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REVIEW ARTICLE

Electroencephalography in epilepsy: look for what could be beyond the visual inspection

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Abstract

Since its starting point in 1929, human scalp electroencephalography (EEG) has been routinely interpreted by visual inspection of waveforms using the assumption that the activity at a given electrode is a representation of the activity of the cerebral cortex under it, but such a method has some limitations. In this review, we will discuss three advanced methods to obtain valuable information from scalp EEG in epilepsy using innovative technologies. Authors who had previous publications in the field provided a narrative review. Spike voltage topography of interictal spikes is a potential way to improve non-invasive EEG localization in focal epilepsies. Electrical source imaging is also a complementary technique in localization of the epileptogenic zone in patients who are candidates for epilepsy surgery. Quantitative EEG simplifies the large amount of information in continuous EEG by providing a static graphical display. Scalp electroencephalography has the potential to offer more spatial and temporal information than the traditional way of visual inspection alone in patients with epilepsy. Fortunately, with the help of modern digital EEG equipment and computer-assisted analysis, this information is more accessible.

Keywords EEG · Quantitative · Source localization · Voltage topography

Introduction

Since its starting point in 1929, human scalp electroencephalography (EEG) has been routinely interpreted by visual inspection of the waveforms using the assumption that the activity at a given electrode is a representation of the activity of the cerebral cortex under it [1]. In many patients, this method of interpretation is enough to localize a focal epileptiform activity to one hemisphere or even one lobe. However, such a method has limitations; for example, sometimes the negative pole of a dipolar map is not exactly above the region of origin and may be remote [1].

In this review, we will discuss some other advanced methods to obtain valuable information from scalp EEG using innovative technologies. These include spike voltage topography of interictal spikes, a complementary tool with the potential to improve EEG localization in focal epilepsies; electrical source imaging, which provides useful information to localize

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the epileptogenic focus in patients with drug-resistant epilepsy; and, quantitative EEG, a computational method that compresses raw EEG data allowing a large amount of EEG information (several hours) to be displayed on a single screen.

Spike voltage topography

Spike voltage topography or 3-D voltage maps of cortical activity of the interictal spikes is a descriptive way of defining dipole localization and orientation of the interictal epileptiform spikes [1]. Epileptiform sharp waves and spikes are usually cortex negative, meaning the dipolar currents flow into the cortex; therefore, a focal epileptiform activity typically produces a dipolar field with two poles, a negative and a positive (http://www.besa.de/wp-content/uploads/2014/06/BESA-Quick-Guide-on-3D-Maps.pdf). Clinical investigations of epileptiform discharges using voltage topography have been ongoing for more than two decades. Published studies have suggested spike voltage topography of interictal spikes as a way to improve non-invasive EEG localization in focal epilepsies [1] (http://www.besa.de/wp-content/uploads/2014/06/BESA-Quick-Guide-on-3D-Maps.pdf). This data can complement other localizing data (e.g., visual inspection of EEG and imaging studies). However, the diagnostic accuracy and value of this technique should be clarified in future studies.

In one study of 34 patients with temporal lobe epilepsy (TLE) (21 patients with mesial temporal sclerosis (MTS) and 13 patients with non-MTS brain MRI findings) [2], the authors observed that interictal spikes with different orientations may be seen in patients with TLE and even orientation of the interictal spikes in one patient may vary from one interictal spike to another [2]. They also observed that characteristics of the voltage topography maps of the interictal spikes between patients with MTS-TLE were different from that in other TLE patients; spikes with polar orientation were observed in patients with MTS-TLE, but not in patients with other brain MRI findings (odds ratio = 6.98, 95% confidence interval = 0.38 to 127.38; $p = 0.07$). Therefore, detecting an interictal spike with a polar orientation in a patient with TLE may increase the possibility of mesial temporal sclerosis as the underlying etiology [2].

