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ORIGINAL ARTICLE

The clinical utility of non-invasive video-electroencephalographic monitoring has been diversifying

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Abstract

Background Inpatient long-term video-electroencephalographic (VEEG) monitoring has been used extensively for differential diagnosis of paroxysmal events. We evaluated the diagnostic yield and clinical utility of VEEG performed in a comprehensive epilepsy center.

Method We retrospectively reviewed all cases of VEEG performed from May 2003 to April 2018. We analyzed the data to determine its clinical utility and diagnostic yield.

Results A total of 1335 cases were reviewed. After excluding 147 cases of intracranial recording and 163 cases with incomplete medical records, 1025 cases of VEEG were included. The mean duration of VEEG was 2.3 ± 1.6 days (range = 1–14). A total of 763 VEEGs documented epileptic seizures or interictal epileptiform discharges (IEDs) to confirm the diagnosis of epilepsy. There were 99 psychogenic non-epileptic seizure, 36 status epilepticus, and 34 VEEGs which revealed generalized or focal slow activities without any clinical seizures or IEDs. VEEG was normal in 170 cases. The diagnostic yield of VEEG varied from 83.4 to 88.4% depending on its definition. The proportion of epilepsy in total cases of VEEG continued to decrease from 77.2 to 61.4%. In contrast, the proportion of normal VEEG steadily increased from 4.1 to 24.1% during the same time period.

Conclusions This study ascertained how useful VEEG is and the utility of VEEG has been diversifying in clinical circumstances beyond epilepsy. VEEG can play a pivotal role in the diagnostic approach to epilepsy and its differential diagnoses.

Keywords Video-electroencephalography monitoring · Epilepsy monitoring unit · Clinical utility · Diagnostic yield

Abbreviations

AED	Antiepileptic drug
BP	Blood pressure
EEG	Electroencephalography
HR	Heart rate
IEDs	Interictal epileptiform discharges
MRI	Magnetic resonance imaging
OH	Orthostatic hypotension
PNES	Psychogenic non-epileptic seizure
POTS	Paroxysmal orthostatic tachycardia syndrome
VEEG	Video-electroencephalographic monitoring

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Introduction

Despite major advances in neuroimaging in the last two decades, electroencephalography (EEG) is still an essential instrument in the evaluation of patients with seizures and various paroxysmal behaviors or events [1]. EEGs have high specificity, but the chances of recording interictal epileptiform discharges (IEDs) during a routine EEG is only 29–55% [2, 3], indicating low sensitivity. Even after repeating routine EEGs up to seven times, the chance of catching IEDs goes up to only 80% [3–5]. The IEDs may be recorded in 0.5 to 2% of healthy subjects with no history of a paroxysmal event [6, 7], although over reading EEGs can lower the specificity in clinical practice [8]. Inpatient long-term video-encephalography (VEEG) monitoring has become an essential tool and the gold standard by providing the means to differentiate paroxysmal events and increase the yield of detecting IEDs [9–11].

VEEG allows for behavioral observation through a video recording that is time-locked with the EEG. The purpose of

VEEG can be divided into presurgical evaluations and diagnostic for any paroxysmal events [9, 11, 12]. VEEG can be considered useful if the prior EEG-based diagnosis is confirmed or altered, or if it provides critical evidence or clues to answer the clinician's questions. Even in the absence of ictal episodes during VEEG, IEDs can provide useful information. The reported diagnostic yield of a VEEG varies from 73 to 85% influenced by patient selection and differences in the definition of diagnostic yield [9, 12, 13].

Although VEEG is extensively performed in comprehensive epilepsy centers, detailed studies about its usefulness and guidelines have been limited to only a few reports [11, 14]. The purpose of this study was to investigate the diagnostic yield as well as the clinical utility of VEEGs performed in a comprehensive epilepsy center through the retrospective review of 15 years of medical records.

