

Ultra-fast fMRI reveals high-frequency fluctuations in response to neuronal discharges

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Target audience: Neuroscientists and neuroimagers with an interest in fast functional imaging and/or epilepsy.

Purpose: There is considerable interest in the development of fMRI methods to detect responses to neuronal activity at faster time scales than canonical hemodynamic responses. Mixed results have been reported on the identification of a fast initial dip (Buxton, 2001) or of fluctuations directly related to neuronal currents (Rodionov et al., 2010; Sundaram et al., 2010). The current study investigates fast responses to epileptic discharges using the ultra-fast MR-Encephalography (MREG) sequence, which performs whole-brain fMRI at a 100 ms temporal resolution (Zahneisen et al., 2012).

Methods: Twelve focal epilepsy patients underwent a 20-minute resting-state fMRI scan at 3 T (Trio Tim, Siemens Healthcare, Erlangen, Germany) with simultaneous 64-channel EEG recordings using an MR-compatible system (BrainProducts, Munich, Germany). Whole-brain fMRI was acquired using the MREG sequence with the following parameters: TR=100ms, TE=36ms, 64x64x64 matrix, 3mm isotropic voxel size. After standard processing of the EEG to remove MRI-related gradient and pulse artifacts, spikes were marked by an expert neurologist and classified into distinct types based on their localization and morphology, if applicable. The fMRI data were preprocessed by regressing out motion, respiratory, and cardiac-related artifacts (Lund et al., 2006). High-frequency BOLD signal power fluctuations were then calculated by high-pass filtering the fMRI time courses with a cutoff frequency of 0.5 Hz, thus removing slow changes usually associated with BOLD hemodynamics, and then computing the signal envelope using the Hilbert transform. Statistical maps were formed showing voxels with significant high-frequency power increases in a 2-second window following the spikes (permutation test, $p < 0.05$ corrected).

Results: 30 distinct spike types were identified among the 12 patients. 20/30 (67%) spike types resulted in the identification of a significant cluster of voxels showing high-frequency BOLD signal power increases shortly following the spikes. The clusters were in areas concordant with the spike topographies and with the patients' clinical profiles (Fig. 1). The remaining 10 spike types did not show significant spike-related high-frequency BOLD signal changes.

Discussion: The high degree of spatial concordance between the identified high-frequency fluctuations and the patients' spike topographies points to a highly specific fast response that is unlikely to be artifactual. While the 100 ms temporal resolution of MREG is insufficient to directly sample epileptic discharges, the fast fluctuations may reflect an effect of oxygen consumption such as that related to the initial dip.

Conclusion: MREG can detect fast fMRI responses associated with neuronal activity with whole-brain coverage. While the mechanisms at the origin of these fast fluctuations remain to be elucidated, this study opens up new avenues for the accurate localization of neuronal activity with high spatial and temporal resolution.

Acknowledgements: This study was supported by the European Research Council advanced grant agreement 232908 and by the Forschungskommission of the University of Freiburg.

References:

- Buxton RB. The elusive initial dip. *Neuroimage*. 2001 Jun;13(6 Pt 1):953-8.
- Lund TE, Madsen KH, Sidaros K, Luo WL, Nichols TE. Non-white noise in fMRI: does modelling have an impact? *Neuroimage*. 2006 Jan 1;29(1):54-66.
- Rodionov R, Siniatchkin M, Michel CM, Liston AD, Thornton R, Guye M, Carmichael DW, Lemieux L. Looking for neuronal currents using MRI: an EEG-fMRI investigation of fast MR signal changes time-locked to frequent focal epileptic discharges. *Neuroimage*. 2010 Apr 15;50(3):1109-17.
- Sundaram P, Wells WM, Mulkern RV, Bublick EJ, Bromfield EB, Münch M, Orbach DB. Fast human brain magnetic resonance responses associated with epileptiform spikes. *Magn Reson Med*. 2010 Dec;64(6):1728-38.
- Zahneisen B, Hugger T, Lee KJ, LeVan P, Reisert M, Lee HL, Assländer J, Zaitsev M, Hennig J. Single shot concentric shells trajectories for ultra fast fMRI. *Magn Reson Med*. 2012 Aug;68(2):484-94.

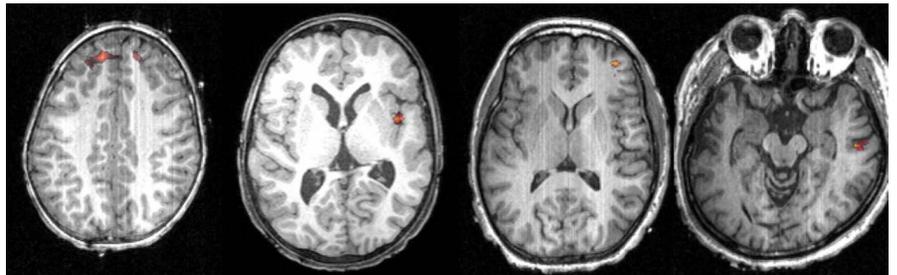


Figure 1. Examples of clusters of high-frequency fMRI signal fluctuations associated with epileptic spikes in 4 representative patients. From left to right: left frontal spikes (maximum F1), right fronto-central spikes (maximum FC2), right frontopolar spikes (maximum Fp2), right temporal spikes (maximum P8). In all cases, the activation cluster is concordant with the spike field. Additionally, in the 2nd example, the activation is within dysplastic cortex.