



## EEG Wave of the Future: The Video-EEG and fMRI Suite?

### Mapping Preictal and Ictal Haemodynamic Networks Using Video-Electroencephalography and Functional Imaging.

Chaudhary UJ, Carmichael DW, Rodionov R, Thornton RC, Bartlett P, Vulliemoz S, Micallef C, McEvoy AW, Diehl B, Walker MC, Duncan JS, Lemieux L. *Brain* 2012;135:3545–3663.

Ictal patterns on scalp-electroencephalography are often visible only after propagation, therefore rendering localization of the seizure onset zone challenging. We hypothesized that mapping haemodynamic changes before and during seizures using simultaneous video-electroencephalography and functional imaging will improve the localization of the seizure onset zone. Fifty-five patients with  $\geq 2$  refractory focal seizures/day, and who had undergone long-term video-electroencephalography monitoring were included in the study. 'Preictal' (30 s immediately preceding the electrographic seizure onset) and ictal phases, 'ictal-onset', 'ictal-established' and 'late ictal', were defined based on the evolution of the electrographic pattern and clinical semiology. The functional imaging data were analysed using statistical parametric mapping to map ictal phase-related haemodynamic changes consistent across seizures. The resulting haemodynamic maps were overlaid on co-registered anatomical scans, and the spatial concordance with the presumed and invasively defined seizure onset zone was determined. Twenty patients had typical seizures during functional imaging. Seizures were identified on video-electroencephalography in 15 of 20, on electroencephalography alone in two and on video alone in three patients. All patients showed significant ictal-related haemodynamic changes. In the six cases that underwent invasive evaluation, the ictal-onset phase-related maps had a degree of concordance with the presumed seizure onset zone for all patients. The most statistically significant haemodynamic cluster within the presumed seizure onset zone was between 1.1 and 3.5 cm from the invasively defined seizure onset zone, which was resected in two of three patients undergoing surgery (Class I post-surgical outcome) and was not resected in one patient (Class III post-surgical outcome). In the remaining 14 cases, the ictal-onset phase-related maps had a degree of concordance with the presumed seizure onset zone in six of eight patients with structural-lesions and five of six non-lesional patients. The most statistically significant haemodynamic cluster was localizable at sub-lobar level within the presumed seizure onset zone in six patients. The degree of concordance of haemodynamic maps was significantly better ( $P < 0.05$ ) for the ictal-onset phase [entirely concordant/concordant plus (13/20; 65%) + some concordance (4/20; 20%) = 17/20; 85%] than ictal-established [entirely concordant/concordant plus (5/13; 38%) + some concordance (4/13; 31%) = 9/13; 69%] and late ictal [concordant plus (1/9; 11%) + some concordance (4/9; 44%) = 5/9; 55%] phases. Ictal propagation-related haemodynamic changes were also seen in symptomatogenic areas (9/20; 45%) and the default mode network (13/20; 65%). A common pattern of preictal changes was seen in 15 patients, starting between 98 and 14 s before electrographic seizure onset, and the maps had a degree of concordance with the presumed seizure onset zone in 10 patients. In conclusion, preictal and ictal haemodynamic changes in refractory focal seizures can non-invasively localize seizure onset at sub-lobar/gyral level when ictal scalp-electroencephalography is not helpful.

### Commentary

Treatment-resistant epilepsy remains a challenge for roughly one-third of patients with epilepsy (1). Although epilepsy surgery provides an excellent treatment option for some patients, the process of identifying proper candidates remains a labor-intensive process. For patients without clear MRI lesions or with discordant MRI and video-EEG data, additional testing is often required to determine if a patient is a candidate for

surgery. The combination of presurgical tests "required" varies between and within comprehensive epilepsy centers and is often guided by the resources available within the region; many centers have developed particular expertise in one or more of these methods (e.g., PET or MEG) and may have limited or no access to another.

Even with the available tools, many patients are poorly localized, leading to extensive invasive intracranial EEG monitoring or no surgery. The quest continues for an improved localization method. The study presented by Chaudhary further explores the role of functional MRI localization of seizures. Although this is not the first study to assess hemodynamic responses to seizures as measured by the blood

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oxygen level-dependent (BOLD) response in fMRI, it reports on their experience with 55 patients undergoing video-EEG fMRI studies specifically for the purpose of capturing and modeling seizures (for a review of previous ictal fMRI studies, see (2)).

The capture of a seizure while in the scanner poses significant technical and logistic challenges; some of these challenges are shared with ictal MEG and SPECT studies, along with video-EEG with either scalp or intracranial electrodes. To maximize the likelihood of capturing seizures, chosen patients had a history of two or more seizures per day at the time of scanning; to minimize the likelihood of motion artifact, patients were excluded with a history of large seizure-related head motion. Even with enrollment targeting patients with daily seizures, only 24 of the 55 patients enrolled (36.3%) had at least one seizure recorded, with only 20 patients reporting their typical seizure.

The video-EEG data were utilized to divide seizures into four phases: pre-ictal (30 seconds prior to ictal onset), ictal onset (the evolution of the ictal pattern on EEG prior to observed clinical features), ictal established (regional and generalized EEG activity and the onset of an observable clinical semiology), and late ictal (EEG slowing seen after the ictal established phase). Seven patients had seizures that could be represented only by a single ictal phase.

For each study, a global maximum BOLD response was defined as the most statistically significant cluster. To assess the localization value of the observed BOLD responses, the concordance between the ictal onset zone and the BOLD responses were defined as: entirely concordant, concordant plus (the global maximum was in the seizure onset zone), some concordance (one BOLD response area was within the seizure onset zone), or discordant (all BOLD responses were outside of the seizure onset zone).

The ictal (7 patients) or ictal onset (13 patients) time period produced the highest degree of concordance with 65% concordant or concordant plus compared with 25% for the pre-ictal phase, 38% for the ictal established phase, and 11% for the late ictal phase. Complete concordance was seen in only three patients for the ictal–ictal onset phase and for one patient in the ictal established phase. Discordant data were seen in nine patients, although this was true for the ictal onset–ictal phase in only three patients.

Three of six patients who underwent intracranial EEG monitoring went on to have a resection. Two had a resection of the BOLD cluster and are currently seizure free, whereas the

BOLD cluster was not resected in the third patient who has continued seizures (1–3 seizure days per year). No discordant data were seen for the ictal onset (4) or ictal (2) periods among the six patients who had intracranial EEG. For the 14 patients for whom intracranial data were not available, discordant data were seen in two of the eight patients with a known structural lesion and in one of six patients with non-lesional neuroimaging.

This case series demonstrates both the promise and limitations of this method of ictal localization. The systematic approach outlined by Chaudhary et al. has improved on the degree of concordance from previous series (3); the authors hypothesized that the superior classification of seizure evolution periods would increase the potential diagnostic yield, and the data presented here support that hypothesis. However, the challenges of capturing seizures while in the MRI, along with the technical expertise to properly analyze the data, make it unlikely that epilepsy monitoring units will soon become video-EEG magnetic resonance suites.

Beyond the relatively narrow lens of the diagnostic utility, however, this technique affords a rich opportunity to explore, as the authors did, both pre-ictal and ictal propagation. As our understanding of the BOLD response and underlying neuronal activity improves, these techniques can provide valuable insights into changes that precede seizures and, potentially, changes that impact seizure spread and semiology. As the authors also point out, only larger studies will allow us to fully explore the value of this approach both diagnostically and scientifically.

by Chad Carlson, MD

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