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Duration of electroencephalographic recordings in patients with epilepsy

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ABSTRACT

Purpose: Previous studies have demonstrated different diagnostic yields with electroencephalography (EEG). Due to the small sample sizes or different patient populations (outpatients or inpatients only) in these previous studies, the clinical use of routine EEG and outpatient/inpatient video-EEG monitoring (VEM) needs further clarification. In this study, we investigated EEGs obtained from patients referred by epileptologists; by comparing the results of different EEG methods, we sought to determine the optimal durations and specific types of EEG recordings for different clinical situations.
Methods: The data from 335 routine EEGs, 281 3 h outpatient VEMs, and 247 inpatient VEMs (>48 h) were reviewed. We analyzed the latency to the first epileptiform discharge or clinical event.
Results: In patients undergoing outpatient VEMs, 48% of the first epileptiform discharges appeared within 20 min, and 64% appeared within 30 min. In patients undergoing inpatient VEMs, 21.2% had their first attack within 3 h. The second peak of event occurrence was during the 33rd–36th h. Only 3.5% of the seizures were recorded after 57 h. The detection rate of epileptiform discharges was higher for 3 h outpatient VEM than for routine EEG (54.1% versus 16.4%, $p < 0.01$). Epileptic and/or nonepileptic events were recorded in 45.8% of the inpatient VEMs, the diagnostic yield of which was higher than for outpatient VEMs ($p < 0.01$). Since the patients in this study had been selected to limit the bias between each group, the diagnostic yield of EEGs in this study are likely to have been higher than those found in routine practice. Patients with generalized epilepsy had a shorter latency to the first epileptiform discharge compared to patients with localization-related epilepsy (mean, 22.1 min versus 33.9 min, $p < 0.05$).
Conclusions: Two-thirds of epileptiform discharges were detected within 30 min of VEM. A 30-min recording is recommended for routine EEG examinations that aim to detect epileptiform discharges. A 3 h outpatient VEM is a reasonable option when a routine EEG fails to detect epileptiform discharges. The latency to the first epileptiform discharge was shorter in patients with generalized epilepsy than in patients with localization-related epilepsy. 48 h of inpatient VEM might be adequate for detecting the target events.

1. Introduction

Electroencephalography (EEG), which remains the gold standard electrophysiological modality for obtaining diagnostic information in patients with epilepsy, helps to determine the syndrome, treatment, and prognosis of the epilepsy. Patients with seizures and generalized spike-wave complexes on EEG recordings have a recurrence rate of 58% at 5 years, but the risk decreases to 26% if they have nonepileptiform EEG.[1] However, initial routine EEGs in patients with epilepsy have a yield of only 29%–56%.[2–4] With subsequent EEGs, the yield can increase to 82%.[3] In contrast, 2.2% of individuals without epilepsy have been reported to have an epileptiform discharge on EEG.[5]

In a specialist clinic, the misdiagnosis of epilepsy in patients with refractory epilepsy can be as high as 26%.[6] Since the introduction of video-EEG monitoring (VEM), [7,8] its high diagnostic value in adult patients with recurrent seizures has been confirmed.[9–15] However, the use of long-term inpatient VEM is limited by its cost, the labor intensiveness of the trained personnel, and the lengthy duration of the monitoring. Several studies have demonstrated the effectiveness of prolonged outpatient VEM in adults.[16–18] Other studies have investigated the latency to the first interictal epileptiform discharge [19,20] in order to help determine the duration of EEG that is required for optimal diagnostic yield. However, some of these studies have had small sample sizes, some have focused only on the VEM yield in outpatients or inpatients,

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and others did not record the time to the first epileptiform discharge. In order to determine the optimal duration of an EEG examination for determining diagnoses, the present study examined data from 335 routine EEGs, 324281 3 h outpatient VEMs, and 247 long-term inpatient VEMs. We present a complete database of the different EEG methods and recommend specific types and durations of EEG recordings for different clinical situations.

