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## The utility of prolonged outpatient ambulatory EEG

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### ABSTRACT

**Purpose:** ILAE guidelines recommend the use of prolonged EEG where the diagnosis of epilepsy or the classification of the seizure syndrome is proving difficult. Due to its limited provision, video EEG monitoring is unavailable to many patients under investigation<sup>1</sup>. The aim of this study was to examine the utility of the alternate investigation of outpatient ambulatory EEG.

**Methods:** In this retrospective study we analysed 324 consecutive prolonged outpatient ambulatory EEGs lasting 72–96 h (4–5 days), without medication withdrawal. EEG data and the clinical record were reviewed to investigate the utility of the investigation.

**Results:** Of 324 studies: 219 (68%) studies gave positive data, 116 (36%) showed interictal epileptiform discharges (IEDs), 167 (52%) had events. 105 (32%) studies were normal. Overall 51% of studies changed management of which 22% of studies changed the diagnosis and 29% of studies refined the diagnosis by classifying the epilepsy into focal or generalised.

**Conclusion:** The present study confirms the diagnostic utility of outpatient ambulatory EEG in the diagnosis of paroxysmal events.

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### 1. Introduction

Many authors have discussed the importance of correct diagnosis and electro-clinical classification in epilepsy in order to prognosticate and utilise antiepileptic medication appropriately. A clinical diagnosis of epilepsy is found to be incorrect in up to 30% of patients.<sup>2,3</sup> The common differential diagnoses of syncope and psychogenic non epileptic attacks (PNEA) are notoriously hard to diagnose, even the witnessed semiology can be misleading.<sup>4,5</sup>

A single 20-min duration routine EEG shows abnormalities in as few as 30–50% of patients with epilepsy. Repeated 20 min studies can increase the yield to 60–70%.<sup>6,7</sup> A sleep EEG after an initial negative routine EEG has been shown by several groups to reveal IEDs in an additional 24–34% of patients.<sup>8</sup> Most studies have concluded that 10% of patients with epilepsy will not show IEDs despite repeated testing with repeated EEG modalities.<sup>9</sup> Before confirmation of diagnosis or correct classification the patient may be on inappropriate medication. There may also be a psychological and financial cost of an incorrect diagnosis in emergency

department attendances, hospital admissions or in sick leave from work.

The ILAE recommends long term EEG monitoring where there is diagnostic uncertainty as to the diagnosis of epilepsy, in confirmed epilepsy in order to classify the epilepsy syndrome, quantify seizures or diurnal and circadian patterns, and to document the electro-clinical basis of seizures prior to epilepsy surgery.<sup>1</sup> The majority of the literature on long term monitoring concentrates on inpatient video EEG monitoring in epilepsy surgery cohorts with severe epilepsy in whom drug withdrawal is carried out. Due to its limited provision, video EEG monitoring is unavailable to many patients under investigation.

The alternate investigation of prolonged outpatient ambulatory EEG is a relatively recent inception as the technology to allow for portable devices only became commercially available in 1979. Outpatient ambulatory EEG does not allow direct observation of the semiology of an event, nor does it provide a safe environment for drug reduction. Where these factors are not relevant, enabling patients to be investigated at home with exposure to their typical seizure provoking factors, make outpatient ambulatory EEG an attractive option.

Initial reports on 4 and 8 channel montages confirmed the reliability and utility of the modality.<sup>10–13</sup> More recently studies have reviewed the utility of computer assisted ambulatory EEG with 1–2 days of monitoring.<sup>14,15</sup> There have been no studies on modern ambulatory EEG units with 32-channel capability for

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continuously recording a standard 10–20 montage together with channels for reference, ground and ECG for prolonged periods at sampling rates and quality comparable to inpatient video EEG recordings. In this study we aim to characterise the utility of outpatient ambulatory EEG in the investigation of paroxysmal events.

## 2. Methods

In this retrospective study we analysed 324 consecutive patients who underwent outpatient ambulatory EEGs, lasting 72–96 h, performed between 2007 and 2010, at the Royal Prince Alfred Hospital in Sydney Australia where clinical follow up data (from subsequent outpatient review) was available.

