Seizure xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Review

Correlation of invasive EEG and scalp EEG

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ARTICLE INFO

Article history:
Received 11 May 2016
Accepted 27 May 2016

Keywords:
Interictal spikes
Source localization
Intracranial recordings
Refractory epilepsy
Epilepsy surgery
Electroencephalography

ABSTRACT

Ever since the implementation of invasive EEG recordings in the clinical setting, it has been perceived that a considerable proportion of epileptic discharges present at a cortical level are missed by routine scalp EEG recordings. Several *in vitro*, *in vivo*, and simulation studies have been performed in the past decades aiming to clarify the interrelations of cortical sources with their scalp and invasive EEG correlates. The amplitude ratio of cortical potentials to their scalp EEG correlates, the extent of the cortical area involved in the discharge, as well as the localization of the cortical source and its geometry have been each independently linked to the recording of the cortical discharge with scalp electrodes. The need to elucidate these interrelations has been particularly imperative in the field of epilepsy surgery with its rapidly growing EEG-based localization technologies. Simultaneous multiscale EEG recordings with scalp, subdural and/or depth electrodes, applied in presurgical epilepsy workup, offer an excellent opportunity to shed some light to this fundamental issue. Whereas past studies have considered predominantly neocortical sources in the context of temporal lobe epilepsy, current investigations have included deep sources, as in mesial temporal epilepsy, as well as extratemporal sources. Novel computational tools may serve to provide surrogates for the shortcomings of EEG recording methodology and facilitate further developments in modern electrophysiology.

1. Introduction

Ever since the first recordings in humans, performed by Hans Berger in 1924 [1], scalp EEG has been a key instrument in epilepsy workup, guiding primary diagnosis, epilepsy classification and treatment. The first intracranial EEG recordings, performed by Reginald Bickford in epilepsy patients in 1948 [2], revealed a striking discrepancy between seemingly negative scalp EEGs and an abundance of epileptic discharges in invasive EEGs. Several subsequent *in vitro*, *in vivo*, and simulation studies have been conducted to clarify the relationship between the epileptic discharges recorded at the cortical level and their scalp correlates, especially in terms of amplitude of the original discharge and extent of the cortical activation.

The correlation of cortical sources with their corresponding scalp EEG discharges is particularly crucial for epilepsy surgery that has since been established as a safe and effective treatment option for pharmacoresistant patients. In this context, scalp EEG is a major localizing tool that determines invasive electrode placement or even surgical resection, whereas invasive EEG constitutes the gold standard for defining the localization and extent of the epileptogenic zone [3]. The current methodology of invasive explorations in epilepsy patients has, however, inherent limitations, thus rendering multimodal comparisons particularly challenging [4]. Subdural recordings offer extensive cortical coverage, but are prone to sampling limitations for deep sources, such as sulcal sources [5–7]. Depth electrode recordings provide information for selected deep structures [7–9], but are plagued from sampling limitations due to incomplete and irregular cortical coverage. The rapid developments in computational studies, including simulation as well as electrical source localization (ESL) methods, address the urgent need to compensate for the

Abbreviations: EEG, electroencephalography; ECoG, electrocorticography; ESL, electrical source localization; MEG, magnetoencephalography; fMRI, functional magnetic resonance imaging; SEEG, stereoelectroencephalography; CT, computer tomography.

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http://dx.doi.org/10.1016/j.seizure.2016.05.018
1059-1311/

shortcomings of both subdural and depth recordings and, most of all, to clarify their correlation with scalp EEG recordings [5,8,10,11].

2. Historical studies

Penfield and Jasper, deriving from intraoperative electrocorticography (ECoG) recordings, were the first to propose that a critical minimum amplitude of cortical activity is necessary for epileptic discharges to be recorded by scalp EEG [12]. They suggested a ratio of 10 to 1 between the amplitudes of cortical and scalp discharges, below which cortical discharges would likely be missed on the scalp, whereas the amplitude of the scalp potentials would increase with the amplitude of the original cortical discharge. This ratio, however, was obtained indirectly by comparing the average amplitude of the routine EEG prior to surgery with the amplitude of the subsequent intraoperative ECoG, and was challenged by others that reported considerably lower ratios.

