



Predominantly nocturnal seizures post temporal lobectomy: Characteristics of an unusual outcome group

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ARTICLE INFO

Keywords:

Epilepsy surgery
Seizure outcome
Temporal lobe epilepsy
Hippocampal sclerosis

ABSTRACT

Purpose: To describe the characteristics of a patient group who, after temporal lobectomy for predominantly diurnal seizures, experience a postoperative conversion from diurnal to predominantly nocturnal seizures, and compare this group to those who continue to have a diurnal seizure pattern postoperatively.

Methods: From a cohort of 470 surgical cases with long-term follow-up, we retrospectively identified 16 patients with a predominantly nocturnal seizure pattern, including five with nocturnal seizures only (median follow-up 21 years) and compared them with 20 predominantly diurnal seizure patients.

Results: Sustained postoperative improvement in seizure frequency was observed in 14/16 cases. Seizure recurrence after surgery occurred within the first postoperative year in 13/16 cases. In all but 3 cases the seizures were all predominantly nocturnal from the time of recurrence, whereas in 3 there was a period of diurnal seizures during the early postoperative years. One patient lapsed back to diurnal seizures after 16 years of predominantly nocturnal seizures. Compared to the predominantly diurnal group, these patients had a significantly later age at seizure onset and were older at the time of surgery.

Conclusion: Patients with predominantly nocturnal seizures comprise a small but distinct post-operative outcome category. Although not formally assessed, this outcome appears associated with improved quality of life, such as with eligibility to drive, with 50% of the sample confirmed as driving. This finding may help with providing prognostic information and counseling to these patients when they are identified postoperatively.

1. Introduction

The effectiveness of anterior temporal lobectomy (ATL) for patients with refractory mesial temporal lobe epilepsy (MTLE) has been well established (Engel et al., 2012; Wiebe et al., 2001). Initial seizure freedom is achieved in about 65% of cases (Wiebe et al., 2001), reducing to 40% after 10 years (McIntosh et al., 2004). Of those who have persisting seizures, a subgroup develops a new seizure pattern with 'nocturnal seizures only' occurring postoperatively, a change from predominantly diurnal seizures pre-operatively. This is recognised in Engel's Classification of postoperative outcome – Engel Class IID (Engel, 1987), and has previously been reported (Faught and Kuzniecky, 1995; Hennessy et al., 2000), though not examined in detail.

We aim to describe the evolution in seizure patterns and clinical characteristics of a patient group who develop a new and long-lasting pattern of predominantly or exclusively nocturnal seizures following temporal lobectomy.

2. Methods

2.1. Procedure

Patients were selected from a consecutive series of 470 cases who underwent anterior temporal lobectomy surgery at the Comprehensive Epilepsy Program at Austin Hospital between 1st Jan 1978 and 1st Jan 2007. Patients were excluded if they had more than one operation.

The pre-operative investigation procedures and surgery have been described previously (Berkovic et al., 1995). Routine post-operative review comprised periodic clinical consultation with a neurologist and neuropsychologist for the first two years (Wilson et al., 1998). Following this, patient epilepsy data was obtained from either ongoing consultations at the Austin, information from other neurologists and relevant health professionals external to the Austin, or 2 yearly telephone interviews with an epilepsy nurse when the former data sources were not available (Bladin, 1992). Data was collected by reviewing patient medical records. These records were prospectively maintained, although the particular samples for this study were identified and

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analysed retrospectively.

2.2. Patients with diurnal-to-nocturnal change

We identified patients who experienced a change from predominantly diurnal seizures to predominantly nocturnal seizures post-operatively. We defined this group as those whose pre-operative seizure pattern was > 90% daytime seizures for a minimum of five consecutive years immediately preceding surgery, but post-operatively developed a pattern of approximately > 80% nocturnal seizures which persisted for a minimum of five consecutive years at any time postoperatively. For those that had rare diurnal attacks the exact proportion was hard to estimate accurately, as it depended on patient or family report. In these cases, frequency of diurnal seizures was approximated by descriptions in medical records such as occurring 'rarely,' which was sufficient for this study. From 470 temporal lobe surgery cases, 17 patients fulfilled these criteria. One patient with chronic co-morbid alcohol excess and irregular post-operative follow up was excluded, leaving 16 patients (8 males) with reliable data for analysis, comprising 3.4% of the total cohort.

We described the diurnal-to-nocturnal change in this group detailing the timing of postoperative seizure recurrence and its persistence over time. We additionally documented the semiology of witnessed postoperative seizures. Engel's classification was used to describe postoperative outcome (Engel, 1987).

To visually represent changes in status over time, we assessed outcome in two-year epochs after surgery.

2.3. Comparison with patients who had no change in seizure pattern

We compared the group with predominantly nocturnal post-operative seizures with patients from the same cohort who did not experience this change. We defined this comparison group, hereafter referred to as 'predominantly diurnal' as those who had > 90% daytime seizures preoperatively, and continued to experience this pattern for a minimum of five consecutive years at any time postoperatively. The first 20 patients matching these criteria were consecutively selected from the surgical database.

