Chapter 48
Use of Full-Band EEG for Noninvasive Ictal Localization

Sampsa Vanhatalo
Department of Clinical Neurophysiology and Epilepsy Surgery Program, University of Helsinki, Helsinki, Finland

Juha Voipio
Department of Biological and Environmental Sciences, University of Helsinki, Helsinki, Finland

Kai Kaila
Department of Biological and Environmental Sciences, and Neuroscience Center, University of Helsinki, Helsinki, Finland

John W. Miller
Departments of Neurology and Neurological Surgery, Regional Epilepsy Center, University of Washington, Seattle, Washington, U.S.A.

Mark D. Holmes
Department of Neurology, Regional Epilepsy Center, University of Washington, Seattle, Washington, U.S.A.

BACKGROUND

Determination of the epileptogenic zone is typically attempted by ictal video electroencephalographic (EEG) recordings with scalp electrodes, correlated with other noninvasive studies, particularly neuroimaging. However, conventional scalp EEG gives often equivocal information about the location of seizure origin, or it is incongruent with other tests, leading to the requirement for invasive recordings (1–4). The spatial resolution of the conventional scalp EEG can be enhanced with existing, but clinically unexploited, source localization techniques (5). However, there remains an obvious need for better noninvasive detection of seizure-related signals that arise in brain structures (e.g., deep temporal lobe and neocortex) typically involved in seizure initiation. It is evident from our recent work that detection of such signals is greatly improved with an extended EEG bandwidth (6). While conventional EEG has a limited bandwidth (typically 0.5–70 Hz), distorting or ignoring slow EEG events, a full-band EEG (FbEEG) that detects all physiological frequencies can be obtained using a DC-coupled (direct current coupled) amplifier and proper electrode–skin interface. This
chapter describes the use of very slow (infraslow), ictal EEG events to locate the epileptogenic zone.

A large number of animal experiments, as well as early invasive recordings on humans, have established that seizures are associated with very slow EEG responses often referred to as DC shifts (7–11). However, until our recent work, there have been no noninvasive studies recording focal seizures with DC amplifiers (6). Other recent studies have used conventional EEG amplifiers together with Ag/AgCl scalp electrodes or metal subdural electrodes. Even with this technical limitation (see section “Technical Requirements and Practical Aspects”), these studies have observed ictal low-frequency fluctuations that were congruent with but more localized than the fast ictal EEG activity (12–14). Thus, both the earlier animal work, as well as the recent clinical recordings, demonstrate the advantage of studying very slow ictal EEG changes and the need to develop practical methods to achieve true FbEEG recordings at the bedside (15,16).

ORIGINS OF SLOW EEG EVENTS

Generation of slow ictal EEG responses likely includes several mechanisms in addition to the intracortical neuronal current loops implicated in the generation of higher frequency oscillations. There is evidence that glial cells may be an important generator of slow DC shifts, which may arise even in gliotic human hippocampus (i.e., with Ammon’s horn sclerosis) (17–21). Several studies have also provided evidence supporting the presence of intracranial, non-neural (i.e., not neurons or glia) generation of slow DC shifts, especially those arising at the blood–brain barrier (22–27). Taken together, it seems likely that the ictal slow DC shifts arise from multiple cellular structures and mechanisms. Since these mechanisms are presumably confined to the volume of brain engaged in the ictus, three-dimensional source localization of the ictal DC shifts may, indeed, have analogies with several neuroimaging modalities [e.g., positron emission tomography (PET) or single photon emission computed tomography (SPECT)].

TECHNICAL REQUIREMENTS AND PRACTICAL ASPECTS

Reliable recording of slow EEG events requires (Fig. 1) a genuine DC-coupled amplifier with sufficiently high input impedance and DC stability as well as a wide enough dynamic range (preferably ±200 mV or higher). Amplifiers with an automatic input offset compensation have been used to extend the dynamic range and to avoid amplifier saturation due to possible artifactual changes or drift of the baseline. The first commercial DC-coupled amplifiers suitable for clinical use have recently become available. Also the electrode–gel and skin–gel interfaces must be DC coupled and sufficiently stable. The electrodes must be nonpolarizable, since all polarizable electrode materials (such as gold, tin, platinum, or steel) are coupled in a mainly capacitive manner to their external environment, which leads to high-pass filtering at the electrode–gel interface (28,29). Among the currently available electrodes only those based on Ag/AgCl are adequate (29), and the sintered contact elements used in our work have proved to be both maintenance-free and very stable in recordings lasting up to several days (6,22,23,29,30). Chloride is required in the gel for stable operation of Ag/AgCl electrodes, hence precluding the use of electrolyte-free gels (29). A stable skin–gel contact requires prevention of gel drying, good attachment of the electrode to the skin, as well as short-circuiting of skin-borne signals [caused by movements and
galvanic skin response (GSR) by penetration of the epithelium through the basal lamina at the recording site (22,31–33).

Implementation of FbEEG recordings into routine clinical practice could be remarkably easy. DC-coupled amplifiers are not more expensive than the current clinical amplifiers, suitable electrode material (Ag/AgCl) is sterilizable and has been in clinical use for decades, attachment of the electrodes on skin is practically as quick as with the conventional electrode types, and finally, sufficient scratching of the skin is so painless that we have successfully done that even with sleeping neonates (30).

