Epilepsy & Behavior 50 (2015) 14–17

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

Gender and age influence in daytime and nighttime seizure occurrence in epilepsy associated with mesial temporal sclerosis

Valmir Passarelli *, Luiz Henrique Martins Castro

Department of Neurology, Hospital das Clinicas, Sao Paulo University, Sao Paulo, Brazil

ARTICLE INFO

Article history:
Received 3 February 2015
Revised 3 April 2015
Accepted 17 May 2015
Available online xxxx

Keywords:
Gender
Age
Mesial temporal lobe epilepsy
Seizures
Circadian

ABSTRACT

Objectives: The aim of this study was to analyze the daytime and nighttime seizure distribution during video-EEG monitoring in patients with epilepsy associated with unilateral mesial temporal sclerosis (MTS) and the role of gender, age, and lesion side on 24-hour seizure distribution.

Methods: We studied 167 consecutive adult (age ≥ 16 years) patients with epilepsy associated with unilateral mesial temporal sclerosis that had three or more recorded seizures during continuous video-EEG monitoring with a minimum recording time period of 24 h. Seizure onset time was classified according to occurrence in six 4-hour periods.

Results: Seven hundred thirty-five seizures were evaluated. We observed two higher seizure occurrence periods: 08:01–12:00 ($p = 0.001$) and 16:01–20:00 ($p = 0.03$). Significantly fewer seizures were observed between 0:01 and 4:00 ($p = 0.01$). Nonuniform seizure distribution was noted in women ($p < 0.0001$), in young patients (less than 45 years of age) ($p < 0.0001$), and in both patients with left ($p = 0.03$) and patients with right mesial temporal sclerosis ($p = 0.008$). Men presented uniform seizure occurrence distribution ($p = 0.15$). Women had fewer seizures than expected and fewer seizures than men between 0:01–04:00 ($p < 0.0001$ and $p = 0.0015$, respectively) and 04:01–08:00 ($p = 0.01$ and $p = 0.03$, respectively). Young patients (age < 45 years) had two seizure occurrence peaks, 08:01–12:00 ($p = 0.016$) and 16:01–20:00 ($p = 0.004$). Middle-aged/old patients (≥45 years) had only one seizure occurrence peak, 08:01–12:00 ($p = 0.012$). Young patients had more seizures than middle-aged/old patients between 16:01–20:00 ($p = 0.04$). No differences were noted between left and right MTS.

Significance: We observed two seizure occurrence peaks: morning and late afternoon/evening. We encountered variations in daytime and nighttime seizure distribution according to gender and age, but not according to side of MTS. Future studies are needed to confirm these findings and to unravel the neurobiological substrate underlying daytime and nighttime variations of seizure occurrence in different age groups and between genders.

1. Introduction

Unpredictability is a dangerous and distressing feature of epileptic seizures. Identification of triggers and patterns of seizure recurrence may allow antiepileptic drug regimen adjustments and adoption of nonpharmacological measures that may help in preventing seizures or minimizing harm and distress associated with seizures [1].

Circadian distribution of seizures is not random: increased and decreased seizure frequency periods are well established in different epilepsy types. Juvenile myoclonic epilepsy is characterized by greater seizure occurrence on waking periods [2], while frontal lobe epilepsies are associated with nocturnal seizures [3].

Circadian rhythms are regulated by complex neuroendocrine interactions influenced by individual characteristics, such as age and gender. Circadian variations in neuronal and endocrine activity may help to explain daytime and nighttime variations of seizure occurrence. A better understanding of the complex regulation of circadian rhythms may help in unraveling factors underlying variability of 24-hour seizure occurrence according to epilepsy type [4].

Afternoon peak of seizure occurrence has been described in temporal lobe epilepsy [5]. Variations according to gender, age, and side of the epileptogenic focus have not been reported, possibly because of inconsistencies in data analysis and insufficient sample sizes.

We analyzed the circadian distribution of seizures during video-EEG monitoring in patients with epilepsy associated with unilateral mesial temporal sclerosis (MTS), and we also evaluated the role of gender, age, and side of the epileptogenic focus on seizure occurrence pattern.

2. Methods

2.1. Subjects

We reviewed the video-EEG monitoring database in our institution in a 10-year period (2004–2014) to identify all consecutive adult

* Corresponding author at: Rua Alves Guimarães, 434 Apto 51, CEP 05410-000, Brasil. Tel.: +55 11 9633 8439 (mobile).
E-mail address: valmirpas@ig.com.br (V. Passarelli).

http://dx.doi.org/10.1016/j.yebeh.2015.05.028
1525-5050/

(age ≥ 16 years) patients with epilepsy associated with MRI-diagnosed (1.0 T or higher) unilateral mesial temporal sclerosis. Patients with dual pathology were not included. We selected patients with three or more recorded seizures during continuous video-EEG monitoring with a minimum recording time period of 24 h.

2.2. Data acquisition

In our tertiary epilepsy center, video-EEG monitoring is carried out continuously over many days. Patients are constantly monitored with EEG and video, supervised by experienced nurses. At least one clinical neurophysiologist analyzes all monitoring data. Seizure semiology and EEG description of sleep or awake state, seizure duration, and time of seizure onset are noted in all seizures. All patients included in the study underwent prolonged noninvasive video-EEG monitoring (Natus-Bio-logic, 32 channels, San Carlos, CA, USA). Electrodes were placed according to the 10–20 system, with additional anterior temporal and subtemporal electrodes.

