Sleep in Patients with Epilepsy

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Sleep disorder is common in all societies, so are in the patients with epilepsy (PWE). In the International Classification of Sleep Disorders (ICSD) published 2001, it is categorized into four main subsidiaries, which are (1) dyssomnias, (2) parasomnias, (3) sleep disorders associated with mental, neurologic, or other medical disorders and (4) proposed sleep disorders [1]. No matter what the final diagnosis is, the results usually are poor quality of sleep and excessive daytime sleepiness. There are complex pathophysiologic mechanisms that underlie the interaction of sleep and epilepsy. These include (1) epilepsy seizure per se, (2) psychotic and psychiatric impact from epilepsy and (3) side effects from antiepileptic drugs (AEDs). In PWE, poor sleep quality causes sleep deprivation, which in turn exaggerates the attacks of seizures and falls into vicious cycles. Thus, it is worth paying attention to this field.

Sleep is an extremely valuable physiological activating technique in epilepsy and is used routinely in the electroencephalographic (EEG) recording. The importance in the activation of epileptiform discharges (EDs) during sleep was first demonstrated by Gibbs and Gibbs in 1947 [2]. It is proposed that non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep have contrasting effects on ictal and interictal EDs. EDs are likely to propagate during NREM sleep, including its synchronized EEG transients, such as K-complexes and sleep spindles. In contrast, REM sleep, with its asyn-chronous cellular discharge patterns and skeletal motor paralysis, is resistant to propagation of EDs and to clinical motor accompaniment. In addition, the preserved skeletal muscle tone in NREM permits seizure-related movement, whereas the lower motor neuron inhibition in REM prevents seizure-related movement [3]. These can explain why clinical seizures and interictal EDs tend to occur in NREM rather than REM sleep.

Seizures markedly activated by sleep including the seizures of frontal lobe origin and the generalized tonic seizures of Lenox-Gastaut syndrome. The epilepsies that having interictal EDs markedly activated during NREM sleep include benign rolandic epilepsy, temporal lobe epilepsy and infantile spasm. While the Landau-Kleffner syndrome and the atypical benign rolandic epilepsy possess the most striking increase of EDs with continuous spike-and-wave complexes during slow wave sleep (CSWS) or electrical status epilepticus during sleep (ESES) in EEG (Figure 1) and absence of normal sleep activities.

On days after nocturnal seizures, patients had more severe excessive daytime sleepiness as compared with days after seizure free nights. As compared with seizure-free nights, nights with seizures were characterized by a reduction of REM and stage 3 sleep, prolonged REM latency and reduced sleep efficiency [4]. These findings held true even on seizure-free nights. Nocturnal generalized seizures would decrease sleep time and REM sleep

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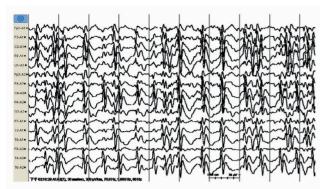
Figure 1. This is the sleep EEG recording in a 10 year-old boy of atypical benign rolandic epilepsy. There are abundant spikes occupying more than 85% of the sleep recording with absence of normal sleep activities. The EEG pattern is highly suggestive of the diagnosis of Electrical status epilepticus during sleep (ESES).

percentage, prolong REM latency, and fragment sleep[5]. Multiple focal seizures in a night also significantly reduced REM sleep. In addition, not only seizures occurring at night but also those occurring during the day can affect sleep architecture, with proved significant reduction of REM sleep and prolongation REM latency in the following nights[6].

Psychological or psychiatric problems, having a high incidence in PWE, may also play a role in disturbing normal sleep. It was reported that 40% of respondents with insomnia and 46.5% of respondents with hypersomnia had a psychiatric disorder. Anxiety disorders were found to be the most common mental disorders [7]. Another study found that 93% of depressed inpatients complained of insomnia[8].

In PWE, depression is the most frequent comorbid psychiatric disorder, with a prevalence of 10% to 20% among patients with controlled seizures and 20% to 60% among those with refractory epilepsy[9,10]. The prevalence of anxiety disorder, panic disorder, obsessive-compulsive disorder and phobias is also high in PWE, with estimates of 3% to 66% [10]. Psychosis consisting of visual or auditory illusions and hallucinations, paranoia, depersonalization, derealization, autoscopy, or delusion is reported in 0.6% to 7% of PWE in the community, and in 19% to 27% of hospital-derived populations [11]. The overall frequency of psychosis among PWE is approximately 7% to 14%. Reports suggest that up to 69% of patients with temporal lobe epilepsy and 72% of patients with generalized epilepsy suffer from personality disorders [12]. Even as benign as juvenile myoclonic epilepsy, 14% was reported to have personality disorders [13].

Sleep disturbance in PWE may be secondary to AEDs they are treated with. Most old AEDs were reported to result in a normalization of the sleep architecture and sleep efficiency [14]. Studies suggest that phenytoin (PHT), phenobarbital (PB), carbmazepine (CBZ) and clonazepam (CZP) can decrease sleep latency. PB and ethosuximide (ESM) can decrease awakening and arousal. CBZ and CZP can decrease wake time after sleep onset. PHT, PB and ESM can increased stage 1 and stage 2 sleep. CZP can increase stage 2 sleep. PHT, CBZ and valproic acid (VPA) can increased slow wave sleep. PB, VPA and CZP can decrease REM sleep. In newer AEDs, gabapentin (GBP) can decrease awakening and arousal but increased slow wave sleep [14].

However, AEDs can also have negative effect on sleep architecture. VPA and ESM can increase awakening and arousal. VPA can increase wake time after sleep onset. PHT, CZP and ESM can decrease slow wave sleep. ESM will increase REM sleep. In newer AEDs, GBP can increase REM sleep, lamotrigine produced somnolence in 14% and insomnia in 6% of patients. Topiramate produced somnolence in approximately 30% of patients treated. Somnolence and insomnia occurred in 18 and 6%, respectively of patients receiving tiagabine[15].

The mechanisms of sleep disorders related to AEDs are complex, some related to their direct sedative effect on central nervous system, and can be ameliorated by gradual escalating the dosages when initiation of treatment. Some are more complicated, for example, the slow wave sleep-enhancing effects were thought to reflect the effect of CBZ on 5-hydroxytryptamine (5-HT) levels or its effect on adenosine receptors that modulate the release of 5-HT and catecholamines [16]. Therefore, it is not difficult to expect that sleep disorders are more prevalent in patients with polytherapy than in those with monotherapy and improved after reducing the number of AEDs.

Under the invention of modern diagnostic tools especially video monitoring with polysomnography, the types and causes of sleep disorders are much easier to be clarified than before. In the paper "Sleep Quality and Daytime Sleepiness in Patients with Epilepsy" by Chen NC et al (Acta Neurologica Taiwanica Vol 21 No 2 June 2011), they adopted self-rated questionales of Epworth Sleepiness Scale (ESS) and the Pittsburg Sleep Quality Index (PSQI) as tools to estimate excessive daytime sleepiness and sleep quality. They had three main findings: (1) Twenty percent of PWE (23/117) in contrast to 7% of healthy controls (2/30) had excessive daytime sleepiness. (2) There is a significantly higher prevalence of poor sleep quality in the partial seizure, non-seizure-free, and polytherapy groups. (3) The poor seizure control was the strongest independent risk factor for poor sleep quality. Their findings are consistent with the studies in the past decades and worth paying appreciation for it has been the first large scale study in Taiwanese PWE (117 cases) ever since. Indeed, the complex relationship between epilepsy and sleep disorder must be addressed in order to provide the best management of sleep disturbance in PWE.

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