Journal of the Neurological Sciences 315 (2012) 33–38

Contents lists available at SciVerse ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Temporal relationship between awakening and seizure onset in nocturnal partial seizures

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ARTICLE INFO

Article history:
Received 26 September 2011
Received in revised form 12 December 2011
Accepted 19 December 2011
Available online 16 January 2012

Keywords:
Sleep
Epilepsy
Awakening
Seizure
Video EEG
Polysomnography
Frontal lobe epilepsy
Temporal lobe epilepsy

ABSTRACT

Clinical awakening can be seen just before or after seizure onsets. In this study we determined the time between onset of seizures and awakening in patients with frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE).

Sixty-eight patients who underwent video-EEG monitoring with simultaneous PSG were retrospectively examined. TLE or FLE patients having seizures during sleep were included. Seizure onset and awakening onset were marked according to clinical and electrophysiological features. The duration between awakening and seizure onset was compared in patients with TLE and FLE.

Twenty-five patients who had been diagnosed with TLE (17) or FLE (8) had a total of 75 seizures during sleep. All seizures except one, occurred during NREM sleep in both TLE and FLE patients. The seizure onsets were before awakening in 49 seizures (FLE: 20, TLE: 29) and the awakening preceded the seizure onsets in 12 seizures (FLE: 3, TLE: 9). The duration between seizure onset and the awakening was shorter in FLE, either in seizures with preceding awakening or not ($p=0.014$, $p=0.015$).

Awakening was mostly seen after onset of seizures rather than before, especially in TLE. But in patients with FLE the duration between seizure onset and awakening was shorter. The localization of epileptic activity may play a role for the timing of awakening mechanisms during nocturnal partial seizures.

1. Introduction

Epilepsy and sleep have a significant influence on each other. In evaluations of that reciprocal relationship between epilepsy and sleep, early observations for the timing of seizures with respect to the sleep cycle concentrated on generalized tonic–clonic seizures [1]. It was found that 19–24% experienced seizures only during nocturnal sleep, while 33–37% occurred both during daytime and nighttime hours [2–4]. According to reports in the last 15 years, in patients with localization related partial epilepsy, 11–26% of temporal lobe epilepsy (TLE) patients had seizures during sleep [5,6]. These rates were higher (37–61%) in patients with seizures originating from the frontal lobe, in frontal lobe epilepsy (FLE) [5,6]. All these nocturnal seizures tend to occur during stage 2 of non-rapid eye movement (NREM) sleep [7,8].

Because of violent behavioral components of seizures, awakening can be seen after seizure onset. In certain epilepsy syndromes (e.g. juvenile myoclonic epilepsy and epilepsy with generalized tonic–clonic seizures on awakening), however, seizures occur soon after awakening [5]. Similarly, in patients with focal epilepsy, 83% of temporal lobe seizures were recorded during times of mini-arousals in a cycling alternating pattern (CAP) [9,10]. Although there are suggestions about seizures in mesial TLE occurring during sleep, related to awakening [11], intracranial recordings showed that arousal actually follows the onset of the seizure rather than preceding it [12]. A close relationship between frontal lobe related events and the EEG synchronized patterns of CAP has also been reported [13]. Therefore a triggering role of CAP on frontal lobe seizures was suggested [13,14].

Although clinical awakening can be seen just before or after the seizure onsets, it is difficult to assess if an arousal precedes a seizure or results from it. Furthermore, cortical centers for awakening are not as clear as those in the brainstem [15,16] to suggest the effect of epileptic tissue localization in the cortex on awakening. In this study we show the distribution of seizures during sleep for the most frequently seen localization related partial epilepsies in adults with TLE and FLE. Our main aim, however, was to determine the time between onset of seizures and awakening. There are a few studies about relationship between arousal–awakening and seizures [10,12–14]. But to the best of our knowledge there is no study about effect of partial seizures, including both FLE and TLE on awakening. Accordingly we discuss the role of the brain regions on awakening mechanisms.

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doi:10.1016/j.jns.2011.12.009

2. Methods

2.1. Subjects and EEG-PSG-video monitoring

There were 226 adult patients who underwent video-EEG monitoring in our center from December 2007 to January 2010. We have a polysomnography (PSG) recording device with video-EEG in one of two rooms and patients were randomly hospitalized in these rooms. In these patients, who were undergoing simultaneous PSG, recordings were retrospectively examined. Patients with TLE or FLE and having seizures during sleep were included. Patients with unclassified seizures or with both temporal and frontal type seizures were excluded. Those with parietal or occipital lobe epilepsy and generalized epilepsy were also not included. Additionally patients with psychogenic nonepileptic attacks, aura, and unavailable PSG recordings were excluded. This study was approved by the ethical committee of our university, and written informed consents were obtained from all subjects before experiments.

The diagnosis of TLE or FLE was discussed in a multidisciplinary case conference including neurologists, neurosurgeons, neuroradiologists, and neuropsychologists. Their clinical and electrographic features of seizures, magnetic resonance imaging (MRI) findings and positron emission tomography, and ictal or interictal single photon emission computerized tomography when available were evaluated. Patients' seizure types and epilepsy syndromes were determined according to the International League Against Epilepsy (ILAE) classifications [17].

