Folded cortical orientation influences the amplitude of BOLD-fMRI: evidence from simulations and experimental data

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TARGET AUDIENCE MR physicists developing models of fMRI signals, MR engineers working towards the development of new fMRI sequences and cognitive scientist using BOLD-fMRI as a research tool.

PURPOSE Detail modeling of gradient echo (GRE) and spin echo (SE) BOLD-fMRI has been limited to uniformly oxygenated vessel network under static condition [1]. A new quantitative two-photon technique [2] allows dynamic tridimensional measurements of the distribution of oxygen in the microvasculature of the cerebral cortex of the mouse. We used this technique to model the BOLD signals from the ground-level principles of MR physics. Our model permitted the computation of individual vascular compartments to the BOLD response (i.e. arterial, capillary and veins) as well as isolating intravascular and extravascular contributions. We also investigated the effect of the folded cortical orientation relative to the main magnetic field of the scanner.

METHODS Six mice were anesthetized with isoflurane. Oxygen-sensitive two-photon measurements were performed as described previously [2]. PO2 measurements were integrated in six Vascular Anatomical Network (VAN) models [3] together with previous arterial dilation measurements [4] during as 2-s forepaw stimulus. The temporal evolution of oxygen saturation (Fig. 1A) was converted to a shift in magnetic susceptibility that was used to compute a magnetic perturbation (ΔB) volume at each time-point following the forepaw stimulation (Fig. 1B). The resulting fMRI signals were computed by simulating the diffusion of 107 protons in the ΔB volume at each time point (Fig. 1C). Spatial gradients were applied during the simulation to produce gradient echo (SE) and spin echo (SE) signals (Fig. 1D).

RESULTS We computed the individual contribution of arteries, capillaries and veins for the six VAN models for B0 ranging from 1.5 to 14T and for two cortical orientations with respect to B0 (Fig. 2A). TE was set to T2 tissue for GRE and T2 tissue for SE. We found that 75-85% of the GRE signal (depending on the cortical orientation) originate from oxygenation changes occurring in the veins at 1.5T and that this number decreases slightly with increasing B0 to plateau at 70-80% at 14T. For SE, the inversion pulse refocuses the signal around larger vessels decreasing the venous contribution to 50% at 1.5T. The individual contribution of the intravascular (IV) and the extravascular (EV) compartment were also computed for two cortical orientations with respect to B0 (Fig. 2B). All EV and IV results are all consistent with previous work by Uludag et al [5]. Our results in Fig. 2A suggested that the same physiological change could produce BOLD responses with different amplitudes across the cortex depending on the spatial orientation with respect to B0 (B0). To confirm this prediction, BOLD-fMRI was measured in humans (n=5) during a hypercapnic challenge. The angle θ was computed for every voxel [6] as shown in Fig. 3A. A scatter plot of the BOLD changes versus θ for all voxels of the gray matter was generated and the mean BOLD change for each θi is shown in Fig. 3B. The amplitude of the BOLD signal followed a cos2(θi) dependence from 0 to 180° and good agreements between simulations and experimental data were obtained for both the shape and the amplitude (40%) of this effect, confirming our theoretical prediction.

DISCUSSION The angular dependence of the BOLD effect can produces a confounding effect when comparing BOLD response from different subjects with different brain morphologies or with different spatial orientations of the head in the MRI scanner. Nonetheless, the method used to map θ in Fig. 3A can be used to correct for this confounding effect by introducing an additional regressor in the statistical analysis.

CONCLUSION Our work shows that modeling fMRI signals from ground-level principles of MR physics can lead to a better understanding of the physiological origin of the BOLD response. This detailed model will serve as a gold standard to test the accuracy of more simplified models and new quantitative fMRI sequences to recover clinically relevant physiological parameters from fMRI measurements.