2. Methods

This was a single-center, retrospective study that was approved by the Institutional Review Board of Chang Gung Memorial Hospital (CGMH; No. 100-3561B) and that was in compliance with the ethical standards that were established in the Declaration of Helsinki. EEGs were recorded in 3 groups of patients with epilepsy with different protocols between July 2010 and June 2011. The groups that underwent routine EEG and 3 h VEM consisted of patients in the outpatient department, and 3-day VEM data were acquired from inpatients.

CGMH is a tertiary referral medical center in Northern Taiwan. Patients with epilepsy who are referred to this center mainly come from the North, but they also come from elsewhere in Taiwan. In local hospitals, patients with probable diagnoses of epilepsy are typically screened by routine EEG examinations. Doctors may then initiate antiepileptic drugs (AEDs) and/or refer patients to tertiary medical centers.

The National Health Insurance system in Taiwan allows for routine EEG examinations with only short durations. At CGMH, a routine EEG typically takes 20 min, of which 10–12 min consists of the actual EEG recording time. Most patients are examined while awake, although some are asked to sleep. Provocation tests that consist of 3 min of hyperventilation and intermittent photic stimulation (3–24 Hz) are included in the routine EEGs. Routine EEGs can be scheduled by neurologists in other subspecialties or by doctors in different fields. In this study, however, we only included patients who were referred from epileptologists and underwent routine EEGs that were indicated for seizure classification.

In contrast to routine EEGs, only patients who are treated by epileptologists undergo 3 h outpatient or 3-day inpatient VEMs. CGMH's epilepsy monitoring unit had 1 outpatient VEM bed and 3 inpatient VEM beds; this number was increased to 5 in 2011. More than 200 patients a year are admitted for long-term VEM, and approximately 30 patients per month undergo 3 h outpatient VEMs. Patients received VEM for one of the following indications: classification of seizures, differential diagnosis of paroxysmal events, presurgical evaluation, postsurgical follow up, assessment for the discontinuation of AEDs, monitoring of status epilepticus, or evaluation of sleep disorders.

During the 3 h outpatient VEM, patients maintained their regular dosages of AEDs, and they were asked to fall asleep without medical induction after hyperventilation and photic stimulation. The VEM ended after a continuous 3 h period. For the 3-day inpatient VEM, patients were admitted for 3 days; occasionally, the length of admission was extended to 7 days or longer if indicated. A dosage-reduction protocol was applied for all patients, except for those who were planning to discontinue AEDs or for the monitoring of status epilepticus. AEDs were reduced to a half dose on the first day, and they were stopped on the second day if no events were recorded. Once the targeted events were recorded twice, the patients were given an additional dose of AEDs, and they were instructed to resume their usual AED regimen.

VEMs were performed with 32- or 64-channel digital video-EEG systems (BMSI 6000, Nicolet Biomedical, Inc., Madison, WI, USA; Nicolet vEEG, CareFusion Corporation, Middleton, WI, USA). The electrodes were arranged according to the international 10–20 system, which included anterior temporal leads (T1 and T2). Sphenoid electrodes were inserted when indicated. Bentonite was used as the media in routine EEGs. Ten20 Conductive Paste (Weaver and Company, Aurora, CO, USA) was used as the media, and Collodion Adhesive (SLE Ltd., South Croydon, UK) was used as the glue in outpatient and inpatient VEMs.

Each day, the entire recording was visually reviewed by 8 epileptologists, and the time to the first epileptiform discharge or the first clinical event was recorded. The definition of interictal epileptiform discharges was paroxysmal spikes or sharp transients (with or without a slow wave component) that could be clearly detected above the background rhythms.[5] The following spikes or sharp waves were surveyed to confirm the epileptiform morphology.[19] If the transients had very short duration, had symmetric upslope and downslope, were not focally located, and occurred only during drowsiness, they were assumed as benign epileptiform transients of sleep. The identified interictal epileptiform discharges and recorded seizures were discussed by all epileptologists in a weekly conference.

