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Analyzing reliability of seizure diagnosis based on semiology

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ABSTRACT

This study aimed to determine the accuracy of seizure diagnosis by semiological analysis and to assess the factors that affect diagnostic reliability. A total of 150 video clips of seizures from 50 patients (each with three seizures of the same type) were observed by eight epileptologists, 12 neurologists, and 20 physicians (internists). The videos included 37 series of epileptic seizures, eight series of physiologic nonepileptic events (PNEEs), and five series of psychogenic nonepileptic seizures (PNESs). After observing each video, the doctors chose the diagnosis of epileptic seizures or nonepileptic events for the patient; if the latter was chosen, they further chose the diagnosis of PNESs or PNEEs. The overall diagnostic accuracy rate for epileptic seizures and nonepileptic events increased from 0.614 to 0.660 after observations of all three seizures ($p < 0.001$). The diagnostic sensitivity and specificity of epileptic seizures were 0.770 and 0.808, respectively, for the epileptologists. These values were significantly higher than those for the neurologists (0.660 and 0.699) and physicians (0.588 and 0.658). A wide range of diagnostic accuracy was found across the various seizures types. An accuracy rate of 0.895 for generalized tonic–clonic seizures was the highest, followed by 0.800 for dialeptic seizures and then 0.760 for automotor seizures. The accuracy rates for myoclonic seizures (0.530), hypermotor seizures (0.481), gelastic/dacrystic seizures (0.438), and PNESs (0.430) were poor. The reliability of semiological diagnosis of seizures is greatly affected by the seizure type as well as the doctor's experience. Although the overall reliability is limited, it can be improved by observing more seizures.

1. Introduction

Misdiagnosis of epilepsy is not uncommon since the symptoms of epileptic seizures are varied and there are many imitators, including physiologic nonepileptic events (PNEEs) and psychogenic nonepileptic seizures (PNESs). The diagnosis of epilepsy is primarily based on a detailed patient history, the reliability of which is limited because important details about the seizures can be described inaccurately or ignored by patients and witnesses [1] and may even be denied by patients with PNESs. Deacon et al. evaluated the diagnostic accuracy based on patient history in a select group of patients with probable drug-refractory temporal lobe epilepsy. They found that epileptologists rarely missed epileptic seizures (high sensitivity, 96%) but frequently misdiagnosed nonepileptic events as epileptic seizures (low specificity, 50%) [2]. The gold standard for seizure diagnosis is video-electroencephalography (VEEG) monitoring to capture typical seizures [3]. However, long-term VEEG is not always readily available, and typical seizures may not be recorded during monitoring. Moreover, epileptic seizures are sometimes not associated with clear scalp EEG changes [4].

A study showed that doctors could interpret seizures more accurately based on semiology than based on descriptions of seizures [5]. Nowadays, doctors are increasingly given "phone video" or "home video" to review by patients and families. Additionally, when doctors encounter patients having seizures, they must depend on analysis of semiology to make a quick diagnosis. However, the reliability of visual diagnosis of seizures has not been well known. Recent studies observed the accuracy of differential diagnosis between epileptic seizures and PNESs based on seizure semiology [6–9]. Seneviratne et al. reported that the accuracy varied greatly among different professional caregivers [6]. A semiological teaching module increased the accuracy of discrimination between epilepsy and PNESs [7,8]. These studies suggested that doctors' experience is important in diagnosis. However, the accuracy of visual diagnosis of seizures may also depend on other factors such as seizure type and the number of seizures witnessed. Here, we sought to systematically evaluate the reliability of semiological seizure diagnosis using a larger sample of seizures (total = 150 seizure videos). We hypothesized that the accuracy of semiological seizure diagnosis may

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be influenced by the number of seizures reviewed and seizure types as well as doctors' experience.

2. Materials and methods

2.1. Patients and seizure videos

A total of 150 seizure videos from 50 patients (Table 1, Supplemental Table 1) were extracted from our VEEG database at the Second Affiliated Hospital, School of Medicine, Zhejiang University. All patients had been recorded simultaneously by two cameras. The 50 patients were selected using the following criteria: (1) they had at least three of the same typical epileptic seizures or nonepileptic events recorded during the monitoring and were adequately interviewed by medical staff at the bedside; (2) the quality of the videos was good enough to clearly observe the eyes, faces, and hands of the patients; and (3) they had a certain diagnosis. The types of epileptic seizures were classified using the semiology classification [10]. Pure epileptic auras were not included since the semiological changes are minimal and difficult to observe on a video. Syncope videos were not included because an insufficient number of ictal events that appeared like syncope were recorded in our VEEG database. The diagnosis of all seizure types was made by the epileptologists in our center on the basis of clinical descriptions, VEEG results, and auxiliary examinations. Psychogenic nonepileptic seizures were diagnosed with the help of psychiatrists.