Other published studies that investigated spike voltage topography have shown mixed and at times conflicting results. In one study [3], the authors studied 15 patients; 10 patients had focal epilepsy of presumed mesiotemporal origin and the other five patients had focal epilepsy with non-mesiotemporal or extratemporal epileptic foci. In all patients, visual inspection of EEG traces demonstrated temporal interictal epileptiform discharges. The authors studied the spike voltage topographies and found that there was no significant difference between the two groups [3]. Nevertheless, in another study of 45 patients with focal epilepsy, significant results were observed [4]. Analyses of spike voltage topographies revealed two distinct patterns—type 1, dipolar (negative fields that were sharply defined, had steep voltage gradients, were located inferiorly, and were associated with distinct, contralateral positive fields) and type 2, non-dipolar (broad negative fields that extended to or beyond the midline, gradual voltage gradients, and less clear or no associated positive fields). Correlations with clinical data and intracranial EEG findings suggested that dipolar spikes and sharp waves originated in mesial temporal structures, while non-dipolar spikes and sharp waves arose from temporal or frontal neocortex [4]. Similar findings have been reproduced in other studies [5, 6]. These authors inferred that spike voltage topography was useful in the presurgical evaluation of patients with focal epilepsy [4].

To summarize, spatio-temporal analysis of spike voltage topography may allow for improved localization of likely cerebral origins of interictal epileptiform discharges in focal epilepsies; hence the use of modern techniques may improve accuracy of dipole localization, which may be helpful in non-invasive EEG localization in presurgical evaluation of the patients with drug-resistant focal epilepsies [1, 7–9].

Electrical source imaging

EEG or electrical source imaging (ESI) is a model-based imaging technique that integrates temporal and spatial components of EEG to identify the generating source(s) of abnormal electrical activity associated with seizures [10]. Electrical source localization allows for further analysis of EEG beyond visual inspection alone and may enhance non-invasive localization accuracy of the epileptogenic zone. In source localization, by reconstructing the electric potentials recorded with scalp EEG, the location of the underlying currents can be estimated and merged with structural images of individual patients. Source localization is typically based on the analysis of interictal epileptiform discharges (IEDs), but can also be calculated from ictal EEG discharges. The latter may be a clinical relevance, as the area of IEDs does not necessarily coincide with the epileptogenic zone [10, 11]. More recently, high-resolution (high density) ESI (HR-ESI) using a high number of recording EEG electrodes (128–256 electrodes) has become available [12].

In one study, ESI was performed on 64 identical right anterior temporal spikes (and 48 homologous left anterior temporal spikes) in a patient with MTS-TLE investigated with simultaneous depth and subdural intracranial EEG and scalp EEG [13]. ESI of individual anterior temporal spikes had limited reliability and validity. However, spike averaging of 8 or more identical spikes prior to ESI reliably produced accurate source solutions localized to the anterolateral temporal neocortex [13]. In a recent study with the goal of assessing the anatomical concordance of electric source localizations of interictal discharges with the epileptogenic zone estimated by stereo-EEG (s-EEG) in 74 patients suffering from drug-resistant epilepsy, the authors found a reasonable concordance of ESI and s-EEG in frontal lobe epilepsy, in patients with negative MRIs and in malformations of cortical development (than in other etiologies) [14]. This could be very helpful for surgical planning for difficult patients with drug-resistant epilepsy [15].

In conclusion, ESI is a complementary technique in localization of the epileptogenic zone in patients with drug-resistant epilepsy, who are candidates for epilepsy surgery. ESI allows recording of all source orientations, is sensitive to deep sources, and is less affected by motion artifacts. However, results of ESI should be interpreted with caution and independent support from other diagnostic techniques is still required before proceeding to resective epilepsy surgery. ESI has been recognized as a useful and accurate clinical tool awaiting further validation [16].