After acquiring data that included seizure type, neuroimaging, purpose of the EEG, and diagnosis or treatment changes after the examinations, we analyzed the latency to the first epileptiform discharge in outpatient VEMs and the latency to the first clinical event (epileptic or nonepileptic) in inpatient VEMs in order to determine the optimal duration of the EEG recordings.

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) for Windows, version 17.0 (IBM Corporation, Armonk, NY, USA). A chi-square test was used to compare the detection rates between the different EEG methods. An independent *t*-test was used to compare the group means of the time to the first epileptiform discharge between the generalized and localization-related epilepsy syndromes. A *p*-value less than 0.05 in a 2-tailed test was considered statistically significant.

3. Results

In total, 2538 patients underwent routine EEGs between January and April 2011; 657 of them were diagnosed with epilepsy, but only 335 were referred from epileptologists. Among them, epileptiform discharges were recorded in 55 patients (16.4%), and seizures were recorded in 2 (0.6%).

During a one-year period, 328 patients who were all referred from epileptologists underwent 3 h outpatient VEMs. Excluding the indications for the differential diagnosis of paroxysmal events, only 281 patients had a diagnosis of epilepsy. Among them, epileptiform discharges were recorded in 152 patients (54.1%), and seizures were recorded in only 15 patients (5.3%). Both the detection rates of the epileptiform discharges and seizures were higher in the group undergoing 3 h VEMs than in the group undergoing routine EEGs ($p < 0.01$).

In the 152 patients with epileptiform discharges that were recorded during outpatient VEMs, 20 (13.2%) had frontal lobe epilepsy (FLE), 78 (51.3%) had temporal lobe epilepsy (TLE), 36 (23.7%) had generalized epilepsy, and 18 (11.8%) had other epilepsies or complex partial seizures of uncertain origins. The mean latency from the beginning of the EEG recordings to the appearance of the first epileptiform discharge was 31.1 min (median, 21 min). The mean latency to the first epileptiform discharge was 39.2 min for patients with FLE, 30.6 min for patients with TLE, 22.1 min for patients with generalized epilepsy, and 42.8 min for patients with other epilepsies. Patients with generalized epilepsy had shorter latencies to the first epileptiform discharge compared to patients with localization-related epilepsy (mean, 22.1 min versus 33.9 min, $p = 0.02$; 95% confidence interval, 1.93 to 21.75). Fig. 1 summarizes the distribution of the latencies to

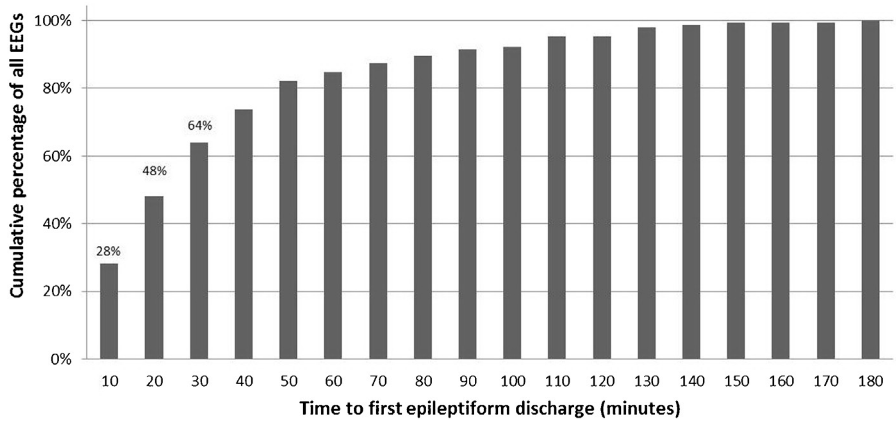

Fig. 1. Time to the first epileptiform discharge in outpatient video-electroencephalography monitoring (VEM).

the first epileptiform discharge in those undergoing outpatient VEMs.