Simultaneous scalp and invasive EEG recordings provided a more suitable setting to determine the correlations of scalp to cortical potentials in the following years. The first combined scalp, subdural and depth recordings for clinical purposes were performed in temporal lobe epilepsy patients by Abraham and Marsan in 1958 [13], verifying that the amplitude of cortical spikes determines their recording by scalp EEG electrodes, at least to a certain extent. The authors proposed that the extent of the activated cortical area, but not the morphology or the duration of the resulting cortical discharge, determines the presence and amplitude of its scalp EEG correlate. Two further studies in animals [14,15] verified the role of the scalp as a spatial averager of electrical activity, exclusively transmitting components common to and synchronous over extensive cortical areas.

Of all studies attempting to determine the extent of cortical activation required to produce epileptic discharges recordable in scalp EEG, that of Cooper et al. [16] has gained the most widespread acceptance, proposing a minimum of 6 cm^2 of synchronized cortical activity. This estimation, however, is based on a head-phantom using *in-vitro* measurements of a piece of fresh cadaver skull, a pulse generator connected to saline-soaked cotton balls placed on the inside of the skull, an artificial dura made of polyethylene, and EEG electrodes recording from the exterior of the skull. The 6 cm^2 estimate of the required extent for cortical sources derived from the area of multiple pinholes punched into the polyethythene sheet, when EEG signals were first recorded from the electrodes on the outside of the skull. Additionally, measurements estimating the source area were made in the absence of EEG background activity, thus rendering any conclusions uncertain.

3. Contemporary studies

3.1. Computational studies

In 1999, Merlet at al. [17] analyzed simultaneous scalp EEG and stereoelectroencephalography (SEEG) recordings and compared dipole localizations with the distribution of SEEG potentials concurrent with scalp EEG discharges. The cortical discharges that corresponded to scalp EEG spikes were never focal but involved 8-21 SEEG contacts for temporal and 15-10 SEEG contacts for extra-temporal sources. Interestingly, no scalp EEG spikes were observed that corresponded exclusively to focal activity limited to mesial temporal structures. The authors concluded that the involvement of lateral temporal neocortex, additional to the mesial temporal structures, is required for the generation of scalp-visible EEG spikes. They further suggested that modeling a scalp-visible EEG spike by a single source located in the mesial aspect of the temporal lobe might be unreliable.

The relationship between the EEG signals and the spatio-temporal configuration of the underlying cortical sources was more recently addressed in the study of Cosandier-Rimélé et al., using a realistic model of simultaneous scalp and intracerebral EEG generation [11]. The proposed model includes both an anatomically realistic description of the spatial features of the sources, as a convoluted dipole layer, and a physiologically relevant description of their temporal activities, as coupled neuronal populations. The authors confirmed that the cortical area involved in scalp EEG spikes is rather large, since a spike-to-background amplitude ratio of >2.8 corresponded to a cortical source of 24 cm^2 for the intracerebral EEG and 30 cm^2 for the scalp EEG. Furthermore, it was shown that the location of the cortical generator relative to the recording electrodes strongly influences EEG signal properties, thus underlining the importance of source geometry in this context.

3.2. Simultaneous multiscale EEG studies

The last decade saw the advent of several novel technologies that derive from interictal EEG spikes, such as electrical source localization (ESL), magnetoencephalography (MEG), and functional magnetic resonance imaging (fMRI) [5,6,9,18–21] rendering the correlation of cortical-to-scalp epileptic discharges even more crucial. At the same time, the advances of EEG technology permitted simultaneous scalp and invasive EEG recordings in the routine workup of epilepsy surgery patients, thus fuelling further research regarding scalp EEG spikes and their cortical substrates.

In a seminal study, Tao et al. [22] analyzed the simultaneous scalp and subdural grid recordings of temporal lobe epilepsy patients, aiming to determine the extent of cortical sources that produce scalp EEG spikes. Cortical discharges with and without scalp EEG correlates were visually identified, and the extent of cortical activation was estimated from the number of electrode contacts demonstrating concurrent depolarization. The authors concluded that cortical sources of scalp EEG spikes commonly involved a synchronous activation of at least 10 cm^2 of gyral cortex, whereas much larger cortical source areas of 20–30 cm^2 corresponded to prominent scalp EEG spikes, and cortical source areas of <6 cm^2 never resulted in scalp EEG spikes.