The two patient groups were examined for differences in clinical variables: sex, history of febrile seizures, presence of convulsive seizures preoperatively, age at seizure onset, age at operation, duration of pre-operative epilepsy, resection side, histopathology, and seizure frequency pre and post-operatively. Histopathology specimens had been reviewed by one pathologist and coded, as for our previous study (Berkovic et al., 1995).

2.4. Statistical analyses

Comparisons between the predominantly nocturnal group and predominantly diurnal seizure groups were made using the Mann-Whitney U test for age at seizure onset, age at operation and duration of pre-operative epilepsy.

The remaining variables were categorical and analysed using either a Fisher's Exact Test or a Pearson's Chi Square test. A significance level of 0.05 was used for all tests.

3. Results

Sixteen predominantly nocturnal seizure patients were identified, comprising 3.4% of our total cohort. Eleven (69%) had at least weekly seizures preoperatively, with bilaterally convulsive seizures in 9/16 (56%). All underwent a standard anterior temporal lobectomy (ATL) (Berkovic et al., 1995), and 15/16 (94%) had hippocampal sclerosis.

Median duration of post-op follow up was 21 years (interquartile range 14.75–22 years, range 10–31 years). Post-operatively, most nocturnal seizure patients experienced a sustained improvement in

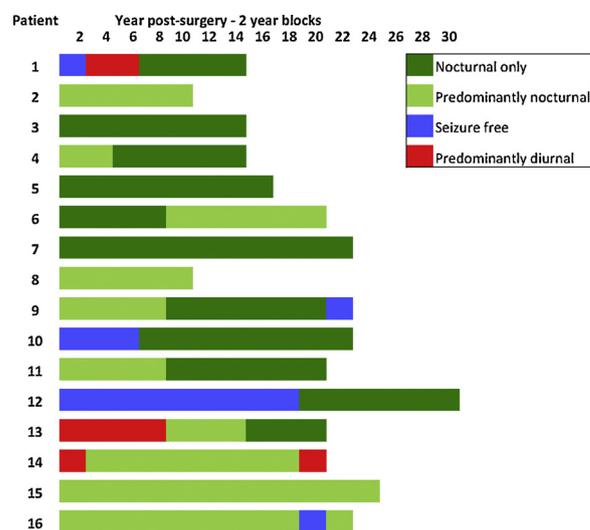


Fig. 1. Postoperative seizure characteristics for nocturnal seizure group.

seizure frequency. At the time of last follow-up, 14 patients (87%) were having monthly seizures or less, with one of these being seizure free.

3.1. Postoperative seizure recurrence and evolution of predominantly nocturnal pattern

Post-operative seizure patterns are illustrated in Fig. 1. Recurrence occurred within 12 months of surgery in 13/16 cases (81%). Patients 1, 10, and 12 experienced an initial seizure free interval of 2–18 years.

Most patients (13/16) had nocturnal seizures from the time of initial seizure recurrence. In patients 1, 13 and 14, there was a period of diurnal seizures before the nocturnal seizure pattern became established. However, one patient returned to diurnal seizures after 16 years of predominantly nocturnal seizures. Five patients had no daytime seizures throughout the entire follow-up period.

In 11/16 patients (69%), the patients had a bed partner who gave a witness description of their seizures. In 12/16 patients, they experienced both focal impaired awareness seizures and bilateral tonic-clonic seizures. The remaining four patients had focal impaired awareness seizures alone. For the five cases sleeping alone, bilateral tonic-clonic seizures were inferred from a history of a bitten tongue, incontinence, post-ictal myalgia or exhaustion.

Among the 16 nocturnal seizure patients, nocturnal only or predominantly nocturnal seizures persisted for a median duration of 16 years from the time of surgery to the last follow-up (IQR 13–20.2 years, range 8–24 years). At the last follow-up only one had lapsed back to diurnal seizures in the context of significant neuropsychiatric difficulties and with some non-compliance with medication. In the previous 12 months from last follow-up, 5 patients had no seizures, 7 had seizures monthly or less and 4 had seizures more than monthly. The median number of anti-epileptic drugs at last follow-up was two.

3.2. Comparison with 'Predominantly diurnal' seizure group

The predominantly diurnal group had a similar median duration of postoperative follow-up of 21 years (IQR = 18–26 years, range 7–29 years). Preoperative characteristics of the two groups (Table 1) were comparable in terms of demographics and risk factors known to influence postoperative outcome (presence of febrile seizures, convulsive seizures, and histology). There was a difference in resection side between the groups, with most temporal resections in the nocturnal seizure group being right sided.

Mean age at seizure onset for the predominantly nocturnal seizure group was over 10 years older than the predominantly diurnal group

Table 1

Preoperative characteristics of the nocturnal versus diurnal seizure groups.