Over a period of 1 year, 247 patients underwent long-term inpatient VEM. Interictal epileptiform discharges were found in 173 cases (70.0%). Clinical habitual events were recorded by video in 113 patients (45.8%), but epileptic seizures were confirmed by ictal discharges in only 86 patients (34.8%). The VEM detection rates of epileptiform discharges and seizures were significantly higher in the inpatient groups compared to the outpatient groups ($p < 0.01$). In the 86 patients whose epilepsy syndromes were diagnosed by epileptic seizures, there were 30 patients (34.9%) with FLE, 31 (36.1%) with TLE, 8 (9.3%) with generalized epilepsy, and 17 (19.8%) with other epilepsies.

After the inpatient VEM, the diagnoses of the patients were changed in 112 of the 247 patients (45.3%), and the treatment was changed in 89 patients (36.0%). Nonepileptic events were noted in 28 patients (11.3%), including 18 patients with psychogenic nonepileptic seizures and 10 patients with physiological nonepileptic events, such as syncope, cardiac arrhythmia, or dystonia. Two patients had both epileptic and nonepileptic events during the recording. One patient was suspected of having a simple partial seizure, but the electrical activities were too small to be recorded by the EEG.

The mean latency to the first clinical event was 17.9 h (median, 14 h). The mean latency to the first epileptic seizure was 19.5 h (median, 17.5 h). Fig. 2 shows the distribution of the latencies to the first clinical attack in the long-term inpatient VEMs.

Tables 1 and 2 summarize the detection rates of the different EEG methods and the latency to the first epileptiform discharge or seizure in patients with different seizure classifications.

4. Discussion

Although many publications have reported EEG findings in patients with epilepsy, the latency from the start of EEG recording to the appearance of epileptiform discharge has rarely been described. The results for the group that underwent 3 h outpatient VEMs revealed that the first epileptiform discharges were detected within 10 min in 28% of patients, within 20 min in 48%, and within 30 min in 64% (Fig. 1). This was consistent with previous studies that reported that 37% to 53% of the first epileptiform discharges occurred within 20 min and that 71% of epileptiform discharges occurred within 30 min.[19,20] However, these previous studies had smaller sample sizes, and they had analyzed latencies with time unit of 20 min or more. The protocols of our routine EEG and outpatient VEM were the same except for the existence of video recording and the duration of examinations: patients underwent hyperventilation and intermittent photic stimulation, and maintained their regular AED dosages during recordings. In addition, patients in both groups all had diagnosis of epilepsy and were

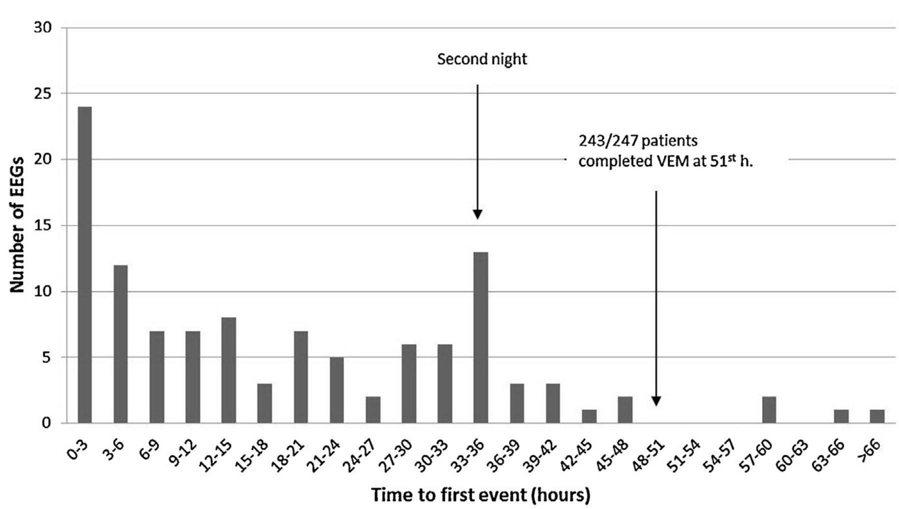

Fig. 2. Time to the first clinical event in inpatient VEM.

