Comparison of Breath Holding Techniques for the Calibration of FMRI Measurements of Oxygen Metabolism

P. Roberts[1], P. Jezzard[1], and D. Bulte[1]

[1]FMRIB Centre, University of Oxford, Oxford, Oxfordshire, United Kingdom

Introduction Different breath hold (BH) techniques have been used by different researchers. The most common are inspiration BHs and expiration BHs (BHs immediately following a normal breath in and a normal breath out respectively), but it is currently unclear which is the better technique to use in fMRI. It is possible that the volume of air in a patient's lungs during a BH may affect the physiological response to the BH. It is also possible that it may affect the magnetic field in the scanner, due to the different susceptibilities of air and body tissues, and thus affect data quality. The aim of the present study is to compare the haemodynamic response to inspiration and expiration BHs of 30 seconds, using simultaneous measurements of the BOLD signal and cerebral blood flow (CBF). The implications for calibration of the $CMRO_2$ model, and applications of the two techniques to research and medicine, are discussed.

Methods Data were acquired from six normal, healthy volunteers (five male, 24±5 years). Images were acquired with a Siemens Trio 3T MRI scanner using a 12-channel RF head receive coil. BOLD and ASL data were obtained in an interlaced sequence. BOLD images were T2 -weighted GE EPI images with TR = 4.5s and TE = 32ms. ASL images were acquired using the Q2TIPS[1] sequence with TR = 4.5s, TE = 23ms, TI1 = 0.7s, TI1stop = 1.2s, and TI2 = 1.4s. For both BOLD and ASL data acquisition, five axial slices were imaged, each of which consisted of a 64x64 matrix of 4x4x6mm^3 voxels. The hypercapnia paradigm consisted of four alternating sequences of inspiration and expiration BHs, each sequence comprising four 30 second BHs, separated by 30s of normal respiration.

Results Following inspiration BHs, the end tidal partial pressure of CO_2 ($ETCO_2$) increased in all subjects. Following expiration BHs, $ETCO_2$ increased in only four subjects. The most probable reason for the absence of an increase in $ETCO_2$ in the other two subjects was their breathing pattern following the BHs. In cases where an increase in $ETCO_2$ was observed, the mean increase was greater for inspiration BHs (19.8±4.9%) than for expiration BHs (13.3±9.6%). The BOLD signal and CBF increased in grey matter (GM) in all subjects during BHs compared with rest for both types of BH. Changes in BOLD and CBF were greater in GM than in white matter (WM), which is consistent with recent studies[2]. The results are shown in Table 1. Values of *M*, the scaling factor required for $CMRO_2$ fMRI, have been calculated as by Hoge et al.[3] with $\alpha = 0.38$ and $\beta = 1.5$. Because of the anomalously high values of *M* calculated for subject 1 for inspiration BHs the data from this subject have been excluded in the average. Values of ΔBOLD are plotted against values of ΔCBF in Fig. 1 (individual subjects, GM). The values of *M* estimated in the present study are comparable with values estimated by Kastrup et al.[4], who estimated *M* as 7±1% using BHs at 1.5T, Chiarelli et al.[5] (in different GM regions: *M* = 6.6±3.4%, 4.3±3.5%, 7.2±4.1%, CO_2 mixed with air at 3T), and Stefanovic et al.[6] (*M* = 7.2±1%, CO_2 mixed with air at 1.5T).

Subject	Inspiration BH			Expiration BH		
	ΔCBF (%)§	ΔBOLD (%)§	M (%)	ΔCBF (%)§	ΔBOLD (%)§	M (%)
1	*7 ± 15*	*1.7 ± 0.4*	*22.2 ± 6.1*	*25 ± 11*	*0.8 ± 0.2*	*3.6 ± 1.1*
2	21 ± 8	2.1 ± 0.5	11.1 ± 2.5	44 ± 14	1.8 ± 0.4	5.3 ± 1.3
3	29 ± 11	2.3 ± 0.4	9.1 ± 1.7	15 ± 12	1.2 ± 0.3	8.3 ± 2.0
4	59 ± 24	1.8 ± 0.3	4.4 ± 1.1	39 ± 20	2.0 ± 0.4	6.4 ± 1.7
5	67 ± 16	2.2 ± 0.4	5.2 ± 1.1	19 ± 13	2.1 ± 0.5	11.8 ± 3.1
6	35 ± 21	1.5 ± 0.4	5.1 ± 1.5	39 ± 12	0.8 ± 0.2	2.5 ± 0.8
Mean ± SD†‡	42 ± 20	2.0 ± 0.3	7.0 ± 3.0	31 ± 13	1.6 ± 0.6	6.8 ± 3.5

Table 1: Changes in ΔCBF and ΔBOLD compared with baseline for the two different types of breath hold in GM. † Errors on inter-subject means are standard deviations on the inter-subject data. ‡ The data from subject 1 have been excluded from any mean calculation. § Errors on individual subject data are half of the inter-quartile range.