The same methodology was applied 2 years later to ictal discharges in temporal lobe epilepsy patients, aiming to delineate the cortical substrates necessary for generating scalp EEG patterns [23,24]. In this study, less than half of subdural EEG ictal discharges presented a scalp EEG correlate, with a mean latency of 0.4 s for seizures of neocortical origin and 7 s for seizures of mesio-temporal origin. Ictal onset was apparently missed in scalp EEG for mesial temporal cortical sources, whereas the delayed ictal pattern occurring in scalp EEG with a latency of up to 16 s mirrored propagation and served rather to lateralize than to localize the cortical seizure onset. The authors concluded that sufficient extent of cortical activation of >10 cm^2 as well as synchrony, gradually achieved in the course of propagation, were required for scalp-recordable EEG patterns, in accordance with their findings for interictal discharges.

The contribution of electrical potentials arising from deep sources to scalp EEG, a crucial issue in the presurgical workup of temporal lobe epilepsy [7,25,26], has recently been addressed in a study of simultaneous scalp and intracerebral EEG [8]. Based on the routine visual analysis of scalp EEG in simultaneous scalp and invasive recordings, it has been previously postulated that interictal [27,28] as well as ictal discharges [29] confined to mesial temporal structures escape detection in scalp EEG. This has been attributed to their deep localization and infolded geometry, leading to a cancellation of electrical potentials, and to the blurring effect of the superimposed neocortical background activity [30–33]. It should be noted that, so far, this key issue has been analyzed in invasive EEG studies performed mainly with foramen ovale or subdural electrodes [27,28,34–38] and only rarely with depth electrodes [13,27,29]. In the study of Koessler et al. [8], it has been confirmed that epileptic discharges arising from mesial temporal sources are not spontaneously visible in scalp EEG. However, mesial temporal sources significantly contribute to scalp EEG, as can be demonstrated by extraction from the respective background activity (Fig. 1).

Whereas all previous *in vivo* studies, both historic and contemporary, have been conducted exclusively in temporal lobe epilepsy, these observations have only recently been extended to extratemporal epilepsy [5]. Extratemporal sources are equally prevalent as temporal sources in pediatric epilepsy surgery and constitute a major challenge in terms of electroclinical correlations and postsurgical outcomes [39–41]. In particular, frontal lobe epilepsy studies have reported 12–37% of patients without any scalp EEG spikes at all, and a predominance of widespread unilateral or even bilateral spikes in the remaining cases [42–45]. Factors contributing to the disparity between scalp EEG spikes and their cortical substrates include the inaccessibility of large parts of the frontal lobe to scalp electrodes, the extent of intralobar and interlobar connections, and the presence of secondary bilateral synchrony. Focal interictal spikes have been observed in scalp EEG mainly in association with dorsolateral frontal sources, whereas medial and orbitofrontal sources have been reported to give rise to bifrontal spikes, if any, with unilateral, albeit often falsely lateralizing, predominance [42,45]. In the study of Ramantani et al. [5], deriving from simultaneous subdural and scalp EEG recordings in frontal lobe epilepsy patients, it was shown that not only dorsolateral but also or- bitofrontal and medial-frontal sources can be detectable in scalp EEG. Both the extent of cortical activation and the subdural spike-to-background amplitude ratio determined the detection of cortical sources in frontal lobe epilepsy.

Dense array recordings, increasingly used in presurgical workup in the last decade though yet unsuitable for long-term recordings, have the potential to significantly increase the sensitivity of scalp EEG. The studies of Yamazaki et al. [37,46],