Table 1
Detection rate of ED in different EEG methods.

	Outpatient VEM	Inpatient VEM	p value
Total patients	281	247	
Patients with ED	54.1%	70.0%	< 0.01
All attacks	5.3%	45.7%	< 0.01
Epileptic seizures	5.3%	34.8%	< 0.01
Nonepileptic attacks	0.0%	11.3%[‡]	
Simple partial seizure	0.0%	0.4%	

ED, epileptiform discharges; VEM, video electroencephalographic monitoring; ‡ including 2 patients with both nonepileptic and epileptic attacks.

outpatients referred from epileptologists in this study. Therefore, 30 min of EEG recording is recommended for routine EEG studies that aim to detect interictal discharges, and this duration may have positive EEG results in two-thirds of the patients.

For statistical reasons, this study analyzed the latency to the first epileptiform discharge relative to time. We note that one pitfall of this study was that the first epileptiform discharges that occurred at the end of a period (e.g., min 19 of the 0–20 min group) offered little information to the epileptologists because the general EEG pattern was not readily identified without subsequent similar epileptiform discharges that confirmed the first one. Therefore, it may be necessary to extend the EEG duration beyond what was suggested by this study in order to obtain the best diagnostic information.

For the latency to the first event that was recorded in long-term inpatient VEMs (Fig. 2), 21.2% of the patients had their first clinical events within 3 h. The second peak appeared during the 33rd–36th h. This was around the second night (22:00–1:00) after admission, and the seizures could have occurred during sleep after the AEDs were halved or discontinued for 1 day. Most patients' events occurred within 48 h. When the duration of the VEM was extended, no events were recorded between the 48th and 57th h, and only 4 events (3.5%) were recorded after 57 h. Therefore, the results of this study suggested that a 48-h inpatient VEM that includes 2 nights of sleep can provide a high yield of recorded events, and another 24 h of VEM would be needed to detect the remaining 3.5% of events.

Table 1 shows the diagnostic yields of different EEG methods. The detection rate of our routine EEG was 16.4%, and the diagnostic yield of 1 routine EEG has been as low as 29% in the literature.[4] In this study, the detection rate of epileptiform discharges in the 3 h VEM was 54.1% if we selected patients with epilepsy only, and this was much higher than the rate of routine EEGs and approached the detection rate of long-term inpatient VEMs (70.0%). In addition, most patients fell asleep during the 3 h VEM, and epileptiform discharges tend to occur during the first 2 stages of non-rapid eye movement sleep.[21–24]

Because this was a retrospective study, we only controlled for some variables in these 3 groups of patients. The distribution of age and the sexual ratio between the patients undergoing outpatient and inpatient VEMs were similar. Both patient groups undergoing routine EEGs and 3 h VEMs were outpatients who had stable seizure control, referred from epileptologists who gave definite diagnoses of epilepsy, and not deprived of their AEDs. Since uncontrolled factors might affect the results for the detection rates, we cannot conclude any specific EEG method is superior to others. We suggest following the general guideline that every patient with epilepsy should receive at least 1 routine EEG examination. If the seizure classification is still in doubt, a 3 h outpatient VEM is more economical than a long-term inpatient VEM, given its high detection rate of epileptiform discharges. However, for the recording of clinical seizures, inpatient VEM had a much higher diagnostic yield (45.8%) than outpatient VEM (5.3%) according to this study.

