Correcting for Expired Carbon Dioxide Level Does Not Improve FMRI Repeatability for Motor Studies

J. W. Ibinson[1], K. M. Vogt[2,3], R. H. Small[3], D. Q. Beversdorf[4], and P. Schmalbrock[5]

[1]Anesthesiology, University of Pittsburgh Medical Center, Pittsburgh, PA, United States, [2]Biomedical Engineering, The Ohio State University, Columbus, OH, United States, [3]Anesthesiology, The Ohio State University Medical Center, Columbus, OH, United States, [4]Neurology, The Ohio State University Medical Center, Columbus, OH, United States, [5]Radiology, The Ohio State University Medical Center, Columbus, OH, United States

Introduction: "Physiologic" noise sources (fluctuations due to normal physiologic processes) dominate the noise structure of FMRI data [1]. Thus, correcting for physiologic noise can yield considerable alterations in the observed activation and reduce the number of false positives. Roys et al [2] showed that by correcting for physiologic noise with a digital filter, the variance in the most active voxel decreased by almost 10% relative to the uncorrected data. In addition, the variability of the BOLD response over several days has been shown to have a variance 3.5 times higher versus scans collected during the same scanning session [3]. End-tidal carbon dioxide ($ETCO_2$) changes have been shown to alter overall global cerebral blood flow and the BOLD response [4], and several works have demonstrated that including $ETCO_2$ directly into the general linear model (GLM) used to determine activation can yield significant correction effects [5, 6]. However, the impact of $ETCO_2$ on the repeatability of FMRI data is not known. This work examines the effect of including $ETCO_2$ in the GLM on the activation pattern variability of FMRI data for a motor task.

Methods: Two healthy, right-handed subjects were studied in this Institutional Review Board approved pilot study. For the functional task, rapidly alternating finger-to-thumb movements of the right hand were used. Each epoch consisted of 30 seconds of finger-tapping followed by 30 seconds of rest. All images were collected on a 3T Intera scanner (Philips Medical Systems, Cleveland, OH) using interleaved GRE EPI with SENSE acceleration, R=2, TR: 3s, TE: 35 ms, flip angle: 90º, matrix: 80x80 interpolated to 128x128, FOV: 23 cm, slice thickness: 4 mm, 35 contiguous axial slices, 90 timepoints. Each session consisted of two functional scans, with the time period in between scans kept as short as possible. The sessions were then repeated twice, on separate days, giving a total of 6 functional scans for each subject. The expired CO_2 waveforms were recorded during scanning and processed to find the end-tidal value that corresponded to each acquisition volume, and these values were used directly in the GLM [5]. Functional activation maps were determined with FSL (FMRIB's Software Library) using clusters determined by Z>2.3 and a corrected significance threshold of P=0.05 for first level analysis. Average activation maps with and without correction were computed within and across sessions separately for each subject and difference maps between the raw and corrected activation patters were computed with FMRIB's Local Analysis of Mixed Effects (cluster analysis with Z>2.3 and P=0.05).

Results: This study examined the effect of $ETCO_2$ correction on the reproducibility of the activation pattern. Model fit, as expected, did improve with $ETCO_2$ correction. The average activation for each subject across all scans, however, changed very little (Figure 1). Only 4.7% of the average maps brain voxels showed a significant change in activation with $ETCO_2$ correction. There were no statistically significant changes in the activation pattern, as determined by multilevel GLM analysis. Furthermore, there was no improvement in the within-session repeat scans in terms of the activation pattern variability (Figure 2).

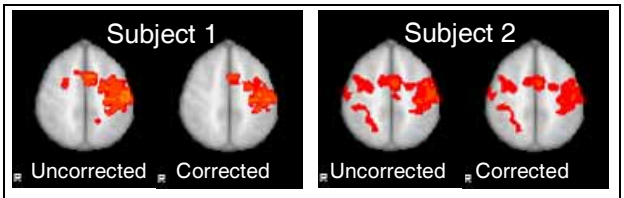

Figure 1. Illustration of $ETCO_2$ correction effects on the average maps for each subject. There is little activation change, and no statistical difference was found.

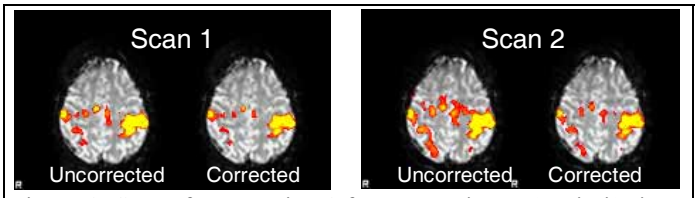

Figure 2. Scans from session 2 for one subject. The similarity of the scan to scan images negates the model improvement of ETCO correction.

Discussion: Although several studies have shown the positive effects that $ETCO_2$ correction can have on activation mapping and statistical model fit, it does not appear that this translates into a significant effect on the activation patterns of this study. The post-correction changes are mild, and no statistically significant effects can be seen on the average maps. There are several possible explanations for this. The activation created by the motor task is among the most robust of all commonly used tasks and this may wash out the effects of $ETCO_2$ correction. In addition, the $ETCO_2$ values for this study did not vary to the extent documented for pain tasks [5]. Therefore, it may not be correct to extend this study's conclusion to other tasks, especially those with less intense activation, like pain tasks. Overall, it has been shown that correcting for $ETCO_2$ has minimal effects on the test-retest repeatability of motor-task FMRI, however its effect on functional imaging of pain or other less intense activations still needs to be studied.

References: 1) Kruger G, Glover GH. Magn. Reson. Med 46:631-637 (2001). 2) Roys SR, Arya R, Gullapalli R. Proc Intl Soc Mag Reson Med 2003; 11:#1833. 3) Aguirre GK, Zarahn E, D'Esposito M. Neuroimage 1998, 8:360-369. 4) Cohen ER, Ugurbil K, Kim SG. J Cereb Blood Flow Metabol 2002, 22:1042-1053. 5) Ibinson JW, Schmalbrock P, Small RH. Intl. Soc. Mag. Reson. Med. 2005; 13:#1569. 6) Wise RG, Poulin MJ, Ide K, Tracey I. Proc Intl Soc Mag Reson Med 2003; 11:#216.