) were collected in PWE.

2.2.1. Questionnaire

Sleep–wake pattern: Subjects were asked to record habitual sleep on workdays and free days including the following information: (i) time to go to bed; (ii) time to get out of bed; (iii) amount of time to fall asleep; (iv) nocturnal sleep time; and (v) daytime nap. Total sleep time was calculated using the sum of nocturnal sleep and daytime nap. The time of mid-sleep (mid-time between sleep onset and sleep end) and social jetlag (difference between the time of mid-sleep on workdays, MSW and the time of mid-sleep on free days, MSF) were also assessed (Roenneberg et al., 2007).

Sleep quality: The Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire that assesses sleep quality and sleep disturbance during a 1-month period (Buysse et al., 1989). It has a total of 19 items, and composed of 7 subscales assessing subjective quality of sleep, sleep latency, sleep duration, sleep efficiency, sleep disturbance, medication use for sleep, and daytime dysfunction. The total PSQI score has a range of 0–21; higher scores indicate worse sleep quality. The PSQI has been shown to be valid and reliable in the Korean population (Sohn et al., 2012).

Chronotype: The Korean version of Morningness–Eveningness Questionnaire (MEQ) (Park et al., 1996) consists of 19 items pertaining to habitual rising and bed times, preferred times of physical and mental performance, and subjective alertness after rising and before going to bed (Horne and Ostberg, 1976). Five questions are time scales divided into 1-h or 15-min interval and fourteen questions are measured on a 4-point Likert-scale. Example questions include “If you went to bed at 11 pm at what level of tiredness would you be?” (four-item answer) or “At what time in the evening do you feel tired and a result in need of sleep?” (time scale). Most questions are preferential, not the actual time. The MEQ scores ranging from 16 to 86, with higher scores reflecting stronger morningness-preference.

Daytime sleepiness: The Epworth Sleepiness Scale (ESS) measures the impact of subjective daytime sleepiness (Johns, 1991). The Korean version of ESS consists of eight items on the subject’s likelihood of falling asleep in a particular situation that is commonly met in daily life. Each item ranges from 0 (no napping) to 3 (high

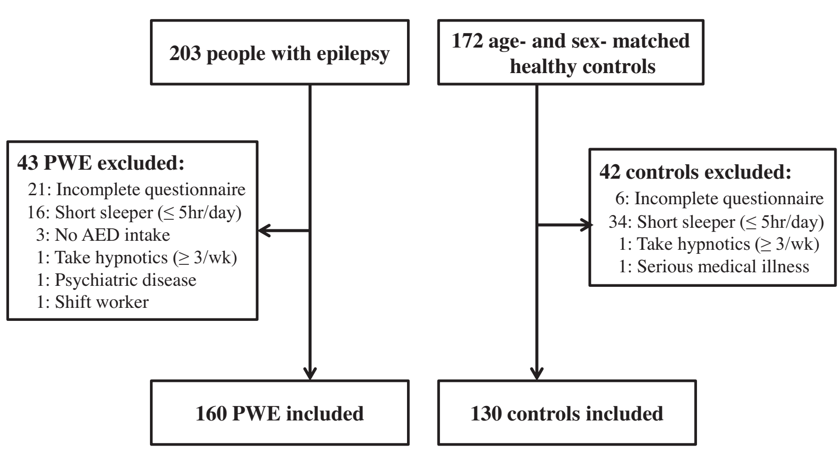

Fig. 1. Study enrollment flow. 208 patients with epilepsy (PWE) who were confirmed by epileptologist were consecutively enrolled. Among them 48 patients were excluded as above. Finally 160 PWE were included. Consecutively 172 healthy controls whose age and gender were matched with patients were also consecutively enrolled. 42 controls were excluded as above, finally 130 persons were included. PWE, patients with epilepsy; AED, antiepileptic drug.