Our study demonstrated that compared to patients with localization-related epilepsy, patients with generalized epilepsy had a significantly shorter latency to the first epileptiform discharge (22.1 min versus 33.9 min), as assessed by outpatient VEM (Table 2). Although the results of our inpatient VEM and previous studies also revealed this tendency,[19,20] they did not reach statistical significance. In clinical practice, a single train of definite interictal generalized discharges is sufficient for the diagnosis of generalized epilepsy. In contrast, for localization-related epilepsy, the interictal discharges are relatively infrequent and sometimes only occur during sleep. Moreover, the first few interictal discharges are often less well formed after the initiation of sleep; therefore, they can be readily identified by experienced epileptologists but not by most neurologists. In other words, patients with localization-related epilepsy may require more extended EEG monitoring in order to obtain a complete picture of their EEG pattern. This inference is supported by a former study that found that 1 day of VEM is sufficient for a diagnosis of generalized epilepsy.[25]

In this study, inpatient VEMs resulted in a diagnosis change for 112 patients (45.3%) and a treatment change for 89 patients (36.0%). This result was comparable to previous reports of the rate of diagnosis change (47.8%) [11] and the rate of treatment change (40.3%) [26] in patients with epilepsy. However, in Ghougassian's study, 58% of the patients had a diagnosis change, and 73% had a management change.[10] This high rate of diagnosis or management change might have been due to the high proportion of patients without epilepsy (30.5%) in their study. Indeed, the greatest change in diagnostic categories after VEM was in the number of patients with nonepileptic seizures, with a 31% absolute increase. This highlighted the difficulty in diagnosing psychogenic nonepileptic seizures without VEM.[27–29] In contrast, patients without epilepsy accounted for only 11.3% of the patients in the present study and 9.4% of the patients in Baheti's study.[11]

Among the 86 patients with epileptic seizures during long-term inpatient VEMs, 8 (9.3%) had generalized epilepsy, 31 (36.1%) had

Table 2
Latency to the first ED in outpatient VEM and to the first seizure in inpatient VEM.

	Outpatient VEM			Inpatient VEM		
	Patients with ED	First ED Mean (min)	First ED Median (min)	Patients with seizures	First seizure Mean (h)	First seizure Median (h)
All patients	152	31.1	21.0	86	19.5	17.5
GE	23.7%	22.1	17.5	9.3%	12.0	10.0
LRE	76.3%	33.9*	23.5	90.7%	20.2	17.5
TLE	51.3%	30.6	23.0	36.1%	27.0	30.0
FLE	13.2%	39.2	29.0	34.9%	16.0	12.5
Others	11.8%	42.8	20.5	19.8%	15.4	9.0

ED, epileptiform discharges; FLE, frontal lobe epilepsy; GE, generalized epilepsy; LRE, localization-related epilepsy; TLE, temporal lobe epilepsy; VEM, video electroencephalographic monitoring.
* $p < 0.05$.

TLE, 30 (34.9%) had FLE, and 17 (19.8%) had epilepsy of another area or multifocal epilepsy. The proportion of patients with generalized epilepsy was lower than that in Ghougassian's study (28%) but higher than in Baheti's study (3.5%). The proportion of TLE cases in our study (36.1%) was also fewer than that in Baheti's study (68.4%) and fewer than the estimated proportion of TLE (66%) in all patients with localization-related epilepsy.[30] This might be explained by the fact that patients with TLE are relatively easily diagnosed based on clinical ictal features and outpatient EEGs, resulting in fewer TLE patients being further referred for long-term inpatient VEM. In support of this explanation, TLE cases comprised 51.3% of the patients who received outpatient VEMs in this study.

5. Conclusions

Two-thirds of epileptiform discharges were detected within 30 min of VEM. Thirty min of recording is recommended for routine EEG examinations that aim to detect epileptiform discharges. A 3 h outpatient VEM is a reasonable option when a routine EEG fails to detect epileptiform discharges. The latency to the first epileptiform discharge was shorter in patients with generalized epilepsy than in patients with localization-related epilepsy. 48 h of video-EEG monitoring might be adequate for detecting the target events.

Competing interests

The authors declare that they have no competing interests.

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