# The BOLD Response to Interictal Epileptiform Discharges

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## INTRODUCTION

Interictal epileptiform discharges (IEDs) are studied routinely in the EEG evaluation of patients with epilepsy. Recently, the recording of EEG in the MR scanner (Ives et al. 1993) has enabled the study of electrographic events with fMRI. It is an exciting possibility because it may allow accurate anatomical localization of the generator of IEDs by correlating changes in BOLD signal and the presence of IEDs recorded with surface EEG. It may also provide information on the mechanisms underlying IEDs, since the metabolic change measured by fMRI is a consequence of the abnormal neuronal activity generating the IED. We studied in a group of selected patients the relationships between IEDs and the BOLD signal using continuous EEG-fMRI.

## MATERIALS AND METHODS

**Functional MRI:** We acquired on a 1.5T MR scanner (Siemens Vision, Erlangen, Germany) 7 to 10 runs of 120 frames, each frame consisting of 25 BOLD 64*64 images, with a TR of 50ms, a voxel size of 5x5x5mm, and a repetition time of 3s.

**EEG recording:** We recorded 21 channels of EEG inside the magnet with an EMR32 amplifier (Schwarzer, Munich, Germany). The EEG was processed offline in order to filter out the scanner artifact (Hoffmann et al. 2000) and enable the marking of IEDs.

**Image analysis:** We performed statistical processing of the images (Worsley et al., 1996; model based on Glover 1999). Images were motion corrected and smoothed (6mm FWHM filter). Slow fluctuations in the MRI signal were modeled with a third order polynomial. We defined regions of interest (ROI) as significant clusters of voxels (t-stat threshold: 4.4).

**Mean HR:** We averaged the BOLD signal following isolated IEDs. BOLD signals were interpolated to obtain one value every second. For each individual BOLD response, the time origin for averaging was taken as the point closest to the corresponding IED (Fig. 1).

**Correlation between responses:** We compared the amplitude of each BOLD response either to the amplitude of the corresponding IED. Amplitudes were measured as the square root of the energy of these signals. We measured the correlation between pairs of ROIs as a function of time.

**Subjects:** Patients were selected on the basis of having focal and frequent interictal spiking. We included in this study only the small subgroup of patients with clear fMRI activations that were spatially consistent with EEG findings.

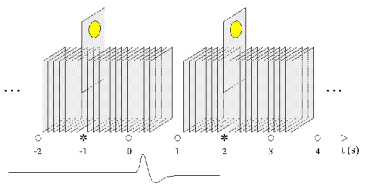


*Figure 1:* Schematic representation of the selection of the BOLD signal time point corresponding to the EEG event. Middle: relative time. Above the time line: two fMRI frames (consisting each of 25 slices; the slice containing the maximum of the ROI is raised). Below the time line: EEG event. Star: BOLD signal sample, circle: interpolated point. The origin of time is taken as the closest point to the EEG event.

*Table1*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Patient** | **EEG activity** | | | **# runs** | | **# IED's** | |
| **# IED's** | | | | **fMRI activation** | | | |
| **Max. t-score** | **# significant** | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | **in average HR** | | | | | | |
| | | | | | | | |
| **voxels** | | | | | | | |
| | | | | | | | |
| A | | L | posterior temporal | | 8 | | |
| 7 | | | | | 6 | | |
| | L | posterior temporal | | | 7.6 | | |
| 20 | | | | | | | |

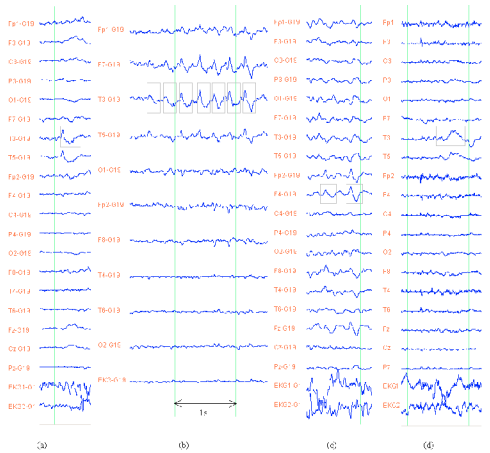


*Figure 2:* Examples of IEDs recorded during scanning and subsequently filtered (gray boxes: time windows and channel used in computing the IED energy). Reference electrodes: (F3+F4)/2.