MRIs were obtained using either 1.5 or 3.0 T scanners (Symphony and Allegra, respectively, Siemens, Erlangen, Germany). The MRI protocol included coronal 3D T1-weighted (W) gradient-echo imaging (MPRAGE) obtained parallel to the brainstem, and fluid-attenuated inversion recovery (FLAIR), and T2-W turbo spin-echo and T1-W inversion recovery images obtained perpendicular to the hippocampi in addition to routine brain imaging.

Each patient was monitored for 3–10 days in a video-EEG monitoring unit using a 32-channel EEG system (Grass-Telefactor). There was not a standard procedure for withdrawal of the antiepileptic drug during monitoring. T1 and T2 scalp electrodes were placed according to the standard 10–20 system. The other parameters recorded included electrooculogram (EOG), submental electromyogram and electrocardiogram (ECG), respiratory effort and airflow, oxyhemoglobin saturation, and anterior tibialis EMG. Digital EEG-PSG systems allow for monitoring 32 inputs, to provide EEG coverage sufficient to define ictal patterns. The studies were manually scored for sleep stages in 30-s epochs with an expanded EEG montage. We do not distinguish between NREM stage 3 and NREM stage 4 sleep, but use the term NREM stage 3/4 to describe slow wave sleep. That defines epochs that have 0.5–2 Hz activity greater than 75 μV amplitude for at least 20% of the epoch. Other standard Rechtschaffen and Kales criteria were used in analyzing the PSGs [18].

Seizures were defined as an EEG pattern that represents a clear change from background frequencies and evolves in frequency and amplitude [19]. The obvious ictal EEG onsets were marked in expanded EEG montage according to the 10–20 system. Remontaging assists in distinguishing epileptic seizures from artifacts. Video monitorings were also evaluated with simultaneous EEG recordings to define seizure semiology and awakening. The onset of semiology was noted on EEG. The first event related to a seizure, whether EEG or semiological changes, was regarded as seizure onset. Seizures with unclear ictal EEG onsets and ictal behavioral changes were not included. Intrusion of sustained alpha activity over 50% of epoch was defined as wakefulness [18,19]. In video recordings any behavior unrelated to seizure semiology or sleep including eye opening was also noted. That onset of awakening was marked on EEG.

The seizures were classified in two groups for analyzing the duration between onset of awakening and ictal beginning. In group 1 the seizure onsets were recorded before awakening, while in group 2 the awakening preceded the seizure onsets.

2.2. Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 16.0). An independent samples *t* test was used for continuous variables. Patients with TLE and FLE were compared for occurrence of seizures in which stage of sleep by Mann–Whitney's *U* test. The duration between awakening and seizure

Table 1
Demographic features of 25 patients with FLE or TLE, and having seizures during sleep.

Patient	Gender	Age (year)	Age onset of the seizures (year)	Antiepileptic drugs	Risk factors for epilepsy	Type of epilepsy
Patient 1	F	17	5	LVT, CBZ	–	FLE
Patient 2	F	21	18	LVT, OXC	FS	TLE
Patient 3	F	25	18	LVT	–	TLE
Patient 4	M	57	25	CBZ, LMG, LVT,	FS, Trauma	TLE
Patient 5	M	20	8	CBZ, P	Trauma	FLE
Patient 6	F	34	7	VPA, LMG, OXC	–	TLE
Patient 7	F	20	3	LVT, CBZ	–	FLE
Patient 8	F	18	15	VPA, LVT	FS	TLE
Patient 9	F	30	10	LVT, OXC	–	TLE
Patient 10	F	23	17	LVT, OXC	FS	TLE
Patient 11	F	58	7	CBZ		FLE
Patient 12	M	25	6	LVT, OXC, LMG	FS	TLE
Patient 13	M	20	14	CBZ	Trauma	FLE
Patient 14	F	27	24	LVT	–	FLE
Patient 15	M	31	1	CBZ	FS	TLE
Patient 16	F	21	17	CBZ, LVT	Trauma	TLE
Patient 17	F	29	18	LVT, TPM	Trauma	TLE
Patient 18	M	17	17	LVT, TPM	FS	TLE
Patient 19	F	37	22	CBZ, LVT	Family history	TLE
Patient 20	M	34	21	OXC, VPA, TPM	–	TLE
Patient 21	M	17	1	CBZ, LVT	Family history	FLE
Patient 22	M	23	13	LVT, CBZ	–	TLE
Patient 23	F	44	28	CBZ, LVT	–	TLE
Patient 24	F	23	11	CBZ, LMG	–	FLE
Patient 25	M	18	7	CBZ, LVT	Family history	TLE

M:Male, F:Female, FS:Febrile seizure, CBZ:Carbamazepine, OXC: Oxcarbazepine, VPA:Valproic acid, TPM:Topiramate, LVT:Levetiracetam, LMG: Lamotrigine, TLE:Temporal lobe epilepsy, FLE:Frontal lobe epilepsy.