Patients and methods

This is a blind-reviewed retrospective research. We reviewed all patients who had VEEGs from May 2003 to April 2018 at a comprehensive epilepsy center of a tertiary university hospital in the Republic of Korea, which provides care for a population of 5.2 million. The VEEG system used for recording was Grass-Telefactor (Grass Technologies, West Warwick, USA) with 64-channel cable telemetry and facilities for recording EEG and electrocardiography. EEG technicians continuously monitored the patients and the EEG throughout the recording. Nurses were always present in case of seizure or emergency intervention. The VEEG, demographic, and clinical data were reviewed.

There were no strict guidelines set for VEEG, but there were three general objectives: (a) presurgical evaluation in patients with refractory epilepsy; (b) seizure classification; (c) diagnostic evaluation of paroxysmal events such as seizure, psychogenic non-epileptic seizure (PNES), sleep disorders (e.g., parasomnia), and paroxysmal dyskinesia. All recordings were conducted on a 24-h basis. Upon admission for VEEG, a detailed history was obtained and the patient underwent a neurological examination. At the start of recording, the patients completed routine activation procedures including intermittent photic stimulation and hyperventilation (3–5 min). Also, serial orthostatic blood pressure (BP) and heart rate (HR) were checked at the bedside during recording. Depending on the patient's seizure type and frequency, antiepileptic drugs (AEDs) were reduced or completely tapered off by an epileptologist during admission. All VEEGs were evaluated by visual inspection without using automatic seizure detection software. Recordings were reviewed daily by a board-certified epileptologist. Patients were discharged if they concluded that they had been taking VEEG for a sufficient period, or if clinically meaningful findings were identified. The length of the admission was generally limited to 3 days unless the epileptologist deemed an extension necessary. Clinically meaningful findings included habitual seizures or events, IEDs, and clinically relevant EEG discharges such as burst suppression, triphasic waves, and focal or diffuse slow activity. IEDs were defined as spikes or sharp waves that are distinguished from the background rhythms clearly, with or without a following slow wave. A spike has a local field potential and a duration of less than 70 milliseconds; a sharp has a duration between 70 and 200 milliseconds. The benign variants or artifacts were excluded. If indicated, a tilt table test with beat-to-beat blood pressure monitoring was performed after VEEG to document orthostatic hypotension (OH) or paroxysmal orthostatic tachycardia syndrome (POTS). Single-lead electrocardiographic monitoring was performed in all patients. However, if cardiac rhythm abnormalities were recorded or in-patients were clinically suspected of abnormal heart rhythm, further cardiac evaluation (i.e., ambulatory electrocardiographic monitoring) was performed. Since this study aimed only at non-invasive monitoring (phase I), we excluded intracranial recordings (phase II). In addition, it is excluded from the analysis if there is a clear limit to the data collection, such as it is difficult to recognize handwritten characters on the scanned paper records and missing record. The results of the latest routine EEG, which were performed within a year before VEEG, were compared with that of the VEEG. If there were any significant events such as severe trauma causing intracranial hemorrhage, encephalitis, brain surgery, or stroke between routine EEG and VEEG, the case was excluded from the analysis.

Statistical analysis was done using SPSS version 22.0 (Chicago, IL, USA). Categorical variables were analyzed with Pearson x^2 test and Fisher exact test; *t*-test was used to analyze continuous variables. Statistical significance was determined at $p < 0.05$.

Results

We reviewed a total of 1335 cases of VEEGs and enrolled 1025 cases after excluding 147 cases of intracranial VEEG and 163 cases of inadequate medical records (Fig. 1). A total of 982 individuals had completed VEEG monitoring. All but 291 patients had prior routine EEGs, 27 patients had two sessions of VEEG, and 8 patients had three. A total of 417 patients with the result of routine EEG were analyzed. There were 233 concordant results between the routine EEG and VEEG, accounting for 55.9%. The most common discordance between routine EEG and VEEG was the change from normal to focal epilepsy ($n = 98$, 53.3% of discordance), followed by from others to focal epilepsy ($n = 54$, 29.3% of discordance). In the classification of epilepsy, 9 generalized epilepsies were

