Hemodynamic and Metabolic Responses to Neuronal Activation and Deactivation in Epilepsy Patients

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Introduction While fMRI BOLD studies of physiological brain activation are often done in surgical epileptic candidates to map the eloquent cortex as well as in parital and generalized epilepsy patients to study the interictal epileptiform discharges (IEDs), there is a paucity of data on the underlying changes in CBF, CBV and $CMRO_2$. The diffuse neurophysiological abnormalities assumed to exist in patients with idiopathic generalized epilepsy (IGE) are commonly believed not to influence the nature of the $CMRO_2$/CBF coupling, and hence the interpretation of BOLD fMRI response. In principle, however, $CMRO_2$/CBF coupling may be disturbed due to medications, the cumulative effect of seizures, and/or the changes in extracellular ion concentrations [3]. To examine this possibility and compare the findings to those of an earlier fMRI study of healthy volunteers [4], we measured hemodynamic and metabolic changes underlying BOLD responses to a unilateral distal motor task, known to induce excitation in the contralateral and inhibition in the ipsilateral primary motor cortex [2], via continuous EEG-fMRI in a group of 7 epilepsy patients with generalized IEDs.

Methods A 1x1x2mm^3 3D RF-spoiled T_1-weighted gradient echo (TR/TE of 22/10 ms) sequence for anatomical reference was followed by an interleaved (5x5x5mm^3; inter-slice gap of 1mm) PASL and T_2^*-weighted gradient echo sequence (TR of 1.8s, TE of 22/50ms for CBF/BOLD) for CBF and BOLD signal measurements. A QUIPSS II scheme was employed with 2 presaturation BASSI pulses [5] 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) performed a right-handed pinch grip at a frequency of 1Hz (in 24 20/60/40s off/on/off sessions), with the target force from 6 to 10% of the subject's maximum voluntary contraction. Thereafter, medical air alternating with graded hypercapnia (up to 8% CO_2, 21% O_2 and balance N_2) 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 fitting the deoxyhemoglobin dilution model [1] to the transformed and averaged CBF data and averaged BOLD data. The task-induced $\Delta CMRO_2$ were calculated using the estimated M and the measured BOLD and CBF data [1].

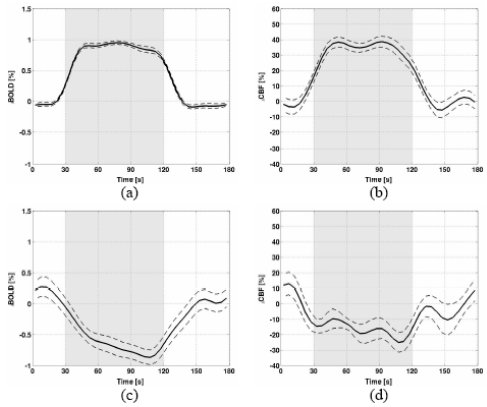

Figure 1: Time courses (low pass filtered, FWHM = 20s) of contralateral BOLD (a) and CBF (b), and ipsilateral BOLD (c) and CBF (d) changes in a subject.

Results Task-induced increases in BOLD signal were observed in the contralateral primary motor cortex (M1) and bilateral secondary motor areas. In contrast, BOLD signal decreased in the ipsilateral M1. A typical set of BOLD and CBF time courses, in both contra- and ipsilateral M1 ROIs of a patient, is shown in Fig. 1. Fig. 2 displays the measured BOLD and CBF data pairs for hypercapnic perturbation and motor task, as well as the calculated iso-$CMRO_2$ contours. The maximum achievable BOLD signal increase (M) was 0.046±0.013 (or ΔR_2^* of -0.9±0.2 s^{-1}). The calculated $CMRO_2$ and the corresponding measured CBF changes are displayed in Fig. 2. The slope of the straight line fit to these data yielded a $\Delta CMRO_2/\Delta CBF$ coupling ratio of 0.46±0.05 (with q of 0.92 indicating an excellent χ^2 fit). The ratio of contra- to ipsilateral CBF responses was significantly (p~0.017) smaller in epileptic patients (2.2±1.3) than in healthy subjects (4.2±2.3) studied earlier [4]. A very similar level of deactivation-induced percent CBF decrease is seen in the two groups, in contrast to a smaller excitation-induced percent CBF increase in the epilepsy patients (*c.f.* Fig. 3).

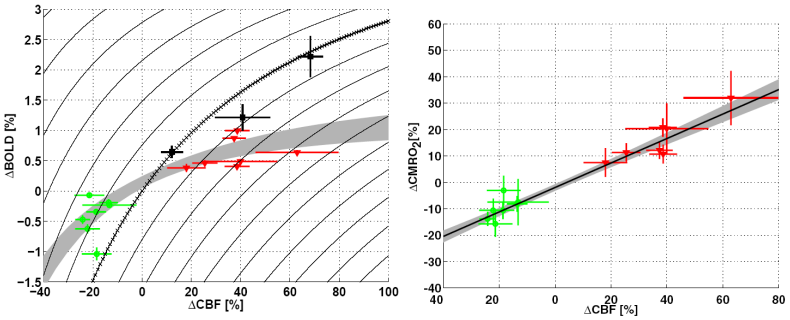

Figure 2: Task-induced changes in BOLD, CBF (left), and $CMRO_2$ (right) signals in the ipsilateral ROIs (green circles) and contralateral ROIs (red triangles), for each patient, with the average hypercapnia data shown as black squares.

Conclusion A consistent linear relationship between task-induced oxygen consumption and perfusion changes in regions of positive and negative BOLD response was observed, with a slope of 0.46±0.05, in close agreement with the 0.44±0.4 coupling ratio found in an earlier study of healthy volunteers [4]. A decreased relative activation- to deactivation-induced CBF change was observed, possibly resulting from the underlying neuronal hyperexcitability. The present findings suggest a preserved coupling between metabolic and hemodynamic processes underlying BOLD increases and decreases in epileptic patients in response to normal functional activation and deactivation and provide no evidence for a disturbance in the interictal cerebral vascular responses in this disorder.

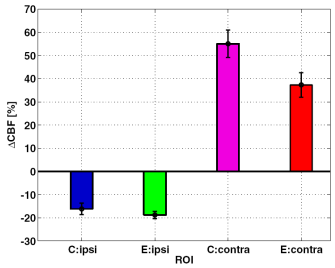

Figure 3: The average, task-induced, percent changes in CBF signal in ipsi- and contralateral ROIs of healthy subjects (C) and epileptic patients (E).

References

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