Measurement of Absolute CBV Change During Brain Activation using Grey Matter Nulled fMRI

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Introduction

MR signal change measured by grey matter nulled (GMN) fMRI [1] is affected by the fraction of CSF in a voxel, resulting in a significant underestimation of any change in absolute CBV. We present a method to determine the blood and CSF signals separately from the GMN fMRI data acquired with two different TRs. Using two TR for data acquisition assures that pure blood signal in a voxel can be quantified and the absolute CBV change to brain activation can be determined accordingly.

Methods and Materials

Consider a two-compartment tissue model consisting of grey matter (GM) parenchyma and CSF in an MRI voxel. After nulling GM signal using an inversion recovery sequence, the MR signal is expressed by

$$S_{GMN} = abs\left[(1 - X_{CSF}) \cdot CBV \cdot C_b \cdot e^{-TE/T_{2,b}^*} \cdot M_{0,b}\left(1 - 2e^{-TI/T_{1,b}} + e^{-TR/T_{1,b}}\right) + X_{CSF} \cdot C_{CSF} \cdot e^{-TE/T_{2,CSF}^*} \cdot M_{0,CSF}\left(1 - 2e^{-TI/T_{1,CSF}} + e^{-TR/T_{1,CSF}}\right)\right] \quad (1)$$

where X_{CSF} is the fraction of CSF in a voxel, C_b and C_{CSF} are the water proton densities in blood and CSF, respectively, $M_{0,b}$ and $M_{0,CSF}$ are the longitudinal magnetisation of blood and CSF in steady state equilibrium condition, respectively, CBV is the fraction of blood volume relative to the parenchymal volume in unit of *ml blood/100 ml parenchyma*, $T_{1,b}$ and $T_{1,CSF}$ are the blood and CSF longitudinal relaxation times, respectively, $T_{2,b}^*$ and $T_{2,CSF}^*$ are the effective transverse relaxation times of blood and CSF, respectively, and TI is the inversion time selected to null GM signal. Because $T_{1,GM}$ = 1122 ms at 3T [2], the corresponding TI for TRs = 3000 and 4000 ms are 703 and 746 ms, respectively.

Let $Y_1 = (1 - X_{CSF}) \cdot CBV \cdot C_b \cdot e^{-TE/T_{2,b}^*} \cdot M_{0,b}$ $Y_2 = X_{CSF} \cdot C_{CSF} \cdot e^{-TE/T_{2,CSF}^*} \cdot M_{0,CSF}$ $A_1 = 1 - 2e^{-TI/T_{1,b}} + e^{-TR/T_{1,b}}$ $A_2 = 1 - 2e^{-TI/T_{1,CSF}} + e^{-TR/T_{1,CSF}}$

Eq. (1) can be written as

$$S_{GMN} = abs\left(Y_1 \cdot A_1 + Y_2 \cdot A_2\right) \quad (2)$$

Since $T_{1,b}$ = 1627 ms [3] and $T_{1,CSF}$ = 3817 ms [4] at 3T, A_1 and A_2 can be calculated for the selected TR. At TR = 3000 and 4000 ms, Eq. (2) can be expressed respectively as

$$S_{GMN}(TR = 3000\,ms) = abs\left(0.140109 \times Y_1 + 0.207896 \times Y_2\right) \quad (3)$$

$$S_{GMN}(TR = 4000\,ms) = abs\left(0.178884 \times Y_1 + 0.294285 \times Y_2\right) \quad (4)$$

Using Eq. (3) and (4), Y_1 and Y_2 at baseline and during activation can be determined. After determining Y_1 at baseline and during activation, the blood signal change can be calculated by

$$\frac{Y_1^{act} - Y_1^{rest}}{Y_1^{rest}} = \frac{(1-X_{CSF}) \cdot CBV^{act} \cdot C_b \cdot e^{-TE/T_{2,b}^{*act}} \cdot M_{0,b} - (1-X_{CSF}) \cdot CBV^{rest} \cdot C_b \cdot e^{-TE/T_{2,b}^{*rest}} \cdot M_{0,b}}{(1-X_{CSF}) \cdot CBV^{rest} \cdot C_b \cdot e^{-TE/T_{2,b}^{*rest}} \cdot M_{0,b}} = \frac{CBV^{act} \cdot e^{-TE/T_{2,b}^{*act}} - CBV^{rest} \cdot e^{-TE/T_{2,b}^{*rest}}}{CBV^{rest} \cdot e^{-TE/T_{2,b}^{*rest}}} \quad (5)$$

At short TE, Eq. (5) can be simplified to

$$\frac{Y_1^{act} - Y_1^{rest}}{Y_1^{rest}} \approx \frac{CBV^{act} - CBV^{rest}}{CBV^{rest}} \quad (6)$$

Eq. (6) shows that the absolute CBV change can be determined after Y_1 at baseline and during activation have been quantified.

Five healthy subjects (aged between 24 and 47) were recruited, each provided a signed informed consent before taking part in the study. Philips Achieva 3T MR system (Philips Medical Systems, Best, The Netherlands) was used for fMRI data acquisition. A single oblique axial slice (5 mm) along the calcarine sulcus was manually selected for fMRI scans. The GMN fMRI scans were performed as follows: single shot GRE-EPI, TR = 3000 or 4000 ms, FA = 90°, FOV = 224x224 mm, matrix = 112x112, SENSE factor = 2.5, TE = 10 ms, and TI = 703 or 746 ms for TR = 3000 and 4000 ms, respectively. 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). Routines under IDL 6.0 (Research Systems Inc., Boulder, CO) were used to determine the signal change from raw data acquired with TR = 3000 ms and the absolute CBV change from data acquired both with TR = 3000 and 4000 ms.

Results

Table 1 shows both the signal changes calculated from the activation maps obtained from the raw GMN data (TR = 3000 ms) and the absolute CBV changes determined from GMN data acquired with two TRs (TR = 3000 and 4000 ms) in the visual cortex. The signal change calculated from raw GMN data was 7.0 ± 1.9 % (mean ± SD, n = 5), which was much less than the absolute CBV change (16.7 ± 5.8 %) computed from the GMN data acquired with two TRs.

Conclusion

Our study demonstrates that the GMN fMRI signal change is affected by the partial volume effects of CSF in activated voxels, and thus, the CBV change will become underestimated. Both blood and CSF contributions in activated voxel can be estimated using the GMN fMRI data acquired with two TRs. Increase in absolute CBV can be determined from measured pure blood signal at baseline and during activation. The absolute CBV change determined by the current approach agrees well with CBV change measured with PET (+21%) in response to visual stimulation [5].

Table 1. Quantification of absolute CBV change.

	Raw Data Signal Change %	Absolute CBV Change %
Subject 1	5.65	18.22
Subject 2	6.45	11.19
Subject 3	9.27	25.42
Subject 4	5.02	11.56
Subject 5	8.70	17.10
Mean±SD	7.0±1.9	16.7±5.8

References

[1] Shen Y, et al; J Cereb Blood Flow Metab 2008 (in press).
[2] Lu H, et al; J Magn Reson Imaging 2005; 22:13-22.
[3] Lu H, et al; Magn Reson Med 2004; 52:679-682.
[4] Donahue M, et al; Proc ISMRM 2006; 459.
[5] Ito H, et al; J Cereb Blood Flow Metab 2001; 21:608-612.