Behaviour of Compartmentalized Diffusion-Weighted fMRI Signal from Human Brain during Hypercapnia

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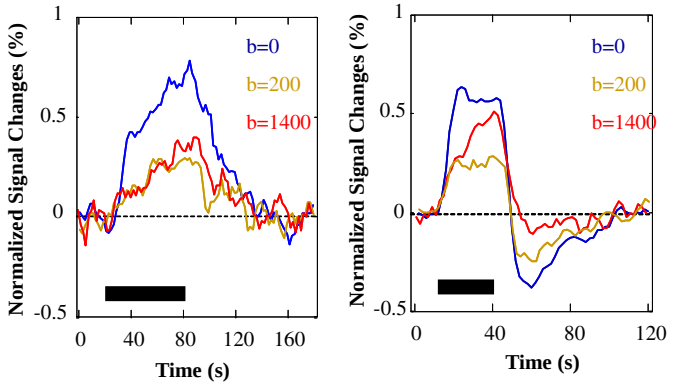
Introduction: A three compartment signal model has recently been proposed for the analysis of diffusion-weighted functional MRI (DW fMRI) time-courses [1,2]. One of these compartments corresponds to the vasculature (IV), while the other two divide the tissue signal into fast- (FDP) and slow-diffusion phase (SDP) contributions. Intriguingly, decomposition of raw visual stimulation data into IV, FDP and SDP time-courses revealed that the poststimulus undershoot (PSU) is mainly confined to the FDP, while the SDP signal is highly correlated with the stimulus and may reflect the neural response uncontaminated by the PSU. It was suggested that the FDP and SDP signal changes originate from the extravascular (EV) BOLD effect [2,3], with the SDP and FDP weighted by BOLD changes in small capillaries and arteriole/venule-sized vessels, respectively. Also, a possible contribution to the SDP from a cell-swelling effect could not be ruled out [4]. To further examine the mechanism of SDP signal changes in DW fMRI, comparison was made of the results of hypercapnia and visual stimulation experiments on the same subjects.

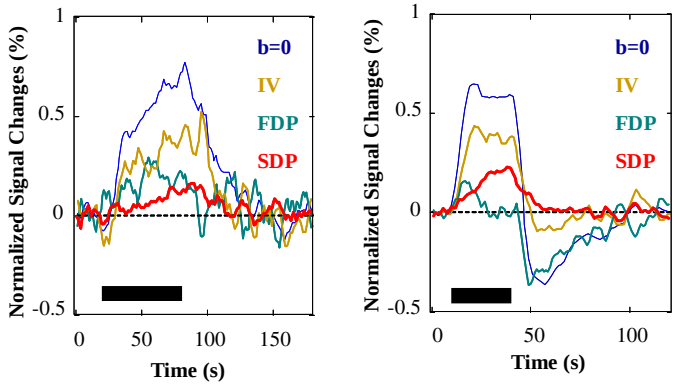
Methods: Seven healthy volunteers (age 20 to 32 years) were scanned on a whole-body 3T MRI system (Excite HD, GE Medical Systems). Images were acquired with a spin-echo echo-planar-imaging (EPI) sequence (TR/TE = 1000 /71.2 ms, 64 x 64 matrix, 3.75 x 3.75 x 4 mm^3 pixel size) with gradient pulses either side of the refocusing RF-pulse (b = 0, 200 and 1400 s/mm^2). During the hypercapnia experiments, 5% CO_2 was administered for 60s followed by 120s rest (2 cycles). The visual stimulation was provided by a black-and-white checkerboard alternating at 8 Hz (4 cycles of 30s activation and 90s rest). The time-courses for both stimuli, obtained from pixels declared activated for the visual stimulus, were decomposed into IV, FDP and SDP contributions by a linear fit to the signal model $S(t_n,b) = S_{IV}(t_n,b) + S_{FDP}(t_n)\exp(-b\,D_f) + S_{SDP}(t_n)\exp(-b\,D_s)$, where $S(t_n,b)$ is the measured signal at time t_n and DW b. Constants D_f and D_s were taken from the literature [5]. The model assumes that $S_{IV}(t_n,b)$ is negligible for $b \geq$ 200 s/mm^2.

Results: Figure 1 shows the raw DW-fMRI signal changes wrt DW for both hypercapnia (Fig 1a) and visual stimulation (Fig 1b). The visual stimulation results are similar to those obtained in previous work [1,2] with a TR of 2s. Note that the hypercapnia time-courses are very similar for b = 200 and 1400 s/mm^2 whereas there is a significant difference between the same time-courses for the visual stimulus. Also, the peak signal change of the hypercapnia time-courses follows a different trend to that observed in [6], which might be explained by the different sequence that was used. The decomposed time-courses are displayed in Fig 2. As expected, the SDP signal change was correlated with the stimulus without any PSU for the visual stimulation (Fig 2b). Although the mean hypercapnic SDP response shows a positive deflection (Fig 2a), the variation across subjects indicates that it is not significantly different from zero.



a. hypercapnia b. visual stimulation

Fig. 1 DW fMRI time courses



a. hypercapnia b. visual stimulation

Fig. 2 Decomposed time courses

Discussion: It is widely thought that hypercapnia alters CBF and CBV without any corresponding neural activation. As the SDP response during hypercapnia is not significant, this suggests that SDP change for visual stimulation reflects the evoked neural activation. However, it remains unclear whether the source is BOLD or some other mechanism such as an intrinsic tissue change.

References:

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