The lack of scalp FbEEG recordings of focal seizures in the literature is mostly due to the technical difficulties in the early pioneering work in the 1960s (34–36). In our experience, this technique is reliable and readily applicable to bedside recordings once the basic technical requirements are met (16,29,37,38). The limitations of the FbEEG technique are mostly similar to those of the conventional EEG. When comparing FbEEG and conventional EEG, the visual appearance of slow artifacts (e.g., eye and tongue movements) are somewhat different due to the lack of high-pass filtering in the former, and hence some experience is needed for their proper identification (6,39,40). Distinguishing between artifacts and seizure-related DC shifts is, however, easy because artifacts have their characteristic waveforms with a typically faster time course (only up to a few seconds) and usually a particular global distribution. Many artifacts can be very efficiently eliminated by using median filters or spatial filters readily available in pertinent analysis softwares (41,42). Skin potentials (“sweat artifacts”) do not cause problems in FbEEG recordings of the present kind because they have been excluded by short-circuiting (see above). Movement artifacts just before and during seizure onset may occasionally make the evaluation of DC shifts difficult. However, most of the movement artifacts can be avoided by firm attachment of the electrodes to the skin (e.g., with collodion), and by using appropriate placing of the reference electrode (e.g., vertex).

**FbEEG RECORDINGS OF FOCAL SEIZURES**

We have recently conducted FbEEG recordings on epilepsy patients undergoing presurgical evaluation (6). Our results have clearly demonstrated that focal seizures are associated with DC shifts confined to the seizure focus (Fig. 2). The ictal DC shifts begin within seconds of electrographic seizure initiation, and they continue throughout
the seizure with the amplitude fluctuating slowly between few tens of microvolts to over a hundred microvolts (Fig. 2). The polarity of the DC shift is typically negative above the ictal focus, and the spatial extent of the shift may ultimately cover several brain regions upon spread of the seizure activity. The relatively large spatial distribution of the ictal DC shifts call for particular attention to how offline re-referencing is performed, and often a computerized source localization (Fig. 3E) may help in getting an unbiased signal location. An examination of a series of temporal lobe epilepsy cases with data from simultaneous intracranial recordings showed that the onset of the scalp-recorded DC shift discloses the side of seizure initiation, and the extent of the DC shift reflects spreading of the seizure activity (Fig. 3). As yet unpublished data based on three-dimensional source analysis have shown that focal DC shifts may appear already before the seizure activity becomes obvious in the conventional EEG (Fig. 3B, C). The geometry of the ictal brain areas is often complex (e.g., in mesial temporal lobe onset seizures), and the polarity of the DC shift in a given derivation may change during the spread of seizure activity (Fig. 3B). Hence, in an attempt to identify and locate DC shifts originating from the seizure initiation focus, DC shifts of either polarity should be sought at and before the electrographic seizure onset.

CONCLUSIONS

Our recent methodological, physiological, and clinical studies have shown that FbEEG is relatively easy and practical at bedside. Ictal DC shifts are consistently seen in scalp recordings, and the DC shifts give information that agrees with seizure lateralization as defined by the other established criteria. Hence, very slow EEG signals may provide invaluable information in noninvasive determination of the side of seizure origin.

Finally, it is notable here that FbEEG records all EEG frequencies. Its wider bandwidth covering low frequencies does not lead to any compromise in recording of fast or even ultrafast events (7a,43). In addition to this, DC-coupled amplifiers have superior artifact tolerance, which per se will likely make them penetrate clinical EEG markets in the near future. Once this new EEG amplifier generation is implemented in the clinic, the actual recording bandwidth will be determined only by the low-frequency compatibility of the skin–electrode interface. Thus, the use
Figure 3  (A–E) FbEEG recording during a left-side onset, complex partial seizure, with simultaneous recording from subdural strip electrodes. Traces in (A)–(C) are all in the same time scale [amplitude bar 200 μV for (A) and (C), 30 μV for (B)], and from the same signal: (A) shows the seizure with FbEEG recording, (B) shows the slow component subtraction of a highpassed [as in (C)] signal from the FbEEG only, whereas (C) demonstrates the signal with conventional settings (i.e., high-pass filtered at 0.5 Hz). Traces in the bottom (D) are selected channels from an intracranial recording, which has been stretched slightly to better illustrate the changes in fast activity. Seizure onset (mesial) and spread (to lateral) in the intracranial EEG are shown with respective arrows, and seizure spread to right mesial TL is shown with an asterisk. Note the prominent positive DC shift in the left temporal derivations after mesial TL activation, and the negative DC shift later after neocortical spread. Three-dimensional analysis (E) of the DC shifts before the onset of fast spiking demonstrates a prominent activity in scalp potential distribution (top figure), as well as in the cortical current source density (middle and bottom; minimum-norm estimate). All derivations in FbEEG are referred to a linked Cz+Pz. Lateral eye movement artifacts before the seizure [marked with ⊕ in trace (A)] have been removed offline in trace (B) before (A)–(C) subtraction in order to improve the visual clarity of the later occurring DC shift. Abbreviations: RST, right mesial TL; RLT, right lateral temporal lobe; LST, left mesial TL; LLT, left lateral temporal lobe. Source: From Ref. 6.
of proper electrodes and electrode–skin contacts (see above and Ref. 29) will permit recordings of all physiologically and clinically relevant EEG frequencies, and FbEEG will most likely become a new clinical standard.

REFERENCES