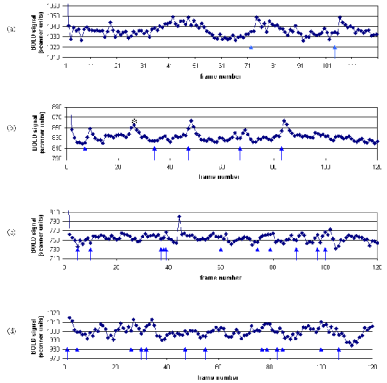


*Figure 4:* The BOLD signal in the ROI of one run for each patient. Arrows: epileptic discharges, star: event that correlate with the HR but not preceded by a scalp IED. Each point corresponds to one 3s frame. (a-d) Patients A-D

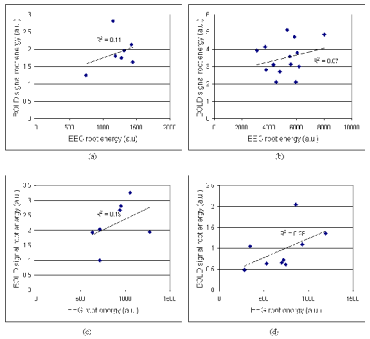


*Figure 6:* Plots of root energy of the BOLD signal versus root energy of the EEG signal for the set of isolated IEDs.

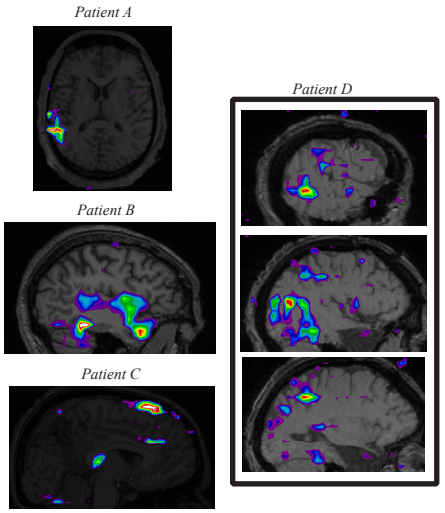


*Figure 3:* Functional MRI activations
(t-stat thresholds: 3 for Patients A, B, C, 1.5 for patient D)

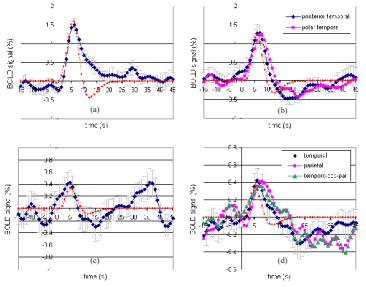


*Figure 5:* Average hemodynamic response and model (dotted lines); (a-d) Patients A-D. The model has been scaled in amplitude for each patient to enable direct comparison. Signals are presented in percent of activation relative to the baseline. For patient B, the model has been convolved with a 5s window to take into account the average burst duration.

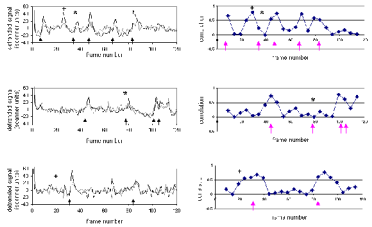


*Figure 7:* Left column: three runs of patient B (black trace: posterior temporal ROI, gray trace: anterior temporal). Right column: corresponding correlation coefficient between the two areas with a 30s sliding window (arrows: epileptic discharges). Plus sign: High correlation between BOLD signals in the absence of scalp IED; Star: low correlation between BOLD signals in the presence of scalp IED.

## RESULTS

Table 1 presents a summary of EEG and fMRI findings. Typical IEDs are shown for each patient on Figure 2. Figure 3 illustrates the activated areas for each patient.

**Bold time course:** For patients A and B, every IED was followed by a clear increase of the BOLD signal. A few BOLD events did not correspond to any visible scalp epileptiform EEG activity (Fig. 4). We observed large slow fluctuations.

**Average HRs:** The HRs were relatively similar to the model of Glover with some notable differences (Fig. 5). Across patients, the maximum signal change varied significantly. For patients with several areas of activation, the average HRs were remarkably similar between ROIs (Fig 5b and 5d).

**Correlation between responses:** There is an indication of a linear relationship between BOLD and EEG responses in patients A, C and D (Fig. 6). The two ROIs of patient B are in general - but not always - correlated around the timing of IEDs and not elsewhere (fig. 7). For some events there is a BOLD response in the posterior temporal lobe and not in the anterior part, but not the reverse.

## CONCLUSION

Epileptic spikes are often considered an important marker of the epileptogenic region, but they are usually considered of no clinical significance in themselves. It has been demonstrated, however, that they can result in a brief cognitive impairment. We show here that in some patients each spike results in a clear hemodynamic response lasting 30 to 40 seconds, whereas in others the response is of much smaller amplitude and duration. This opens the door to a new differentiation between spikes possibly having different mechanisms and significance. We have also shown that the HR of epileptic spikes can be somewhat different from the standard model and different from patient to patient. This will result in more complex analysis procedures, since the standard model is not likely to be optimum.

## ACKNOWLEDGEMENTS

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## REFERENCES

Glover G.H. Neuroimage 9(4):416-29 (1999).

Hoffmann A., Jager L., Werhahn K.J., Jaschke M., Noachtar S., Reiser M. Magn. Reson. Med. 44(5):791-8 (2000).

Worsley K.J., Marrett S., Neelin P., Vandal A.C., Friston K.J., and Evans, A.C. Hum. Brain Map. 4:58-73 (1996).