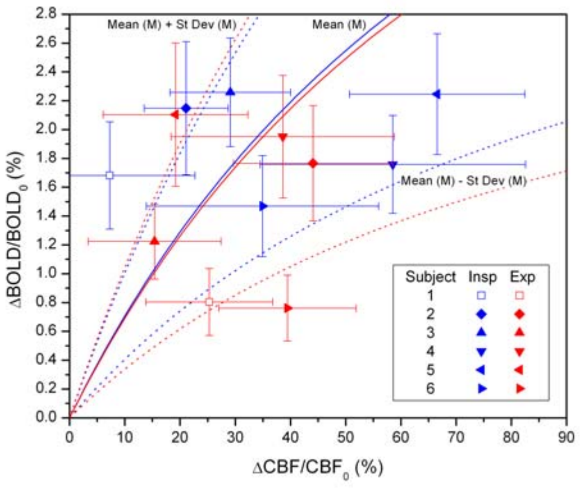

Fig. 1*. Individual subject ΔBOLD signal vs. ΔCBF in GM. Blue and red points and curves represent inspiration BHs and expiration BHs respectively. The solid curves are plotted using inter-subject mean values of M, and the dotted curves are plotted using inter-subject means ± st devs.*

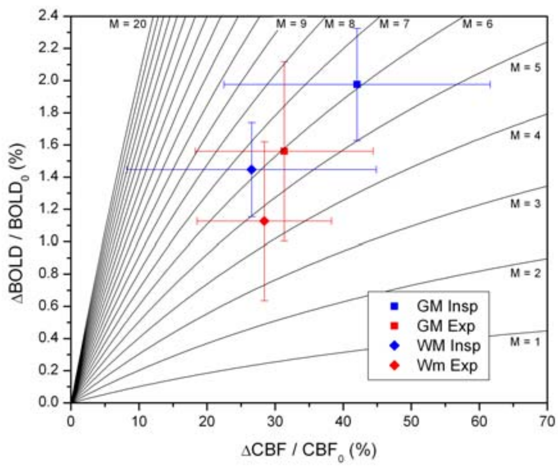

Fig. 2. *Inter-subject mean changes in BOLD and CBF. Error bars show inter-subject standard deviations. Curves are plots of isometabolic Hoge[3] model with values of M between 1% and 20%, plotted at 1% intervals.*

Discussion and Conclusions Both techniques produced similar values of the calibration constant *M*, with similar uncertainties, which are all comparable with recent literature values.[4-6] Despite the possible differences that $\Delta ETCO_2$ may be lower for inspiration BHs, and group estimates of *M* may be more precise for expiration BHs, the values of *M* calculated in the present study were similar for both techniques, and had similar uncertainties. Although further study with more subjects would be required to confirm or refute these observations, the present study suggests that there are no significant advantages of using either technique for calibration of the $CMRO_2$ model. CBF and the BOLD signal increased for both techniques in GM and WM. Signal changes were greater for inspiration than for expiration BHs, and greater in GM than in WM. No conclusive advantages of either BH technique were found. In light of this result, it is suggested that inspiration BHs are preferable, for the simple reason that they are easier for subjects to tolerate.

1. Luh, W. M. et al. Magn. Reson. Med. 41, 1246-1254 (1999).
2. Rostrup, E. et al. Neuroimage 11, 87-97 (2000).
3. Hoge, R. D. et al. Magn. Reson. Med. 42, 849-863 (1999).
4. Kastrup, A. et al. Magn. Reson. Med. 42, 608-611 (1999).
5. Chiarelli, P. A. et al. Magn. Reson. Med. 57, 538-547 (2007).
6. Stefanovic, B. et al. Neuroimage 22, 771-778 (2004