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Rolling in the Deep: Surface EEG Seizures Viewed Through the Lens of Stereo EEG

Intracerebral Correlates of Scalp EEG Ictal Discharges Based on Simultaneous Stereo-EEG Recordings

Ferrand M, Baumann C, Aron O, Vignal JP, Jonas J, Tyvaert L, Colnat-Coulbois S, Koessler L, Maillard L. *Neurology*. 2023 Mar 24:10.1212/WNL.0000000000207135. doi:10.1212/WNL.0000000000207135. Epub ahead of print. PMID: 36963841.

Background and objectives: It remains unknown to what extent ictal scalp EEG can accurately predict the localization of the intra-cerebral seizure onset in pre-surgical evaluation of drug resistant epilepsies. In this study, we aimed to define homogeneous ictal scalp EEG profiles (based on their first ictal abnormality) and assess their localizing value using simultaneously recorded scalp EEG and Stereo-EEG. Methods: We retrospectively included consecutive patients with drug-resistant focal epilepsy who had simultaneous stereo-EEG and scalp EEG recordings of at least one seizure, in the epileptology unit in Nancy, France. We analyzed one seizure per patient and used hierarchical cluster analysis to group similar seizure profiles on scalp EEG and then performed a descriptive analysis of their intra-cerebral correlates. Results: We enrolled 129 patients in this study. The hierarchical cluster analysis showed six profiles on scalp EEG first modification. None was specific to a single intra-cerebral localization. The "normal EEG" and "blurred EEG" clusters (early muscle artifacts) comprised only five patients each and corresponded to no preferential intra-cerebral localization. The "temporal discharge" cluster (n = 46) was characterized by theta or delta discharges on ipsilateral anterior temporal scalp electrodes and corresponded to a preferential mesial temporal intra-cerebral localization. The "posterior discharge" cluster (n = 42) was characterized by posterior ipsilateral or contralateral rhythmic alpha discharges or slow waves on scalp and corresponded to a preferential temporal localization. However, this profile was the statistically most frequent scalp EEG correlate of occipital and parietal seizures. The "diffuse suppression" cluster (n = 9) was characterized by a bilateral and diffuse background activity suppression on scalp and corresponded to mesial, and particularly insulo-opercular, localization. Finally, the "frontal discharge" cluster (n = 22) was characterized by bilateral frontal rhythmic fast activity or pre-ictal spike on scalp and corresponded to preferential ventrodorsal frontal intra-cerebral localizations. Discussion: Hierarchical cluster analysis identified six seizure profiles regarding the first abnormality on scalp EEG. None of them was specific of a single intra-cerebral localization. Nevertheless, the strong relationships between the "temporal", "frontal", "diffuse suppression" and "posterior" profiles and intra-cerebral discharges localizations may contribute to hierarchize hypotheses derived from ictal scalp EEG analysis regarding intra-cerebral seizure onset.

Commentary

Stereotactic electroencephalography (stereo EEG) offers an opportunity to study in situ brain physiology and pathology, even in regions "invisible" by scalp recordings.[1] Yet, stereo EEG signal acquisition requires meticulous attention to trajectory planning. In that regard, preimplantation scalp recordings play a cardinal role in deciding the need for further investigation and the shape that this will take. Background knowledge of scalp-intracranial EEG correlations can assist in careful navigation of such decisions and has therefore attracted increased scientific interest in the past decades.[2]

The current study[3] expands our knowledge in the field by examining simultaneous surface-stereo EEG recordings from 129 patients with drug-resistant epilepsy (DRE) undergoing surgical evaluation. Patients with poor scalp EEG coverage, noninterpretable scalp EEG, no seizures, and nonlocalizing stereo EEG seizures were excluded. For each patient, the most representative seizure was analyzed on the scalp by 2 epileptologists blinded to the stereo EEG recordings and intracranially by group consensus during a multidisciplinary conference. In addition to its morphology and topography, other ictal characteristics such as duration and latency between intracranial and surface EEG seizures were evaluated. Hierarchical cluster analysis identified 6 scalp EEG seizure patterns ("normal," "blurred," "temporal," "posterior," "diffuse suppression," and "frontal"). None of them was specific to a single intracerebral topography.