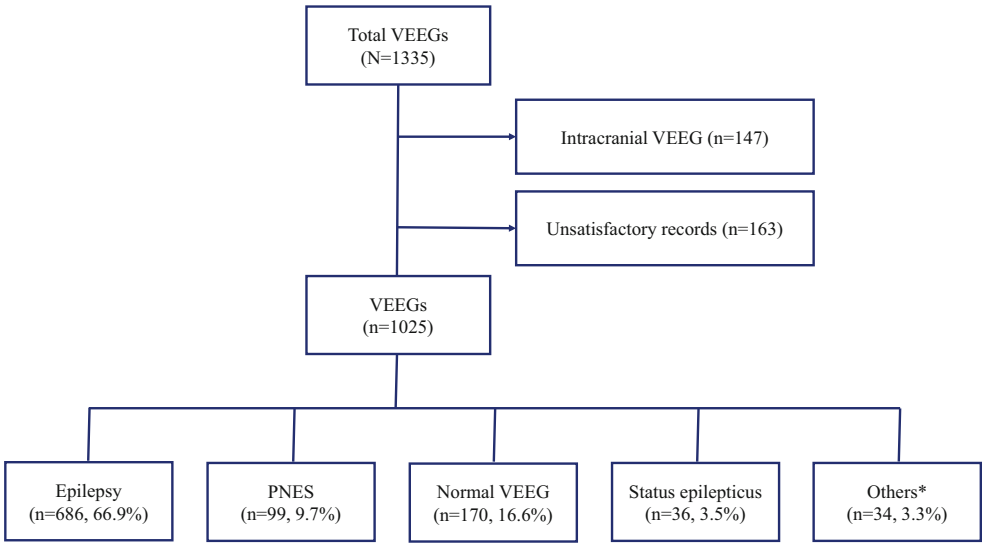

Fig. 1 Enrollment plan and results. The diagram shows the final diagnoses of patients who underwent VEEG. *Others, cases of generalized or focal slow activity on electroencephalography without a seizure or an interictal epileptiform discharge. VEEG = video-electroencephalography monitoring; PNES = psychogenic non-epileptic seizure

changed to focal (4.8% of discordance), and 3 focal epilepsies were changed to generalized (1.6% of discordance) after VEEG. The localization of IED changed in 95 cases, but this did not change the diagnosis (all were focal epilepsy). The mean age of patients was 36.5 ± 18.9 (range = 0.5–89), and 505 (51.4%) were female. Brain imaging including computed tomography and magnetic resonance imaging (MRI) demonstrated potentially epileptogenic lesions in 321 (32.7%) patients. Eight hundred thirty-nine cases (82.0%) were referred by epileptologists, 143 cases (14.0%) by neurosurgeons, and 43 cases (4.2%) by general neurologists. For the 15 years, the numbers of presurgical evaluation, seizure classification, and diagnostic evaluation of paroxysmal events were 414 (40.4%), 242 (23.6%), and 369 (36.0%), respectively. There is an increasing annual trend in the total number of VEEGs as shown in Fig. 2. The number of VEEGs increased from 197 to 289 to 539 every 5 years from 2003 to 2018, respectively. During this period, the respective numbers of each group had also increased: 152, 203, and 331 in epilepsy; 19, 38, and 42 in PNES; and 3, 8, and 25 in status epilepticus. In addition, normal VEEGs were 8, 32, and 130, respectively. The proportion of epilepsy among total cases of VEEG during the sequential 5-year periods continued to decrease: 152 out of 197 (77.2%), 203 of 289 (70.2%), and 331 of 539 (61.4%), respectively. During the same period, the proportion of normal VEEG studies steadily increased: 8 out of 197 (4.1%), 32 of 289 (11.1%), and 130 of 539 (24.1%).