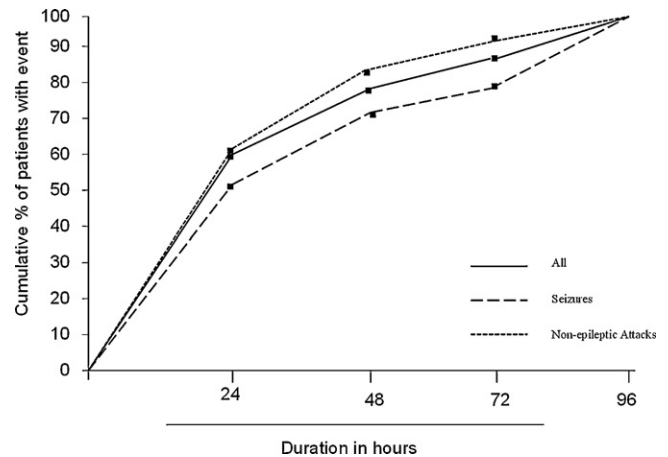
EEG and ECG data was acquired using the ProFusion ambulatory digital 32-channel EEG system (Abbotsford, Australia) using the standard 10–20-electrode placement. The system has a patient activated event button. All patients were recorded as outpatients. Each patient was recorded once for between 72 and 96 h. Patients kept a diary of clinical events and witness accounts and returned once every 24 h for electrode care, data download and battery change. No home video was recorded. No patients underwent drug tapering or withdrawal. The EEG was analysed independently page-by-page by 2 EEG trained neurologists for the presence of interictal EEG abnormalities and for EEG changes during events. The epileptiform discharges and epileptic seizures were classified as focal with or without secondary generalisation or generalised as typical for symptomatic generalised epilepsy or primary generalised epilepsy.<sup>16</sup> The patients' clinical record was analysed for pre test diagnosis, indication for test (diagnosis, classification and seizure frequency), post-test diagnosis and change of management, age, sex, and age at first seizure, seizure frequency, antiepileptic drug use and MRI results.

Epilepsy duration (years) and latency to IED (minutes) were log-transformed to remove skewness, thus achieving approximate normality of these analyses. Determinants of "recording an event", "new information" and "seizure" were estimated using univariate and multivariate logistic regression models. Determinants of "latency to events" were ascertained by an analysis of covariance (ANCOVA). All of the data were analysed with SAS version 9.2 (SAS Institute).

## 3. Results

We reviewed 324 consecutive patients undergoing 5-day ambulatory EEG between 2007 and 2010 where clinical follow up data was available. There were 192 (60%) females, 132 (40%) males with a mean age of 39 years (range 12–79). 195 were on antiepileptic drugs and 129 were not. 81 had abnormal MRI scans (including hippocampal sclerosis, gliosis following head injury or brain resections), 210 had normal MRI scans and in 33 the results of MRI were not available. The mean duration of symptoms (since the first event) at time of monitoring was 12 years (range 1–64 years, mode 1 year). The frequency of events reported by patients showed a mean of 10 per month. The indication for the ambulatory EEG was diagnostic in 193 (60%), classification of epilepsy in 96 (30%) and to confirm the frequency of subclinical seizures in 35 (10%). The provisional diagnosis was epilepsy in 210 (65%), a non-epileptic diagnosis in 109 (35%).

**EEG results:** Of the 324 studies, 219 (68%) of EEG studies gave positive data (EEG abnormalities and/or events). 105 (32%) of EEG studies were normal (neither EEG abnormalities nor events). Of the 324 studies: 122 (38%) showed evidence for epilepsy, 116 (36%) showed IEDs, 52 (16%) had IEDs but no epileptic seizures, 6 (1.9%) had epileptic seizures but no IEDs and 64 (20%) had IEDs and typical events. Of the 64 studies with IEDs and typical events, 45



**Fig. 1.** The latency to recording events (in the 167 of 324 patients who had events). Data expressed as percentages of patients who had any event (black line), seizures (blue line) or non epileptic attacks (red line) against time in hours from onset of recording.

(70%) showed epileptic seizures and IED, 15 (23%) showed both PNEA and IEDs and 4 (7%) showed both PNEA and epileptic seizures and IEDs.

167 (52%) had typical events. On the basis of witness accounts and EEG interpretation of the 167 studies with events, 51 (31%) were epileptic seizures, 96 (57%) were PNEA, 4 (2%) had both PNEA and epileptic seizures and 16 (10%) were syncope.

