Investigation of Positive and Negative BOLD Responses to Interictal Epileptiform Discharges

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Introduction Interictal epileptiform discharges (IEDs) are a very specific marker of epilepsy, traditonally been studied with electroencephalography. More recently, fMRI has been deployed in conjunction with EEG to improve the localization of the irritative zone [3, 5]. However, the physiological changes determining the BOLD response to interictal epileptiform dischages (IEDs) are still incompletely understood and very little is known about the source of the reported regional negative BOLD responses to IEDs [1, 2, 6]. In the present study, hemodynamic and metabolic changes underlying BOLD responses to IEDs were examined via continuous EEG-fMRI in a group of epilepsy patients with generalized IEDs.

Methods A 1x1x2mm^3 3D RF-spoiled T_1-weighted gradient echo (TR/TE of 22/10ms) sequence for anatomical reference, was followed by an interleaved PASL and T_2^* weighted gradient echo sequence (TR of 1.8s and TE of 22/50ms for CBF/BOLD) for CBF and BOLD signal measurements. The latter acquisition covered 8 slices (5x5x5mm3; inter-slice gap of 1mm), positioned to include the primary motor cortices as well as the regions showing most prominent BOLD changes in the prior EEG-fMRI experiment. A QUIPSS II scheme was employed with 2 presaturation BASSI pulses in the imaging region and an adiabatic BASSI inversion pulse, with TI_1 of 700ms and TI_2 of 1300ms. Seven patients with generalized IEDs (6 with IGE, 1 with parietooccipital epilepsy) were examined. Medical air alternating with graded hypercapnia (up to 8% CO_2, 21% O_2 and balance N_2, which produced an average end-tidal CO_2 increase of 17±4 mmHg) was administered in 1/3/2min blocks. All the examinations were performed on a Siemens 1.5T Magnetom Sonata system. A common maximum achievable BOLD signal change (M) was estimated from hypercapnia data by linear fitting of the deoxyhemoglobin dilution model [4] to the transformed and averaged CBF data and averaged BOLD data. EEG was reviewed by an experienced electroencephalographer, who identified the IEDs according to their spatial distribution and morphology. The BOLD and CBF responses to IEDs were estimated by fitting the signal within each ROI (showing a statistically significant correlation with the IED events) using a Fourier basis set. Within each subject, the peak BOLD and CBF changes from all regions of interest satisfying this criterion were averaged before the $\Delta CMRO_2$ estimation was done. The IED-induced $CMRO_2$ changes were calculated using the estimated M in combination with the measured BOLD and CBF data [4].

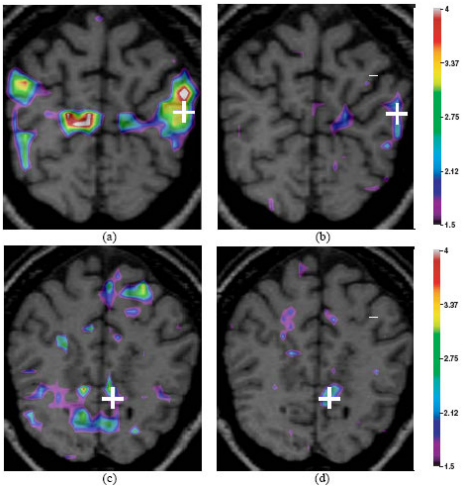

Figure 1: Sample BOLD (left) and CBF (right) t-value maps in a subject, overlaid on the corresponding anatomical slices. The regions of positive responses are shown in the top row; the regions of negative responses, in the bottom row. The centers of mass for the overlapping regions are shown with a cross hair.

Results The maximum achievable BOLD signal increase (M) for the seven subjects was 0.046±0.013, corresponding to a ΔR_2^* of -0.9±0.2s^{-1}. Only 2 of the 6 subjects who exhibited epileptiform activity in the course of the scanning session also showed sufficiently co-localized (*i.e.* at most 5mm separation between their respective ROI centers of mass) statistically significant changes in both BOLD and CBF to allow for $\Delta CMRO_2$ estimation. These included right parietal and right cuneus regions in one subject; and bilateral frontal, left occipital, bilateral precentral, left precuneus and right cuneus regions in the other subject. Sample t-value maps from subject 1 are shown in Fig. 1. The average BOLD and CBF data are displayed in Fig. 2. The optimal linear fit between the corresponding $CMRO_2$ estimates and the CBF data is displayed in Fig. 2, yielding a $\Delta CMRO_2/\Delta CBF$ coupling ratio of 0.48±0.17 (q=0.80).

Conclusion We observed normal hemodynamic responses to hypercapnic perturbation in a group of epilepsy patients with generalized IEDs. A consistent linear relationship between oxygen consumption and perfusion changes in regions of positive and negativeBOLD responses to IEDs was found, with a $\Delta CMRO_2/\Delta CBF$ coupling ratio of 0.48±0.17, in close agreement with the 0.44±0.4 coupling ratio found earlier in healthy volunteers [7]. The current findings suggest a preserved coupling between metabolic and hemodynamic processes underlying BOLD increases and decreases induced by interictal epileptiform activity, in line with the general notion of epilepsy as a disorder of neuronal circuitry rather than cerebral metabolism or hemodynamics.

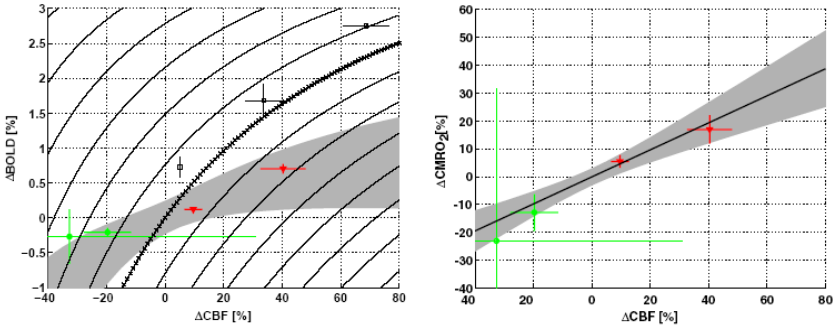

Figure 2: IED-induced changes in BOLD, CBF (left), and $CMRO_2$ (right) signals in the ipsilateral ROIs (green circles) and contralateral ROIs (red triangles) for each patient, with the average hypercapnia data shown as black squares.

References

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