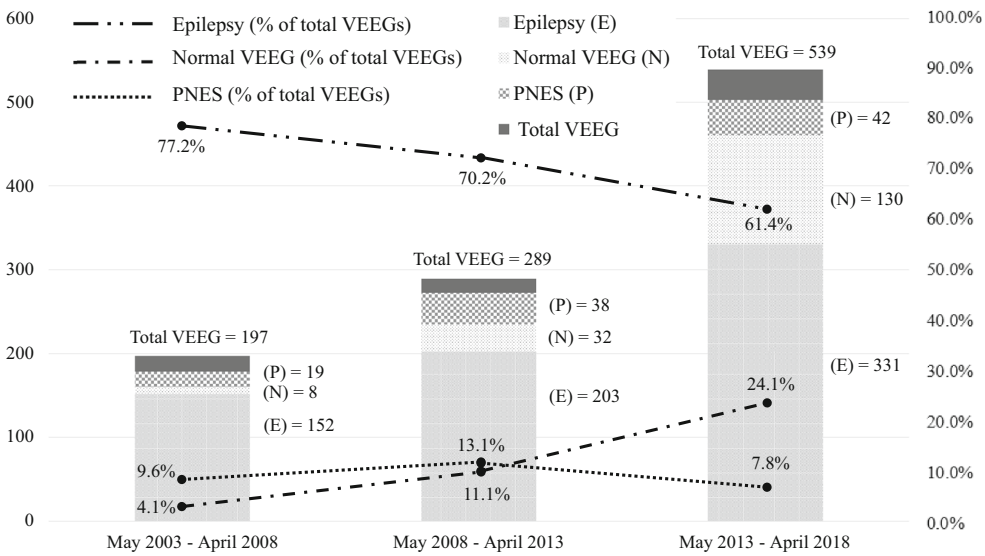

Fig. 2 Trends in the number of VEEGs and their results over time. The changes are shown in three 5-year time spans. The number of total VEEG has been increasing, and the absolute numbers of epilepsy, PNES, and normal VEEG also have been increased, respectively. Interestingly, although the proportion of epilepsy in total VEEG has been steadily decreasing, the normal VEEG has been steadily increased to reach a quarter of the total over the last 5 years. VEEG, video-electroencephalography monitoring; PNES, psychogenic non-epileptic seizure

VEEG findings

The mean duration of VEEG was 2.3 ± 1.6 days (range = 1–14 days, mode 1). A total of 686 VEEGs documented either epileptic seizures or IED and were considered diagnostic of epilepsy (Table 1). There were 99 definite cases of PNES of which 41 also had a diagnosis of epilepsy based on prior evidence of IEDs and/or epileptic seizure. Additional cases included 36 status epilepticus with electrical seizures recorded during VEEG. Cases classified as "Others" accounted for 34 with either generalized or focal slow activity on the VEEG, but no seizures or IEDs. "Others" included 26 slow activity, 2 burst-suppression patterns (both were post-hypoxic encephalopathy), 4 triphasic waves (one was hepatic encephalopathy, another one was hyponatremia, and the others could not distinguish between hepatic encephalopathy and AED-induced confused mentality), and 2 background suppressions (one was stroke, the other was encephalitis).