We reviewed the latency to events observed within 96 h of recording (Fig. 1). For any event, irrespective of diagnosis, 58% were seen within 24 h, 78% within 48 h, 87% by 72 h and 100% by 96 h. Latency to recording epileptic seizures was 51% within 24 h, 70% within 48 h, 79% by 72 h and 100% by 96 h. Latency to recording PNEA was shorter: 60% within 24 h, 82% within 48 h, 92% by 72 h and 100% by 96 h although this did not reach statistical significance (ANCOVA).

**Clinical effect of EEG results:** Of the 324 studies, 146 (45%) confirmed the pre test diagnosis of epilepsy, syncope or psychogenic non epileptic attacks. 93 (29%) studies refined the diagnosis (by classifying the epilepsy as focal or generalised) and 85 (26%) studies changed the diagnosis. 16 (5%) diagnoses were changed from epilepsy to syncope, 51 (16%) diagnoses changed from epilepsy to psychogenic non epileptic attacks, 10 (3%) diagnoses were changed from PNEA to epilepsy and 4 (1%) patients had diagnoses changed from epilepsy to epilepsy and PNEA.

**Determinants of EEG results and clinical outcomes:** Determinants of recording an event vs. no event were analysed (Table 1). Multivariate analysis showed that a higher frequency of reported events and a test indication of classification of the epilepsy were the only significant determinants of recording an event during the study. No other factors were independent determinants.

Determinants of recording an epileptic seizure vs. PNEA (excluding other diagnoses such as syncope) were analysed (Table 2). Multivariate analysis found no pre-test patient factors could differentiate between the likelihood of recording epileptic seizures vs. PNEA. The indication for the test was the only significant determinant of recording epileptic seizure vs. non-epileptic event. Epileptic seizure was more likely if the indication was to classify epilepsy or to confirm the frequency of events. PNEA was more likely if the test indication was diagnostic.

Determinants of latency to recording an event (in days) were analysed. There were no pre-test factors that were significant determinants of latency. Multivariate analysis showed generalised epilepsy to have a shorter latency to seizures during monitoring. Whilst this was statistically significant the number of cases was

**Table 1**

Determinants of recording an event vs. no event were analysed using univariate and multivariate logistic regression models.

	Crude		Multivariate-adjusted	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Age (years) <sup>*</sup>	0.88 (0.71–1.08)	0.23	0.97 (0.67–1.41)	0.88
Sex (female vs. male)	1.28 (0.84–1.95)	0.26	1.00 (0.51–1.95)	0.99
Log of epilepsy duration (years) <sup>*</sup>	1.25 (0.97–1.61)	0.09	1.14 (0.80–1.63)	0.48
Reported frequency (vs. 0 per 28 days)				
0.4 per 28 days	3.96 (0.74–21.28)	0.11	0.58 (0.23–1.46)	0.25
1 per 28 days	8.44 (1.85–38.44)	0.006	0.99 (0.50–1.96)	0.99
4 per 28 days	14.24 (3.20–63.28)	0.001	1.15 (0.60–2.18)	0.68
10 per 28 days	24.73 (4.25–143.98)	0.0004	1.84 (0.55–6.17)	0.33
28 per 28 days	60.75 (13.36–276.17)	<0.0001	5.04 (2.56–9.92)	<0.0001
Lesion on MRI (yes vs. no)	1.81 (1.09–2.99)	0.02	1.68 (0.82–3.44)	0.15
Antiepileptic drug (yes vs. no)	1.16 (0.76–1.79)	0.49	1.12 (0.49–2.54)	0.79
Provisional diagnosis (vs. non-epilepsy)				
Epilepsy	0.88 (0.56–1.38)	0.57	1.58 (0.61–4.05)	0.34
Both epilepsy and non-epilepsy	4.30 (0.87–21.18)	0.07	4.26 (0.42–43.59)	0.22
Indication (vs. diagnosis)				
Classification	0.46 (0.28–0.73)	0.001	0.26 (0.10–0.63)	0.003
Frequency	1.47 (0.71–3.03)	0.30	1.79 (0.51–6.22)	0.36

<sup>\*</sup> odds ratio for continuous variables represent a difference of a SD (15.6 years for age and 1.26 for log-transformed epilepsy duration).

**Table 2**

Determinants of recording a seizure event vs. a non epileptic attack were analysed using univariate and multivariate logistic regression models.

