Partial Volume Effects of CSF and White Matter in Grey Matter Nulled Functional Magnetic Resonance Images

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Introduction: Grey matter nulled (GMN) fMRI [1] is a recently developed fMRI technique based on nulling grey matter (GM) MRI signal using an inversion recovery (IR) approach. The GMN fMRI method can reveal changes in cerebral blood volume (CBV) associated with brain activation. However, the GMN fMRI, like any IR approaches to suppress a given T_1 component (e.g. VASO fMRI [2] by nulling the blood signal), suffers from partial volume effects due to components with differing T_1s. In brain parenchyma, these components include cerebrospinal fluid (CSF) and white matter (WM). In this study, we examined the partial volume effects of CSF and WM to evaluate the option for quantitative assessment of CBV change by the GMN fMRI.

Methods and Materials: In GMN fMRI, the GM signal is suppressed when the inversion time (TI) matches the null GM magnetisation based on the inherent T_1. After suppression of GM signal, the remaining magnetisation comprises contributions from blood, CSF and WM. At TI used in GMN fMRI, blood and CSF magnetisations are negative, where the CSF signal is much larger than that of blood. In contrast, the WM magnetisation signal at TI in GM nulled situation is positive. The blood signal is the target of being measured for GMN fMRI. However, the contributions from CSF and WM will inevitably affect the accuracy of such a measurement. We have now established a model to determine the effects of CSF and WM, including possible changes in their compartment sizes during brain activation. The signal change in GMN fMRI is modelled by $\Delta S/S = (X_{gm,act}S_{par,gm}^{act} - X_{gm,rest}S_{par,gm}^{rest} + X_{wm,act}S_{par,wm}^{act} - X_{wm,rest}S_{par,wm}^{rest} + X_{csf,act}S_{csf}^{act} - X_{csf,rest}S_{csf}^{rest})/(X_{gm,rest}S_{par,gm}^{rest} + X_{wm,rest}S_{par,wm}^{rest} + X_{csf,rest}S_{csf}^{rest})$, where S_{csf}, $S_{par,gm}$ and $S_{par,wm}$ are CSF, parenchymal GM and WM signal respectively, and X_{csf}, X_{gm} and X_{wm} are the fraction of CSF, GM and WM within a voxel, respectively. The fractions of CSF, GM and WM satisfy that $X_{gm,rest} + X_{wm,rest} + X_{csf,rest} = 1$ and $X_{gm,act} + X_{wm,act} + X_{csf,act} = 1$ for resting and activation state, respectively. Considering that $S_{csf}^{act} = S_{csf}^{rest}$ is generally satisfied because of absence of perfusion in CSF, the expression can be simplified to $\Delta S/S = [X_{gm,act}S_{par,gm}^{act} - X_{gm,rest}S_{par,gm}^{rest} + X_{wm,act}S_{par,wm}^{act} - X_{wm,rest}S_{par,wm}^{rest} + (X_{csf,act} - X_{csf,rest})S_{csf}^{rest}]/(X_{gm,rest}S_{par,gm}^{rest} + X_{wm,rest}S_{par,wm}^{rest} + X_{csf,rest}S_{csf}^{rest})$. Note that the signal from GM parenchyma after nulling the GM magnetisation contains contributions from vascular blood only and is represented by Eq.[1]. The WM signal can be expressed by Eq.[2] and the CSF signal by Eq.[3].

$$S_{par,GM} = \sum_i CBV_{GM,i} \cdot C_{blood} \cdot M_{blood,i}(TR,TI) \cdot e^{-TE/T_{2,blood,i}^*} \quad [1]$$

$$S_{par,WM} = \left(C_{par,WM} - \sum_i CBV_{WM,i} \cdot C_{blood}\right) \cdot M_{WM}(TR,TI) \cdot e^{-TE/T_{2,WM}^*} + \sum_i CBV_{WM,i} \cdot C_{blood} \cdot M_{blood,i}(TR,TI) \cdot e^{-TE/T_{2,blood,i}^*} \quad [2]$$

$$S_{CSF} = C_{CSF} \cdot M_{CSF}(TR,TI) \cdot e^{-TE/T_{2,CSF}^*} \quad [3]$$

where i denotes the arteriole, capillary or venule, M_x (TR, TI) is the longitudinal magnetisation of x component after applying a spatially non-selective inversion pulse, C is the water proton density and CBV is the fraction of blood volume relative to the parenchymal volume in unit of ml blood/ml parenchyma.