Normal VEEG

One hundred seventy VEEGs were normal. The final clinical diagnoses in these cases were based on a combination of clinical history, medical examination, and prior diagnostic tests including ambulatory electrocardiographic monitoring, echocardiography, tilt table test, orthostatic BP measurement, and brain imaging (mainly MRI). Therefore, 29 patients with normal VEEG findings with a mean duration of 1.3 ± 0.5 days were still diagnosed with epilepsy. Of the 11 cases diagnosed with sleep disorders, 7 had periodic limb movement disorder, 3 rapid eye movement sleep behavior disorder, and 1 sleep-related myoclonus. VEEG during the day provided sufficient information for diagnosis. Sixty-eight cases had syncope consisting of 31 OH, 21 POTS, 13 cardiogenic syncope, 2 coughing-induced syncope, and 1 micturition syncope. In the case of the syncope, VEEG was performed for an average of 1.5 ± 0.6 days. Fifteen patients were diagnosed with paroxysmal dyskinesia and 2 with hemifacial spasm. There were 4 cases of recurrent transient ischemic attack, all of whom had Moyamoya syndrome. In these cases of movement disorders and Moyamoya syndrome, the symptoms were confirmed within 1 day. Three migraineurs underwent VEEG as they had hemiplegic migraine mimicking focal seizures; one of these patients had IEDs on EEG but no epileptiform discharge during hemiplegic attack. Thirty-eight subjects remained without any discernible diagnosis despite the average of 2 days or more (2.1 ± 0.8) of VEEG, and were eventually categorized as "Undetermined." The final diagnoses of cases of normal VEEG are summarized in Table 2.

Epilepsy

In total, 803 cases were finally diagnosed with epilepsy, 763 of whom had epileptic seizures (396, 51.9%) or IEDs only (367, 48.1%) on VEEG (Table 4). The mean duration was 2.5 ± 1.7 days. Generalized and focal epilepsy were 51 and 635, respectively. Although there were no epileptic seizures or IEDs during VEEG for 40 cases, they met the diagnostic criteria based on prior evidence and clinical history (11 cases with slow EEG activity and 29 cases with normal VEEG) of two or more unprovoked seizures or status epilepticus. In addition, 41 cases of definite PNES showed IEDs and/or coexisting epileptic seizures during the VEEG. The classification of epilepsy cases is summarized in Table 3.

Table 1 The results of video-electroencephalography monitoring

Results of VEEG	Cases *n* = 1025 (%)	1st 5 years[a] = 197 (%)	2nd 5 years[a] = 289 (%)	3rd 5 years[a] = 539 (%)
Epilepsy	686 (66.9)	152 (77.2)	203 (70.2)	331 (61.4)
Focal	635			
Generalized	51			
PNES (definite)[b]	99 (9.7)	19 (9.6)	38 (13.1)	42 (7.8)
PNES in epileptics	41			
PNES only	58			
Normal VEEG	170 (16.6)	8 (4.1)	32 (11.1)	130 (24.1)
Others[c]	34 (3.3)	15 (7.6)	8 (2.8)	11 (2.0)
Status epilepticus	36 (3.5)	3 (1.5)	8 (2.8)	25 (4.6)

VEEG, video-electroencephalography monitoring; *PNES*, psychogenic non-epileptic seizure

[a] Five-year spans: 1st 5 years, May 2003–April 2008; 2nd 5 years, May 2008–April 2013; 3rd 5 years, May 2013–April 2018

[b] Documented by VEEG

[c] If there was generalized or focal slow activity but no seizure or IED

Table 2 Underlying disorders in patients with normal video-electroencephalography monitoring findings

The final diagnosis of normal VEEGs	VEEG duration (days)	Cases $n = 170$ (%)	% of VEEG total
Epilepsy but normal VEEG[a]	1.3 ± 0.5	29 (17.1)	2.8
Sleep disorders	1.0 ± 0.0	11 (6.5)	1.1
Periodic lime movement disorder		7	
RBD		3	
Sleep myoclonus		1	
Syncope	1.5 ± 0.6	68 (40.0)	6.6
Orthostatic hypotension		31	
POTS		21	
Cardiogenic syncope		13	
Coughing-induced syncope		2	
Micturition syncope		1	
Movement disorders	1.0 ± 0.0	17 (10.0)	1.7
Paroxysmal dyskinesia		15	
Hemifacial spasm		2	
Miscellaneous	1.0 ± 0.0	7 (4.1)	0.7
Transient ischemic attack[b]		4	
Migraine		3	
Undetermined (e.g., possible PNES or vasovagal syncope, and an isolated event of seizure or LOC)	2.1 ± 0.8	38 (22.4)	3.7