2.3. Data analysis

Sleep and wakefulness state and seizure onset time were noted in all seizures. Seizure onset time was classified according to the occurrence in the following time periods: 0:01–04:00, 04:01–08:00, 8:01–12:00, 12:01–16:00, 16:01–20:00, and 21:00–0:00. We analyzed the patient's age at the time of hospital admission (young: <45 years; middle-aged or old: ≥45 years), gender, and mesial temporal sclerosis side (left or right).

Antiepileptic drug (AED) schedule and tapering and patient's activity level could not be controlled for, because changes to medication regimens and activity levels were individualized according to the physicians' decisions.

Antiepileptic drug use on admission was characterized by the number of current total and sedative AEDs (barbiturates, benzodiazepines, and topiramate). Antiepileptic drug loads were calculated with the following formula: AED1 / sAED1 + AED2 / sAED2…AEDn / sAEDn = AED load. The numerator represents total daily AED dose, and the denominator represents a standard AED dose [6]. Adopted standard AED doses were as follows: phenobarbital = 100, phenytoin = 300, carbamazepine = 600, oxcarbazepine = 900, valproate = 750, clobazam = 15, clonazepam = 2, topiramate = 200, primidone = 250, lamotrigine = 200, and gabapentin = 900.

The number of seizures experienced by each patient was analyzed with Rosner's extreme studentized deviate test for multiple outlier detection (significance level: $p < 0.05$). Outliers were excluded from the study.

Seizure occurrence according to time periods in the total sample and in each group was tested for nonuniformity with χ^2 statistics. Nonparametric binomial test was used to test if numbers of seizures in each of the six time periods were significantly different from the expected. Initially, the total sample was tested; then, distribution according to gender, MRI laterality (left; right), and age (young; middle-aged/old) were evaluated. Between-group comparisons were performed with the z-test. Significance was established at p-values < 0.05.

3. Results

One hundred seventy-two patients fulfilling study criteria were identified. Five patients were considered outliers and were, therefore, excluded. Thus, 167 patients were studied, 77 men (46.1%), mean age 38.5 ± 11.3 years, 84 (50.9%) with left mesial temporal sclerosis. Seven hundred thirty-five seizures were evaluated, with a mean of 4.4 ± 1.5 seizures per patient. Women had proportionally more seizures during wakefulness than men (Table 1).

Nonuniform seizure distributions within the 24-hour period were noted in the total sample ($p < 0.0001$), in women ($p < 0.0001$), in young patients ($p < 0.0001$), and in both patients with left ($p = 0.03$) and patients with right mesial temporal sclerosis ($p = 0.008$), but not in men or in patients aged 45 or more years.

We observed two periods of higher seizure occurrence: 08:01–12:00 and 16:01–20:00. Additionally, patients had significantly fewer seizures in the period between 0:01 and 4:00 a.m. (Fig. 1).

Men and women had more seizures in the 16:01–20:00 period. Women also had more seizures in the 08:01–12:00 period. Women had significantly fewer seizures in the 0:01–04:00 and 04:01–08:00 periods (Fig. 2).

Young patients had the same seizure occurrence profile as that of the total sample. Seizure occurrence in patients 45 years or older did not deviate from the uniform distribution, according to χ^2 analysis. However, when taking succession of time periods and binomial test analysis into account, patients aged 45 years or older seemed to follow a unimodal distribution of seizures, with an 8:01–12:00 peak. Age group comparisons showed that that the middle-aged/old (≥45 years) group had proportionally fewer seizures in the 16:01–20:00 period (Fig. 3). Appendix A demonstrates day/night seizure distribution according to age grouping by every 10 years (16–25; 26–35; 36–45; 46–55; 56 or more).

Patients with left and right MTS showed no difference in day/night seizure distribution (Fig. 4).

4. Discussion

The influence of daytime and nighttime patterns of distribution and sleep state on epileptic seizure occurrence is well recognized, with description of predominately diurnal or nocturnal epileptic seizures [7]. Twenty-four-hour distribution of focal-onset seizures is influenced by the seizure onset region [8]. Gender or age has not been previously associated with daytime and nighttime seizure distribution.

Afternoon seizure peak and predominant seizure occurrence during wakefulness have been reported in epilepsy associated with mesial temporal sclerosis [5,7]. Higher seizure occurrence in the periods 7:00–10:00 and 16:00–19:00 has been reported [7], a finding that is in

Table 1
Demographic and video-EEG monitoring data test results for 167 patients with unilateral MTS.

n = 167	Women (n = 90)	Men (n = 77)	p	Total sample
Age median (95% CI)	38.5 (36.2–40)	38 (34.4–43)	0.43	38 (37–40)
Left MTS n (%)	41 (45.7)	44 (57.0)	0.18	85 (50.9)
Number of seizures n (%)	386 (52,5)	349 (47,5)	0.17	735
Awake seizures n (%)	316 (81.8)	255 (73)	0.004	571 (77.7)
Seizure duration — seconds median (95% CI)	80.8 (55.3–105.4)	63 (48.9–82.2)	0.25	67.6 (56.9–96.1)
Generalized seizures n (%)	58 (15.0)	47 (13.4)	0.63	105 (14.3)
Number of AEDs median (95% CI)	3 (2–3)	3 (2–3)	0.76	3 (2–3)
AED load median (95% CI)	1.5 (1.3–1.6)	1.4 (1.3–1.6)	0.68	1.5 (1.3–1.5)
Sedative AED load median (95% CI)	1.3 (1.1–1.6)	1.3 (0.7–1.4)	0.33	1.3 (1.1–1.3)

Legend. n: Number of patients; CI — confidence interval; AED: antiepileptic drug; MTS: mesial temporal sclerosis.