	Crude		Multivariate-adjusted	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Age (years) <sup>*</sup>	1.13 (0.78–1.64)	0.51	0.48 (0.22–1.04)	0.06
Sex (female vs. male)	0.61 (0.30–1.22)	0.16	1.00 (0.28–3.55)	0.99
Log of epilepsy duration (years) <sup>*</sup>	1.62 (1.02–2.59)	0.04	0.92 (0.41–2.02)	0.83
Reported frequency (vs. 0 or 0.4 per 28 days) <sup>**</sup>				
1 per 28 days	4.33 (0.61–30.57)	0.14	0.16 (0.01–2.34)	0.18
4 per 28 days	0.87 (0.14–5.55)	0.88	0.35 (0.03–4.15)	0.40
10 per 28 days	1.00 (0.11–8.95)	0.99	0.29 (0.01–6.54)	0.44
28 per 28 days	0.65 (0.11–3.92)	0.64	0.99 (0.10–9.98)	0.99
Lesion on MRI (yes vs. no)	2.89 (1.36–6.13)	0.006	0.53 (0.15–1.88)	0.33
Antiepileptic drug (yes vs. no)	2.69 (1.20–6.00)	0.02	1.54 (0.32–7.33)	0.59
Provisional diagnosis (vs. non-epilepsy)				
Epilepsy	8.84 (2.93–26.65)	0.0001	0.84 (0.13–5.32)	0.85
Both epilepsy and non-epilepsy	5.12 (0.70–37.26)	0.11	0.76 (0.06–9.10)	0.83
Indication (vs. diagnosis)				
Classification	10.15 (4.20–24.55)	<.0001	0.13 (0.02–0.70)	0.02
Frequency	11.92 (3.88–36.61)	<.0001	0.07 (0.01–0.49)	0.008
Number of events recorded > median(3)	1.45 (0.72–2.90)	0.30	0.52 (0.13–2.11)	0.36
Latency to event (days) <sup>*</sup>	1.41 (1.01–1.97)	0.04	0.81 (0.41–1.61)	0.54

<sup>\*</sup> odds ratio for continuous variables represent a difference of a SD (15.6 years for age, 1.26 for log-transformed epilepsy duration and 1.05 for latency to event).

<sup>\*\*</sup> 0 and 0.4 were combined because event number was 0.

small. With non-epileptic events only the number of events recorded was a determinant of the latency to the first event.

*Financial costs of outpatient ambulatory EEG vs. inpatient video EEG:* In our unit we have compared the cost of outpatient aEEG with inpatient vEEG. In order to determine this we calculated the costs for staff wages, clinic or inpatient space, consumables and equipment depreciation. In our unit, inpatient video EEG costs \$948 (AUS) for each 24-h period. Outpatient ambulatory EEG costs \$237 (AUS) for each 24-h period. In our department, inpatient videoEEG therefore costs 4 times as much to perform.

#### 4. Discussion

We evaluated the utility of ambulatory EEG in the investigation of paroxysmal events. The present study shows that ambulatory EEG changed or refined the diagnosis in 51% of patients. Of those events recorded during a 96 h EEG, 58% were recorded within 24 h and 78% within 48 h.

Two previous studies have been performed on the utility of ambulatory EEG recorded for 1–2 days. Most recently a study on computer assisted ambulatory EEG in 502 patients showed 47% with events of which 13% were epileptic seizures and 87% non-epileptic.<sup>15</sup> Morris et al.<sup>14</sup> reviewed 344 patients with computer assisted EEG, recorded for a median duration of 1.4 days. Their study showed a 48% event rate: 20% of which were epileptic seizures and 80% non-epileptic. Overall their study reported a clinical usefulness of 75%. Our study shows similar rates of event detection although our ratio of epileptic seizures to non-epileptic events was much higher at 30%. This may reflect patient selection criteria, but also may reflect the advances in ambulatory EEG technology allowing for 32 channels over the previous 16 channels and thus a full standard 10–20 montage. Both the above studies recorded EEG for shorter periods than our study. As psychogenic non-epileptic attacks are overrepresented in the first 24 h this may also be a factor. From our data, 42% and 22% of first events would have been missed if the recording were for 24 or 48 h respectively.

Multiple studies on inpatient video EEG have characterised the diagnostic utility of video EEG although there has been no randomised comparison with ambulatory EEG. One study has looked at assessments with both video and ambulatory EEG carried out during an inpatient admission with drug withdrawal (patients may have had video EEG, ambulatory EEG or both) but the patients were not randomised.<sup>17</sup> Of 364 first EEG assessments, they described a change or refinement of diagnosis in 133 (37%) although many of their admissions were pre-surgical or for medication changes. Of those referred for diagnostic clarification, 71% had a change or refinement of the diagnosis. They calculated the duration of EEG required to change management as 78 h of ambulatory EEG and 60 h of video EEG. In another study of 131 patients where inpatient video EEG was recorded for a mean period of 5.6 days, events were recorded in 69%, and 43% showed interictal discharges.<sup>18</sup> In this video EEG study the diagnosis was altered or refined in 58% of patients, similar to the 51% in our study.