RBD, rapid eye movement sleep behavior disorder; *POTS*, paroxysmal orthostatic tachycardia syndrome; *PNES*, psychogenic non-epileptic seizure; *LOC*, loss of consciousness

[a] Patients with established diagnosis of epilepsy

[b] The four patients were all Moyamoya syndrome

Diagnostic test characteristics

In this study, the sensitivity and specificity of VEEG for diagnosing epilepsy (recording epileptic seizures or IEDs) were 95.0% and 99.6%, respectively. We considered the 763 cases with identified IEDs or epileptic seizure as true positive cases (635 focal epilepsy, 51 generalized epilepsy, 41 PNES with coexisting epilepsy, and 36 status epilepticus) (Table 4). The only false positive was the case of hemiplegic migraine who also had IEDs on EEG. False-negative cases included the 40 cases with two or more previous unprovoked seizures but normal VEEG ($n = 29$) or slow EEG activity ($n = 11$). Excluding those with a final diagnosis of epilepsy who had normal VEEG, there were 221 cases of true negative including 38 Undetermined, 58 definite PNES without IEDs, 17 movement disorders, 68 syncope, 11 sleep disorders, 23 Others, and 6 Miscellaneous. One case of hemiplegic migraine out of 7 Miscellaneous cases had IED, but no epileptiform discharge during the symptomatic period. Based on the clinical history of recurrent unprovoked seizures or status epilepticus before the VEEG, 11 subjects out of 34 "Others" were epileptics (Table 4). Accordingly, the diagnostic yield of VEEG for epilepsy in this study was 83.4% ((1025-1-40-38-68-23)/1025). The positive and negative predictive values of VEEG were 99.9% (763/(763 + 1)) and 84.7% (221/(40 + 221)), respectively. Nevertheless, there were 119 out of 1025 VEEGs in which VEEG alone could not find significant clinical information: epilepsy but normal VEEG ($n = 29$), OH ($n = 31$), POTS ($n = 21$), and Undetermined ($n = 38$). Therefore, the diagnostic yield of VEEG for clinical utility was 88.4% ((1025-29-31-21)/1025).

Table 3 The classification of final diagnosis with epilepsy

Epilepsy	Cases $n = 803$	%
Generalized epilepsy	51	6.4
Focal epilepsy	635	79.1
PNES in epileptics	41	5.1
Status epilepticus	36	4.5
Epilepsy with slow activity only (i.e., without a seizure or an IED)	11	1.4
Generalized slow activity	4	
Regional slow activity	7	
Epilepsy but normal VEEG	29	3.6

PNES, psychogenic non-epileptic seizure; *IEDs*, interictal epileptiform discharges; *VEEG*, video-electroencephalography monitoring

Table 4 Diagnostic test characteristics

VEEG	Epilepsy	
	Present ($n = 803$)	Absent ($n = 222$)
Positive ($n = 764$)	763 = focal epilepsy (635) + generalized epilepsy (51) + PNES in epileptics (41) + status epilepticus (36)	1 = hemiplegic migraine with IEDs
Negative ($n = 261$)	40 = epilepsy but normal VEEG (29) + slow activity only (11)	221 = undetermined (38) + definite PNES without IEDs (58) + sleep disorders (11) + syncopes (68) + movement disorders (17) + transient ischemic attacks (4) + migraines (3) + generalized or regional slow activities (23)

PNES, psychogenic non-epileptic seizure; *IED*, interictal epileptiform discharge; *VEEG*, video-electroencephalography monitoring

Discussion

This study showed that the indication of VEEG has been diversified over time and has been used more widely in clinical practice. Since VEEG is a time- and labor-consuming, expensive instrument, its clinical utility needs to be evaluated. Previous studies of VEEG have analyzed between 100 and 400 cases conducted within 2 or 3 years [9, 12, 13, 15, 16]. Our study expands the scope by including a larger set of VEEGs performed over 15 years.