2.2. Video observations

Forty doctors from six tertiary referral hospitals were invited and agreed to participate in the study. The participants included 20 physicians in internal medicine (hereafter called physicians), 12 general neurologists, and eight epileptologists. All the epileptologists had worked in epilepsy centers for at least two years, and they had a mean practice time of 11.2 years postgraduation. Most of them finished epilepsy fellowship training in recognized epilepsy centers (Cleveland Clinic, U.S.A.; Montreal Neurological Institute, Canada). The 12 general neurologists and 20 physicians had a mean practice time of 5.2 years and 6.4 years, respectively, postgraduation. All participants were informed that all three seizures from the same patient were of the same type. They were blinded to any clinical information of the patients. The three seizures from each patient were presented to participants consecutively in a fixed order. After observing the first seizure video for each patient, the participants analyzed the seizure semiology and chose the answer of "epileptic seizure" or "nonepileptic event". If they answered "nonepileptic event", they had to choose whether it was PNESs or PNEEs in the next step. When the second or the third seizure video from the same patient was presented, the participants reconsidered the diagnosis of "epileptic seizure" or "nonepileptic event" based on the semiology of the current seizure and previous seizure(s) together. The participants were not allowed to change their previous answers when observing the next seizure. Using this approach, the participants made choices for all three videos of each patient.

Table 1
Semiological descriptions of seizures.

Seizure type			50 (total)
Epileptic			37 (subtotal)
	Dialeptic		2
	Simple motor	Tonic	6
		Clonic	4
		Myoclonic	5
		GTCS	4
	Complex motor	Hypermotor	9
		Automotor	5
		Gelastic or dacrystic	2
Nonepileptic			13 (subtotal)
	PNES		5
	PNEE	Sleep disorders	3
		Movement disorders	5

GTCS, generalized tonic–clonic seizure; PNES, psychogenic nonepileptic seizure; PNEE, physiologic nonepileptic event; dialeptic seizure, the main ictal manifestation is an alternation of consciousness; hypermotor seizure, the main ictal manifestations consist of complex movements involving the proximal limbs and trunk; automotor seizure, the main ictal manifestations consist of automatisms involving the distal limbs or the mouth.

2.3. Standard protocol approvals and patient consent

This study complied with the institutional review board ethical guidelines of our hospital (Second Affiliated Hospital, School of Medicine, Zhejiang University) and was approved by the ethics committee. Written informed consent for education and research purposes was obtained from all patients who participated in the study.

2.4. Statistical analysis

We calculated sensitivity, specificity, and accuracy of the diagnosis. In calculating the accuracy for all the seizures and the specificity of the epileptic seizures, participants were considered to be correct if they correctly selected "nonepileptic event", even if their subsequent choices of PNESs or PNEEs were not correct. In calculating the accuracy of each specific epileptic seizure type, the answer was considered correct when the reviewers chose "epileptic seizure". In calculating the accuracy of PNESs or PNEEs, the answer was considered correct when the reviewers chose "nonepileptic event" and further properly chose PNESs or PNEEs in the next step. The accuracy for each seizure type or event type was calculated by using the following formula:

$$\text{Accuracy} = \frac{\text{Number}_{\text{correct}}}{\text{Number}_{\text{total}}}$$

where $\text{Number}_{\text{correct}}$ is the number of the seizures or events correctly identified and $\text{Number}_{\text{total}}$ is the total number of specific seizure type or event type.

Repeated measures analysis of variance or nonparametric tests were used in the statistical analysis. The statistical methods used are further described in corresponding figure captions. A p value < 0.05 was considered to be statistically significant.

3. Results

3.1. Overall diagnostic reliability

The overall diagnostic accuracy rate for epileptic seizures and nonepileptic events increased slightly from 0.614 to 0.660 after observations of all three seizures ($p < 0.001$, Fig. 1). Interestingly, observing more seizures yielded significant increases in diagnostic accuracy for the neurologist group ($p < 0.001$) and for the physician group ($p < 0.05$) but not for the epileptologist group. The diagnostic accuracy of the epileptologists was significantly better than that of the neurologists ($p < 0.005$) and physicians ($p < 0.001$). Diagnostic accuracy did not differ significantly between the neurologist group and the physician group. After the observation of all three seizures, the accuracy rates of epileptologists, neurologists, and physicians were 0.780, 0.670, and 0.606, respectively.

Both diagnostic sensitivity ($p < 0.005$) and specificity ($p < 0.05$) improved with observing more epileptic seizures. The epileptologists performed better than the physicians ($p < 0.05$) and neurologists ($p < 0.05$) in terms of the diagnostic sensitivity and specificity. However, no statistically significant difference was found between the neurologists and the physicians. Further analysis revealed no significant difference in the diagnostic accuracy of the neurologist and physician groups across seizure types. Hence, we combined the physician and neurologist groups into one "nonepileptologist group" in the following study.