In our study, none of the pre test clinical variables were shown to be determinants of the type of event recorded. As would be expected, psychogenic non epileptic attacks were more likely if the test indication was diagnostic and epileptic seizures were more likely if the referring clinician requested the investigation for electroclinical classification of epilepsy. Many previous studies have failed to show patient factors that predict psychogenic non epileptic attacks over epileptic seizures.<sup>19</sup> Whilst there is an association with previous psychological life events this is not a reliable determinant and one must remember that both epilepsy and PNEA may coexist. For the present time we will have to rely on the outcome of EEG investigations to differentiate between these diagnoses.

Pre test clinical variables including the presence or absence of antiepileptic drugs and MRI results did not predict which patients would have a short latency to recording events ( $p < 0.05$  ANCOVA). The patients' reported frequency of events has been studied in both ambulatory and video EEG as a determinant of latency to events during monitoring. As in the present study, this has been shown to be a very poor predictor of latency to events during monitoring.<sup>20</sup>

Whilst there was a trend towards shorter latency to psychogenic non epileptic attacks, overall there was no statistically significant difference between the latency to events irrespective of the diagnosis. This is in contrast to other inpatient studies on psychogenic non epileptic attacks, which suggest a shorter latency to first event.<sup>21</sup> This difference may be due to the reported suggestibility of events in clinical situations such as a video-monitoring unit.<sup>22</sup> Multivariate analysis showed generalised epilepsy to have a shorter latency to seizures during monitoring. There were a small number of cases of generalised epilepsy and this group included some cases of symptomatic generalised epilepsy where frequent seizures were recorded which will skew the data. Overall 58% of events were seen within 24 h, 78% within 48 h, 87% by 72 h and 100% by 96 h. Therefore 22% of events were seen in the second half of a 96 h recording. This is in contrast to the latency to interictal epileptiform abnormalities. In this situation 95% of IEDs seen in a 96 h EEG will be seen in the first 48 h.<sup>23</sup>

There are limitations to our data set: we do not have data on the delay from the last seizure to EEG monitoring and although most patients will have undergone a 20-min routine EEG prior to referral to the epilepsy clinic we do not have this data. Both these factors may change the likelihood of detecting an event or an IED in epileptic patients. Furthermore, we are unable to confirm the increase in pick up of IEDs during a prolonged ambulatory EEG over a routine 20-min EEG. We have included a diverse group of patients in the study to reflect the range of patients investigated in a specialist epilepsy clinic.

The DMC Neurophysiology Subcommittee of the ILAE recommend the use of hospital based long term monitoring where the

diagnosis of epilepsy or the classification of the seizure syndrome is proving difficult.<sup>1</sup> This guidance also states that "ambulatory outpatient and community-based LTM may be used as a substitute for inpatient LTM in cases where the latter is not cost-effective or feasible or when activation procedures aimed at increasing seizure yield are not indicated."

There are innate limitations to outpatient ambulatory EEG recordings. The technique relies upon diary data and witness accounts of events to help interpret the EEG rather than objective video data. There may be occasions when the history and witness account suggest psychogenic non epileptic attacks and the EEG seizure is obscured by motor artefacts. Furthermore artefacts may be confused with IEDs or epileptic seizures by the less experienced observer. In these instances the correlation of video with EEG is essential. The use of home video recording to supplement outpatient ambulatory EEG has not been studied but may overcome some of these limitations. In general ambulatory EEG has been poorly studied given its widespread use in clinical practice. For example there are no studies directly comparing inpatient video EEG with outpatient ambulatory EEG and this represents an important future research direction.

## 5. Conclusion

Whilst video EEG will remain the gold standard for confirming the electrophysiology underlying a given event, this may be unnecessary for the initial diagnosis of paroxysmal events. The present study confirms the diagnostic utility of outpatient ambulatory EEG in the investigation of paroxysmal events. Given the limited provision and higher cost of inpatient video EEG, outpatient ambulatory EEG represents a practical initial investigation in the investigation of paroxysmal neurological events.

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