The mean duration of our recording was 2.3 ± 1.6 days, consistent with previous studies [9, 15, 16]. The prevalence of PNES in this study was 9.7%, which was lower than in some previous studies (more than 30%) [9, 13], but higher than others (approximately 6%) [15, 16]. Sleep disorders in previous studies accounted for 3 to 10% [15, 16], but only 1.1% in this study. This difference might be due to ethnic background, referral bias, clinical criteria, and the presence of sleep clinic and polysomnography.

The inherent value of VEEG, a high positive predictive value, is based on information including EEG, video, and single-lead electrocardiography. Therefore, we were able to confirm various differential diagnoses of epilepsy including cardiogenic syncope, sleep disorders, hemiplegic migraine, and movement disorders. The VEEG was inconclusive per se for clinical utility in only 119 cases, and the diagnostic yield of VEEG for clinical utility increased to 88.4%. The 29 cases of epilepsy with normal VEEG had an average VEEG duration of 1.3 ± 0.5 days. It is likely that extended VEEG, up to 2 or 3 days [11], would have resulted in further clinically significant findings. Also, the diagnostic yield of VEEG can be improved by a combination of detailed clinical history, physical examination, and other diagnostic modalities such as brain imaging, cardiac evaluation, orthostatic BP with HR, and tilt table test. Clearly, valvular heart disease cannot be confirmed by VEEG; however, the single-lead electrocardiography during VEEG may detect the arrhythmia, which may cause syncope (e.g., sinus pause). Serial measurement of orthostatic BP and heart rate also may detect orthostatic hypotension and POTS. It is very important to confirm that the EEG is normal when the patient feels the symptoms or pre-symptoms (e.g., pre-syncopal dizziness). This is the reason why we should record electrocardiography and should measure orthostatic blood pressure and heart rate during at bedside VEEG. There was an increasing trend in the total number of VEEGs and numbers of each group over the years. Interestingly, the proportion of epilepsy among total cases of VEEG during the sequential first and last 5-year periods decreased from 77.2 to 61.4%. During the same periods, the proportion of normal VEEG studies steadily increased from 4.1 to 24.1%. These findings support the increasing utility of VEEG in a more diverse clinical setting. VEEG has been used as a tool for differential diagnosis of a variety of paroxysmal disorders such as syncope, movement disorders, and sleep disorders. VEEGs were even used in a case of fluctuating consciousness, which helped determine the causes to be subclinical seizures and/or status epilepticus [17, 18]. Overall, the main use of VEEG was presurgical evaluation (40.4%) during the past 15 years, however, the long-term data demonstrated in this study ascertains that the clinical utility of VEEG is diversifying beyond epilepsy.

There are a few limitations of this study. Since this is a retrospective study that excluded the cases of insufficient medical records and the patients admitted to the epilepsy monitoring unit were all selected by physicians, selection bias should be considered. The need for VEEG, however, means that the differential diagnosis of the case is difficult enough to require extra efforts for the diagnosis. In these cases, VEEG provided important clinical information. Second, the VEEG reviewer was not in a blind situation, which might affect the interpretation. Third, since phase I VEEG does not provide the complete localization of the epileptogenic zone, the classification of epilepsy is not confirmative.

Conclusion

In practice, physicians tend not to plan additional tests (such as VEEG) unless there is uncertainty. Besides, the verification of the diagnosis is obtained not by a single examination but by

careful consideration of the clinical information and the examination results. VEEG is not an omnipotent diagnostic tool; however, VEEG may provide critical information in clinical practice. This study is significant in the sense that more than 1,000 VEEGs over 15 years were analyzed; therefore, we believe that this study is representative of the paradigm of clinical use and diagnostic yield of VEEG. VEEG has proven to be useful in multiple ways that have exceeded its original intended use, and its indication has been diversified over time.

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Compliance with ethical standards The study was approved by the ethics committee of the Keimyung University Dongsan Medical Center. The need for written informed consent was waived due to the study's retrospective design.

Conflict of interest The authors declare that they have no conflict of interest.

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