In epilepsy the correct diagnosis of the syndrome and the identification of the irritative zone are of great interest since it is necessary for correct treatment and eventually surgical intervention. This irritative zone is not only involved in the epileptic crises, but also produces fluctuating interictal activity. Interictal activity fluctuates spontaneously, has typical EEG signatures, and is assumed to mostly result from activity in sharply delimited regions. Therefore, a method that detects random events with high temporal and spatial resolution is needed. This is provided by simultaneous EEG/fMRI recordings. Combined EEG/fMRI has indeed been demonstrated to be a valuable tool to delineate the irritative zone defined as the area with altered BOLD during epileptiform activity (Krakow et al., 1999 or Salek-Haddadi et al., 2006). The identification of epileptiform activity has so far been based on subjective selection of ‘suspicious’ events, simplifying the epileptiform activity to an on/off phenomenon. While this has been successful in a reasonable amount of cases, this approach is certainly loosing sensitivity because it subjective, does not take into account the variance in the length and amplitude of the single interictal epileptic discharges (IED) and cannot account for intermittent rhythmic discharges. Moreover, subthreshold IEDs are not accounted for.

Our study has therefore used an Independent Component Analysis (ICA) to identify epileptiform activity continuously. The decomposition of the EEG into ICA components separates normal physiological EEG activity from components representing artifacts (e.g. eyeblinks, scanner noise, cardioballistogram, etc.) and, most important for our purpose, it isolates factors representing epileptiform activity (Iriarte et al., 2006; Jung et al., 2000). The temporal evolution of these epileptiform ICA factors can then again be correlated with the fMRI BOLD signal. This has the advantage that the epileptiform ICA factors include also subthreshold epileptiform activity and account for the length and the amplitude of separate IEDs. Moreover, the ICA based identification eliminates the need to manually select single events, which is cumbersome and error-prone. We expected that this should increase the sensitivity of the method as compared to the conventional approach using a binary (on-off) predictor for the BOLD signal.

Twenty patients with different types of focal and generalized epilepsy syndromes were investigated in a 3T Siemens Magnetom Trio MR scanner. Simultaneously a 92 channel EEG was recorded with 3 MR compatible BrainAmp amplifiers. To avoid aliasing of the scan pulse artifact, the EEG sampling was locked to the clock of the MR scanner using the Brain Products SyncBox (Mandelkow et al., 2006). Additionally, a second EEG dataset was recorded outside the MR environment. MR scan pulse artifact correction was performed according to the average artifact subtraction (AAS) method described by Allen et al. (2000). Afterwards the EEG recorded outside the scanner and the MR scan pulse corrected EEG were combined and decomposed using an ex-tended infomax ICA algorithm (Delorme and Makeig, 2004). Thereby the outside recorded EEG provides a baseline for the ICA algorithm to learn the uncontaminated EEG. This improved the separation of factors and yielded a small set of ICA factors with little spectral amplitude outside the scanner and markedly increased amplitude inside the scanner. This is the behavior that we expected for factors related to scanner and cardioballistic artifacts.

Two experienced neurophysiologists selected the factors coding for epileptiform activity based on their temporal dynamics (activity at the same timepoint as IEDs present in the original EEG) and their load on the electrodes (e.g. scalp distribution). The factor rated as most accurately meeting the criteria was considered for further analysis. The absolute amplitude of the selected ICA factor was convolved with a double gamma hemodynamic response function (HRF) to account for neurovascular coupling. This convolved signal used to compute voxelwise correlations with the BOLD signal. As covariates motion in six directions (translation and rotation along the X, Y and Z-axis) were used. To validate our hypothesis that our more physiological predictor may increase the sensitivity, we also analyzed each patient with the conventional approach.

The ICA separated artifacts from physiological and pathological activity in each patient. In seventeen of twenty patients, the BOLD correlates of epileptic activity were in accordance with the suspected EEG sources, the clinical semiology and, if present, the structural lesions. In those cases that were clinically equivocal, the BOLD correlates helped to establish the proper diagnosis of the underlying type of epilepsy. In one patient who suffered from temporal lobe epilepsy, the affected hippocampus could be identified by the BOLD correlates of rhythmic delta activity. This is a case where the conventional approach typically fails. Overall, we could demonstrate that the ICA based approach increased the sensitivity for proper lateralization in our very heterogeneous group of patients with diverse types of epilepsies form 50% (conventional approach) to 80% (ICA approach).

The ICA EEG/fMRI approach is a safe, non-invasive and easily applicable technique, which can be used to identify regions with altered hemodynamic effects related to IEDs as well as intermittent rhythmic discharges in different types of epilepsy.
References


Graphical overview of analysis procedure and an example of results for one patient with temporal lobe epilepsy.