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Yet, the "temporal" cluster was typically ipsilateral in the theta/delta range and corresponded preferentially to mesial temporal localization, the "posterior" cluster was ipsilateral or contralateral alpha range or slow frequencies corresponding preferentially to temporal localization (though occipital and parietal seizures were typically in that group too), the "diffuse suppression" cluster was typically bilateral and corresponded to mesial and insulo-opercular localization and the "frontal" cluster was characterized by bilateral fast frequencies corresponding preferential to a frontal localization. The short and longest seizure duration were seen with the "normal" and the "temporal" scalp EEG profile, respectively.[3]

The strengths of this study[3] are the investigation of a relatively large number of patients with diverse pathologies. The recordings were concurrent and extensive. A thorough cluster analysis methodology was deployed to reconcile the extensive heterogeneity. On the other hand, correlations were retrospective and limited by the available intracerebral electrodes that were implanted based on individualized electroclinical hypotheses and anatomical constraints ($\sim$60% of the cases achieved seizure freedom eventually). Despite all good intents for an unbiased approach, the reviewers of both the scalp and the intracranial EEG recordings were not blinded to the patients' clinical and radiological data ($\sim$65% of the cases were lesional). Albeit representative, a single seizure was evaluated per patient, introducing selection bias, particularly since individualized anti-seizure medication withdrawal or rescue drugs administration may have inevitably affected some of the collected variables (e.g., intracranial-scalp EEG propagation/latency and seizure duration). Finally, when drawing conclusions about scalp EEG utility, one should also remember that straight-forward cases were not implanted and, hence, excluded from this analysis. Conversely, several implanted cases did not have adequate scalp EEG coverage to be included, although they did not substantially differ in their characteristics from those that did.[3]

These methodological considerations notwithstanding, this study highlights the value of concurrent scalp-intracranial EEG in the presurgical evaluation of patients with DRE. At the same time, it acknowledges that scalp EEG is not flawless and that careful integration of semiological and radiological information is needed to define a cogent hypothesis about the epileptogenic zone. Prior simultaneous surface-intracerebral EEG comparison have corroborated that scalp EEG detects stereo EEG seizures only 1/3 of the time when they are focal aware or subclinical, particularly if their duration is brief.[4] Due to high skull resistivity and because of the distance between the cortical source and the sensors, scalp EEG seizure patterns are often overshadowed by background EEG activity or artifacts.[5] The extent of the cortical area engaged in the ictal discharge, as well as the topography and geometry of the cortical generator have been each independently linked to the seizure recording with scalp electrodes.[2] Unsurprisingly, scalp EEG is a poor spatial localizer and even lateralizer.[6] No ictal scalp pattern corresponds to a specific intracerebral pattern.[7] Contrary to the current study that showed a brief lag between the scalp and the stereo EEG recorded seizures, prior studies showed a mean delay of 14 seconds.[4] As a result, ictal signs appeared on average with a lag of 14 seconds after scalp EEG onsets, while that time was nearly doubled for stereo EEG onsets.[4] The presence of an insufficient electrographic latency or discordant location and EEG pattern between scalp and stereo EEG recordings was associated with a lower chance of successfully detecting the seizure onset zone.[8]

As also shown in this study where approximately ¼ of the initial cohort had poor coverage or uninterpretable waveforms, concurrent scalp EEG recordings during stereo EEG evaluations are not always straight-forward. To maximize recording time, application of the scalp leads right after the stereo EEG implantation is desirable but often constricted by operative time and need for unobstructed post-implantation imaging to guide reconstruction of stereo EEG electrodes positioning. Recording duration may be further limited due to concerns related to comfort and risk of infection. Full scalp EEG coverage may be confined by stereo EEG electrodes entry points. Interpretation may be affected by suboptimal positioning compared to standard locations and skull defects or the omnipresent challenges that physiologic, instrumental, and environmental artifacts pose.[7]

Nevertheless, standardizing the simultaneous recording between scalp and intracranial EEG in invasive presurgical evaluations offers multiple benefits. It facilitates identification of different states allowing for better characterization of physiological activity in wakefulness and sleep.[1] It also enables clarification of ambiguous interictal patterns such as artifacts and normal variants that can be occasionally misinterpreted for pathologic abnormalities.[1] In patients with unilateral implantations, it can provide noninvasive coverage of the contralateral hemisphere, partially mitigating the risk of false seizure lateralization.[9] In patients with scalp onsets before stereo EEG onset, it raises a red flag of suboptimal implantation strategy.[4] In patients with seizures induced by potential traumatic effect during electrode implantation, it allows for comparison of their morphology with the previously recorded ictal patterns during the phase I investigation, allowing for correct identification of the patient's habitual seizures.[1] Last but not least, it increases our understanding of the complexity of epileptogenic networks and their association with clinical outcomes.[4]

Future directions in the field of scalp-intracranial EEG interrelations include expansion to frequencies beyond the Berger range (e.g., infra-slow activity and high-frequency oscillations),[10] integration of high resolution, source localization and computational EEG analysis techniques,[5] decoding of the role of subcortical structures (e.g., thalamic or basal ganglia nuclei),[11] exploration of the spatiotemporal dynamics of seizures through simultaneous multimodal investigations with structural and functional neuroimaging incorporating ictal semiology,[2] and characterization of maturational aspects specific to underlying pathophysiology.

As astutely stated, "intracerebral electrodes suffer from some degree of tunnel vision, although what they see through the tunnel is very distinct and precise."[12] Correlating the light at the end of the tunnel with that in the beginning of it provides us with a brighter roadmap in the quest for the epileptogenic zone.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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