	Nocturnal sz		Diurnal sz	p-value
	n (%)	n (%)	n (%)	
Male	8 (50)	6 (30)		0.12**
Febrile sz	5 (31)	8 (40)		0.73*
Convulsive sz	9 (56)	17 (85)		0.12*
Sz frequency	daily	3 (19)	2 (10)	} 0.92**
	weekly	12 (75)	12 (60)	
	monthly	1 (6)	6 (30)	
Resection side	Right	10 (62)	4 (20)	0.01*
Histology	HS	15 (94)	16 (80)	0.45*
	NSP	1 (6)	3 (15)	
	FTL	0	1 (5)	
TOTAL	n	16	20	
mean (IQR),range				
Age sz onset	15.7(3-27), 1-35	6.0(1.4-7.5), 0.7-21		0.01
Duration preop epilepsy	22.9(16-28.5), 5-42	21.8(14.7-25.7), 18-26		0.99
Age surgery	37.6(28-45), 16-50	27.8(22.5-32), 16-46		0.01

*Fisher's exact.

**Pearson's Chi Square.

HS = Hippocampal sclerosis.

NSP = No specific pathology.

FTL = Foreign tissue lesion.

(15.7 vs 6 yrs, $p = 0.01$). Associated with this was an older age at surgery for the predominantly nocturnal group (37.6 vs 27.8 yrs, $p = 0.01$). Duration of pre-operative epilepsy did not differ between the groups.

4. Discussion

This retrospective study was borne out of the clinical observation that a proportion of patients experience 'nocturnal only' seizures post temporal lobectomy. This is not only of neurobiological interest, but is clinically relevant as a freedom from diurnal seizures may confer psychosocial benefits such as permission to drive in many countries (Drazkowski, 2007). Conversely, it is widely known that nocturnal convulsive seizures carry an increased risk of SUDEP (Van der Lende et al., 2018).

We identified 16 such cases within a cohort of 470 subjects who had undergone temporal lobe resection for refractory seizures. This supports the value of the Engel category IID indicating such an outcome (Tonini et al., 2004). Our cohort has an advantage of regular and very long-term follow-up compared to other comprehensive epilepsy programs (McIntosh et al., 2004; Mihara et al., 2018), allowing for capture of changing seizure patterns over time.

A methodological issue is that, even with our prospective 2 yearly follow-up, it was difficult to be sure that all night time seizures were in sleep. Moreover, some patients had rare seizures in wakefulness, often with a trigger such as unusual stress or illness. Further, with a strict definition of nocturnal "only", the longer the follow-up, the greater attrition in this group, as one diurnal seizure will disqualify the case from that group. We therefore chose to include cases that were 'predominantly nocturnal' rather than just 100% nocturnal. At least within this group, representing 3.4% of our cohort, the pattern was maintained long term, in 15/16 patients. Two cases begun with a period of diurnal seizures, and three begun with seizure freedom, after which the

nocturnal pattern was established. From the three that begun with seizure freedom, one case had 2 years of seizure freedom followed by a period of diurnal seizures, before nocturnal seizures became established.

The factors determining a 'nocturnal only' outcome are unclear. In comparison to the 'diurnal group', we found a later age of seizure onset, a later age at surgery, more right sided resections, and a non-significant trend for a lower proportion of cases with pre-operative convulsive seizures. These observations suggest that the nocturnal only group have an intrinsically different and potentially less severe epilepsy. Sleep is a well-known activator of focal seizures. If the nocturnal only group is indeed intrinsically less severe, they might be regarded as having 'controlled diurnal' seizures, yet nocturnal seizures occasionally recur. Indeed there is a recognized group of 'nocturnal only' temporal lobe epilepsy (Bernasconi et al., 1998). The predominance of right-sided resections was a surprise - this could be a surrogate for the more extensive removals done on the non-dominant hemisphere.

Limitations of the study include the small sample. Additionally, as with most studies involving patient recollection and reporting of events, a reliance on patient awareness and recall of seizures may tend to underestimate the number of seizures actually occurring. If the seizure was recorded in a diary soon after it was identified, this may reduce the rate of forgetting. However, patients with frequent seizures are unlikely to maintain such a diary over the long-term due to the effort required. In addition, there can be uncertainty of the occurrence (either missed or a false positive) of an unwitnessed nocturnal seizure when the seizure is inferred based on the patients postictal symptoms the following morning. When the patient does not have a nighttime observer, portable and compact (e.g. wrist-watch) electronic seizure detection and recording devices may be of assistance in more accurately recording convulsive seizures. Compared to nocturnal convulsive seizures, a nocturnal focal seizure may be harder to identify by a witness, and may have fewer postictal symptoms the next morning for the patient, making them more likely to be missed.

Predictors of seizure freedom have been intensively investigated, but remain somewhat controversial, with inconsistencies between studies (Jobst and Cascino, 2015; McIntosh et al., 2004; Tonini et al., 2004). They have not been studied within sub-categories of patients with post-operative seizure recurrence. More attention to this may be warranted as the 'nocturnal seizures only' outcome may be of relevance to psychosocial outcome as our strong, but unmeasured, impression is that these patients have improved quality of life, including the ability to drive. If post-operative nocturnal seizure outcome can be predicted or identified early post-operatively, this may allow for greater prognostic information for neurologists and associated patient counselling.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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