Feasibility of fully simultaneous EEG/PASL/BOLD-fMRI for characterisation of hemodynamic responses to pathophysiologic and physiologic neuronal activation in epilepsy patients

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Introduction

In epilepsy diagnostics encephalographic recordings of interictal epileptic discharges (IEDs) play an important role in presurgical planning. For a better spatial localization these IEDs can be correlated with blood oxygen level dependent (BOLD) signal recorded in a combined EEG/fMRI measurement. However the correlated signal from epileptogenic regions, especially the frequently observed negative BOLD signal is not completely understood to date. They could be explained with at least three different scenarios:

A decreased metabolism could be accompanied by an overcompensating cerebral blood flow decrease as a 'normal' negative BOLD response. Second, epileptic activity could produce an increased metabolism without adequate blood flow change resulting in a negative BOLD effect. And third, the oxygen consumption could stay constant throughout the IED event while at the same time a reduced local blood flow is induced.

In order to differentiate these sources of negative BOLD response a fully simultaneous measurement of cerebral blood flow (rCBF), and EEG/BOLD fMRI is desirable, which we implemented by a combined EEG and dedicated pulsed arterial spin labelling (PASL) MRI examen. To demonstrate the feasibility of this method we examined 2 patients with different pathologies underlying their epileptic symptoms and characterized the BOLD responses that negatively correlated with epileptic activity.

Materials and Methods

We acquired data from 2 patients: One patient with a focal epilepsy due to a bilateral occipital dysplasia and interictal generalized spike waves (GSWD) with an occipital maximum and a second patient with absence epilepsy and typical GSWD with frontal maximum.

The measurements were performed on a 3T MR-scanner (Siemens TRIO) with a circular polarized transmit/receive head coil. A continuous 32 channel MR-compatible EEG (BrainAmpMR, www.brainproducts.com) was recorded inside the magnet while acquiring functional MR measurements simultaneously. rCBF and BOLD were detected using a PASL sequence with PICORE labeling [1] at an echo time of 25ms, suitable for both BOLD and rCBF measurements. An effective TR of 2×2.5ms = 5 ms (control + label image) was used. We recorded two runs: one with eyes closed and one using visual stimulation. Visual stimulation consisted of a passive viewing task with stimuli tailored to the gross location of the epileptogenic region in each individual patient (flickering checkerboard for occipital foci).

This targeted stimulation allowed for characterization of the relationship between ΔrCBF/rCBF and ΔBOLD/BOLD for three different scenarios:

1. GSWD driven hemodynamic responses in a ROI comprising the epileptogenic region
2. responses to visual stimulation in a ROI that was unaffected by GSWD
3. responses in a ROI that was affected by GSWD and reacting to stimulation as well

Gradient artefacts caused by the scanner in the EEG were subtracted offline using Analyzer 1.05 software (www.brainproducts.com) and then GSWD were marked after visual inspection. The analysis of MR-data was performed using Brainvoyager QX (www.brainvoyager.com) and an in house plugin for calculation of rCBF (subtraction of labeled from control images) and BOLD-data (averaged images). Statistical analysis used a rapid event related design with GSWD occurrence or the sensory stimuli as predictors. ROIs were defined by thresholding the statistical maps at $p<0.05$ (false discovery rate, FDR). An additional ROI was defined for the overlap of the GSWD ROI and the stimulus defined ROI. This allowed the analysis of scenarios 1-3.

Results and Discussion

In the two patients we found GSWD in the EEG recordings and correlating negative BOLD activation at a threshold of 0.05 (FDR) in the related MR measurements. In both cases the related flow changes in the identified ROIs were also negative (red scatter plot, fig. 1). Under visual stimulation these ROIs showed a positive stimulus related BOLD activity as well as a positive flow change in the stimuli ROI (fig. 1, blue) and in the stimuli+GSWD ROI (fig. 1, green). For the two patients under investigation we can therefore discard the possibility of increased metabolism without a sufficient vascular response as the source of negative ΔBOLD. However, ΔBOLD/BOLD versus ΔrCBF/rCBF charts exhibited a deviation from the predictions of the deoxyhemoglobin dilution model[2] for the negative going GSWD correlated BOLD signals.

These preliminary study shows the feasibility of simultaneous PASL/BOLD and EEG measurements.

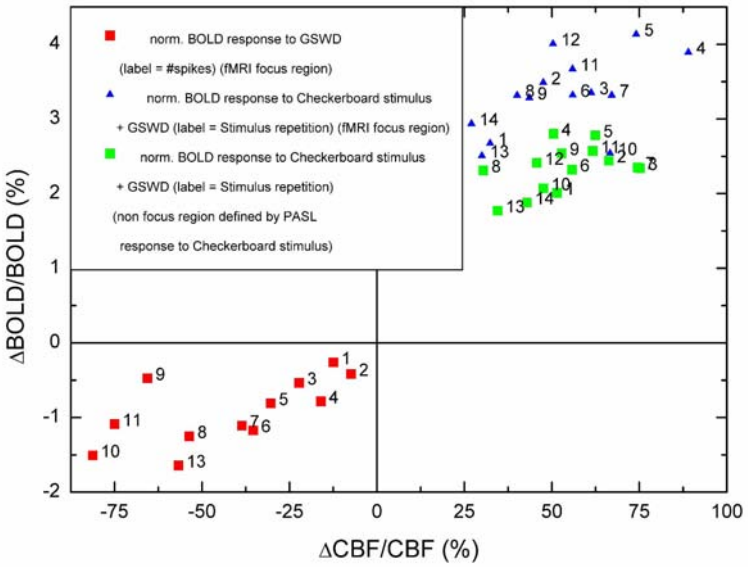

Fig. 1: BOLD MRI signal versus CBF showing the response to GSWD and Checkerboard stimulus

References

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