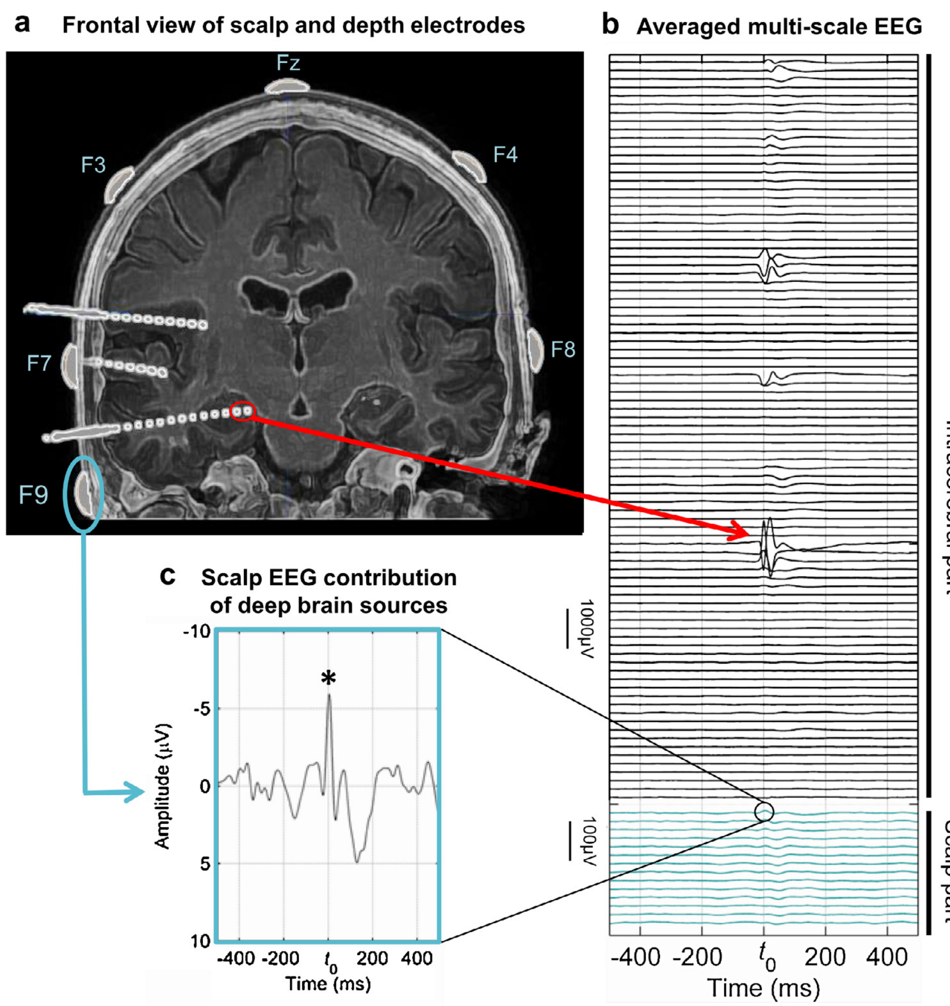

Fig. 1. Contribution of multiscale EEG recordings to the detection of deep (mesial) epileptic sources in an illustrative case of temporal lobe epilepsy [8] (a) Schematic illustration of a coronar MRI-CT co-registration with the six scalp (names in blue) and three intracerebral electrodes (trajectories in white) used for multiscale EEG recordings. Intracerebral electrodes presented 5 to 15 platinum multi-contacts. Scalp electrodes consisted of sterile silver–silver chloride disks. Intracerebral contacts circled in red were situated in the mesial part of the temporal lobe and indicated the position of the epileptic source. (b) Averaged multiscale EEG signals derived from 368 epileptic events, confined in the mesial part of the temporal lobe, automatically detected and marked (t_0). The maximum mean amplitude was -826 μV and the signal-to-noise ratio 20.4 dB. (c) Enlarged view of the scalp signal in the averaged multiscale EEG recording. The mesial epileptic source contribution to the scalp part of the multiscale EEG was recorded with maximum amplitude in the F9 scalp electrode. The star indicates that the corresponding averaged multiscale EEG signal recorded from the F9 scalp electrode at t_0 was statistically significant ($\alpha = 0.05$).

deriving from simultaneously recorded 256-channel dense array EEG and intracranial EEG provide 45% detection rates for mesial temporal and 56% for neocortical extratemporal spikes by visual inspection of the scalp EEG. Interestingly, mesial temporal lobe spikes detected in these dense array EEG recordings presented a considerably higher amplitude compared with detected neocortical spikes.

4. Conclusion

The spatio-temporal resolution of scalp EEG apparently has intrinsic limitations in the localization of its corresponding cortical sources. The decoding of interrelations between cortical sources and their scalp EEG correlates is of cardinal importance for the development and validation of novel diagnostic tools such as ESL, MEG, and fMRI that may constitute potent surrogates for invasive recordings in the future.

Conflict of interest: none.

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