Quantitative EEG

Quantitative EEG (QEEG) refers to the mathematical processing of raw EEG data that allows the compression of several hours of raw EEG into a graphic representation to be displayed on a single screen, in contrast to only 10 to 20 s of routine EEG inspection. Visualizing large amounts of compressed EEG data can provide an overview of the temporal evolution of EEG findings over prolonged periods of time. QEEG parameters are often referred to as "trends"; features of commonly used QEEG trends are based on frequency, rhythmicity, asymmetry, and amplitude. For example, on the frequency-based trends, seizures are represented as an increase in frequency and amplitude and appear as a transient increase in power at the frequencies seen during the evolution of the seizure. QEEG simplifies the information by providing a static graphical display, in a way that may render it easily interpretable. One study found no significant differences in the ability of neurophysiologists, EEG technologists, and neuro-ICU nurses to detect seizures on QEEG panels [17]. This suggests that QEEG may offer utility as a bedside monitor for detection of potentially significant electrographic events (e.g., seizures). To explain the benefits of QEEG more in depth, we have to mention that interpreting ICU-EEG recordings is a labor- and time-intensive task; continuous-EEG (c-EEG) recording in critically ill patients generates a large volume of data on a daily basis; for example, a single 24-h recording, when viewed with 15-s display/page, contains 5760 pages of data. Even if reviewed at a speed of five pages per second, it would require approximately 20 min to screen a 24-h study. In reality, the time required ends up being substantially higher when one includes the need to evaluate abnormal or changing patterns, artifacts, video assessment for clinical events, etc. One study found that QEEG-guided review of the raw EEG was able to shorten the review process time by 78% [18]. In addition, interpretation of c-EEG requires a level of subspecialty training in neurophysiology that makes bedside interpretation of raw EEG by ICU staff very difficult. This can lead to significant delays in the recognition of seizures (particularly of non-convulsive seizures and non-convulsive status epilepticus) and appropriate management of critically ill patients. However, these workflow-related limitations can be overcome to some extent with the use of QEEG, as this technique expedites and simplifies the review process significantly. QEEG enhances the ability of the medical team to rapidly assess the effectiveness of treatment when managing recurrent seizures and status epilepticus in critically ill patients.

Multiple studies have investigated the sensitivity of QEEG for seizure detection both in adults and children, but significant methodological heterogeneity has led to a wide range of reported outcomes, making fair comparisons very difficult. Studies evaluating individual QEEG trends in adults or pediatric populations report a wide range of sensitivities for seizure detection (44–83%) [18–23]. Results are even promising when interpretation is performed by non-neurophysiologists with some training in QEEG (pediatric or adult neurology residents, general neurologists, intensivists, and neonatologists), with sensitivities of 41 to 89% [17, 24–26].

However, use of QEEG has historically been controversial for several reasons. For example, selection of segments of the recorded EEG that are free of artifacts, drowsiness, normal variants, and dubious clinical significance becomes critical in quantitative analysis [27]. EEG characteristics may affect QEEG sensitivity; therefore, QEEG should not be a substitute for reviewing raw EEG by an expert. However, by guiding the raw EEG review, QEEG offers significant time savings, while it has acceptable levels of sensitivity and false-positive rates. Treatment decisions should be made on the basis of raw EEG interpretation by neurophysiologists.

Currently, the main use of QEEG is for detection of electrographic seizures, although other uses (e.g., cognitive decline in Parkinson's disease or obstructive sleep apnea syndrome) are being pursued [28, 29]. A variety of other neurological and psychiatric conditions have also been studied using QEEG methods, including dyslexia, dementia, schizophrenia, obsessive-compulsive disorder, substance abuse, and many others [27].

Conclusions

To summarize, scalp electroencephalography has the potential to offer more spatial and temporal information than the traditional way of visual inspection alone. Fortunately, with the help of modern digital EEG equipment and computer-assisted analysis, this information is more accessible. Spike voltage topography of interictal spikes is a potential way to improve non-invasive EEG localization in focal epilepsies. Electrical source imaging is also a complementary technique in localization of the epileptogenic zone in patients who are candidates for epilepsy surgery. Quantitative EEG simplifies the large amount of information in continuous EEG by providing a static graphical display. These are just some of the examples of the great potentials of the information provided by scalp EEG recordings beyond the visual inspection alone. There are also other innovative methods including neural network architecture analysis [30], graph theory methodology [31], machine learning [32], and others [33, 34] to scrutinize EEG signals. A variety of neurological and psychiatric conditions are under investigation using these innovative methods [35, 36].

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Compliance with ethical standards

Conflict of interest Ali A. Asadi-Pooya, M.D., consultant: LLC and UCB Pharma; Honorarium: Cobel Daru; Royalty: Oxford University Press (Book publication). Paul Boon, M.D., has received consultancy and speaker fees from UCB Pharma, LivaNova, Medtronic, and Eisai.

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