To determine the partial volume effects of CSF and WM, we consider two cases where a voxel consists of either GM + CSF or GM + CSF + WM. For each case, we further consider two conditions under which the fractions of components that either change or remain as a constant upon brain activation. Under condition when fraction sizes change, we consider that $\Delta X_{csf}/X_{csf,rest} = -2\%$ to demonstrate this effect. In case of a voxel consisting of GM + CSF, we cover a range of CSF fractions from 0 to 0.3. In case of a voxel consisting of GM + CSF + WM, we cover the same range of CSF fractions and consider a fixed WM fraction of 0.02. CBV values in GM for baseline and activation were taken to be 0.05 ml/ml and 0.066 ml/ml respectively [3], giving a 32% increase in CBV. TR = 3 s and TE = 10 ms were used in the simulation and experiments. A typical GM T_1 = 1122 ms [4] at 3T was adopted, corresponding to a TI of 703 ms at TR = 3 s. Detailed parameters used in the simulation are given in Table 1. Eight normal subjects (five males, three females, aged between 24 and 51) were recruited with signed informed consent before taking part in the study. fMRI scans were performed on a 3T MR system (Philips Medical Systems, Best, The Netherlands). The fMRI scan data were acquired as follows: single shot GE-EPI, TR = 3 s, FA = 90°, FOV = 224 mm, matrix = 112x112, SENSE factor = 2.5, slice thickness = 5 mm, TE = 10 ms, and TI = 703 ms. A single oblique axial slice covering the primary visual cortex was manually selected. Visual stimulation consisted of 45 s OFF and 45 s ON in two cycles with B/W checkerboard flashing at 8 Hz. Seventy five dynamic images were acquired for each fMRI scan within a period of 225 s. Activation maps were obtained using FEAT (FMRI Expert Analysis Tool), part of FSL package (http://www.fmrib.ox.ac.uk/fsl). A routine under IDL 6.0 (Research Systems Inc., Boulder, CO) was used to determine the signal change amplitudes.

Table 1. Parameters used in the simulations.

Parameter		GM	WM	CSF	arteriole	capillary	venule
Proton Density (C)		0.89	0.73	1	0.87	0.87	0.87
T_1 (ms)	baseline	1122	758	3817	1627	1627	1627
	activated	1122	758	3817	1627	1627	1627
T_2* (ms)	baseline	47.28	53	1442	123	36	21
	activated	48.15	53.3		123	43	31
CBV (ml/ml)	baseline	0.05	0.035				
	activated	0.066	0.0404				
CBF (ml/100g/min)	baseline	57	22.8				
	activated	96.9	38.76				

Results: Figure 1 shows the relative GMN signal change as a function of CSF fraction ($X_{csf,rest}$) at baseline, with and without a change in CSF fraction upon brain activation for the GM + CSF and GM + CSF + WM voxels. As shown, the GMN fMRI signal changes gradually decrease as $X_{csf,rest}$ increases and are substantially smaller than that in the absence of CSF partial volume ($X_{csf} = 0$) when $X_{csf,rest} \geq 0.1$. For the case with a change in CSF fraction ($\Delta X_{csf}/X_{csf,rest} = -2\%$), the relative signal change is even lower for both voxel types. With a small partial volume of WM ($X_{wm,rest} = 0.02$), the relative signal change is much larger (by 71%, not show) than that without WM partial volume (42%) when $X_{csf} = 0$. However, as $X_{csf,rest}$ increases, the WM partial volume effect gradually decreases. Instead, the increased CSF fraction becomes a dominant factor influencing the GMN signal change. Relative signal change of 42% from pure GM ($X_{csf} = X_{wm} = 0$) is larger than that of the true CBV change (32%) due to T_2* effect at TE = 10ms. At a typical $X_{csf,rest}$ = 0.1 [5], relative GMN signal changes with and without CSF fractional change are 6.7% and 8.2% for a voxel consisting of GM + CSF, respectively. Similarly, for a voxel consisting of GM + CSF + WM, the respective GMN signal changes are 6.9% and 9.0%. For both voxel types, the relative signal change with a concomitantly altered CSF fraction upon brain activation is smaller than that without such a change. In addition, relative signal change is slightly larger for a voxel consisting of WM. GMN fMRI experiments with visual stimulation on eight healthy volunteers at 3T showed that the relative signal change was 7.4 ± 2.0%. This value closely matched a simulated voxel consisting of GM + CSF + WM (6.9%) undergoing a change in CSF fraction to activation.

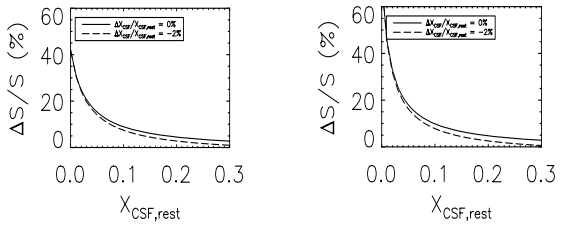

Figure 1. GMN fMRI signal change as a function of resting CSF fraction ($X_{csf,rest}$) with and without a change in CSF fraction during brain activation for (a) GM + CSF and (b) GM + CSF +WM voxels.

Conclusion: Both simulated and experimental results demonstrate that the partial volume effects by CSF and WM for GMN fMRI are significant. Partial volume effect by CSF results in underestimation of the CBV change. In contrast, the contamination by WM to the GMN fMRI will overestimate the GMN signal. However, the effect by WM is greatly superseded by a small CSF contamination in a voxel. A possible change in CSF fraction during brain activation will further reduce the true CBV change estimated by GMN fMRI.

Reference: [1] Shen Y, et al; Proc. ISMRM 2007; 27. [2] Lu H, et al; Magn Reson Med 2003; 50:263-274. [3] Gu H, et al; NeuroImage 2006; 30:377-387. [4] Lu H, et al; J Magn Reson Imaging 2005; 22:13-22. [5] Donahue MJ, et al; Magn Reson Med 2006; 56:1261-1273.