Comparison between end-tidal CO_2 and tidal volume changes calculated from the respiratory motion tracing used for correction of respiratory fluctuations in a functional MRI experiment with normal breathing and hyperventilation

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Introduction: Variations in end-tidal carbon dioxide ($ETCO_2$) are known to be correlated to BOLD signal changes as a result of cerebral blood flow (CBF) adjustments driven by the arterial CO_2 concentration that is reflected in expired air [1]. This suggests that measuring expired CO_2 concentration could be an important addition to the respiratory motion and pulse plethysmography tracings commonly recorded for FMRI physiologic noise correction [2]. However, because CO_2 sampling is not included as a component of MR scanner hardware, collecting this data is technically challenging. A simpler alternative measure has been suggested, derived from the respiratory motion tracing, that accounts for changes in respiratory volume over time (RVT), presumably modeling $ETCO_2$ [3]. This FMRI study employs conditions of paced breathing and hyperventilation that uncouple respiration from $ETCO_2$. Under these conditions, the MR signal changes were more widely correlated to the $ETCO_2$ values than to the calculated RVT values.

Methods: Eight healthy adults (aged 23-53), underwent whole-brain FMRI with a Philips 3T scanner using GRE EPI with parameters: SENSE=2, TR=3s, TE=30ms, 90º flip, FOV=24cm, voxel size=3.75x3.75x4mm, 35 contiguous interleaved axial slices. The functional scan was 10.5 minutes, during which subjects viewed graphical cues to pace their breathing rate and depth. The scan consisted of eight 1 minute conditions: 1-FREE (subjects paced their own breathing rate and depth), 2-NORMAL (rate=15/min), 3-RAPID (24/min), 4-DEEP (12/min at double the normal tidal volume), 5-RAPID&DEEP (25/min at double volume), 6-DEEP, 7-RAPID, and 8-NORMAL. The last 2.5 minutes were a free-breathing recovery period. During scanning, waveforms were recorded for: respiratory motion, finger pulse, and expired CO_2. Image data were preprocessed with FSL, including motion correction and temporal filtering, and then corrected for respiratory and cardiac related signal fluctuations using slice-wise RETROICOR [2]. For each breath in the respiratory timecourse, the RVT value was calculated as the difference in respiration amplitude divided by the respiratory period, $\mathbf{RVT = (R_{max} - R_{min}) / T_R}$. The RVT and $ETCO_2$ value for each breath were interpolated to the beginning of the next TR interval. Two 3-function basis sets were created using FLOBS [4] with a range of peak times that best modeled the optimal transfer functions, based on the literature [1,5], for RVT and $ETCO_2$ and the MR signal changes they induce. The RVT and $ETCO_2$ timecourses were convolved with their respective basis sets and modeled using FSL ($Z > 2.0$, $p < 0.05$). The shape and peak time for both could vary by voxel, allowing optimal model fit.

Results: Compared to initial baseline, subjects' $ETCO_2$ decreased by 35%, paralleling a 105% increase in RVT (both significant, $p < 0.05$), as shown in Fig. 1. The two timecourses were inversely correlated to one another ($r = -0.61$). In parallel to the breathing patterns cues, the RVT timecourse was relatively symmetric about the RAPID&DEEP condition. This shape was not mirrored in the $ETCO_2$ timecourse, which showed lower average values for each repeated breathing condition during its second occurrence, compared to its first. Representative slices from the group average map of voxels correlated to the RVT and $ETCO_2$ regressors are shown in Fig. 2. In MNI standard space, $ETCO_2$ was more strongly (max $Z = 4.62$) and diffusely (132,287 voxels) correlated to the FMRI data than RVT (max $Z = 4.07$, with 24,702 significant voxels).

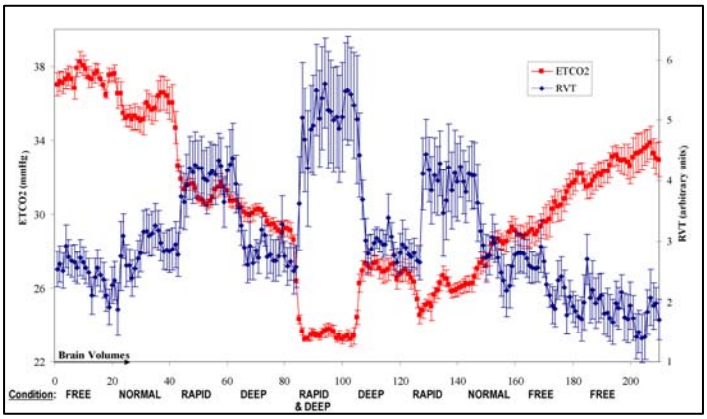

Fig. 1 – Plot of all-subject average interpolated $ETCO_2$ and RVT values calculated for each imaging TR interval. Error bars indicate ± the standard error across subjects. Note that the timecourses were inversely correlated ($r = -0.61$) but differ in shape and symmetry.

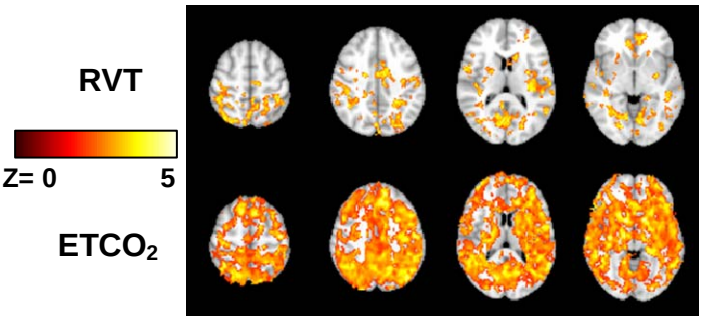

Fig. 2 – Four selected slices of the average maps showing significant correlation to the RVT (top) and $ETCO_2$ (bottom) regressors overlaid on the MNI standard brain.

Discussion: In this study, the respiratory pattern was controlled using graphical cues that effectively uncouple respiration from its normal $ETCO_2$-linked control mechanism. The hypocapnia induced by the RAPID&DEEP condition persists throughout the second half of the experiment, resulting in lower $ETCO_2$ values but similar RVT values when comparing the first and second occurrences of the NORMAL, RAPID, and DEEP conditions. This uncoupling explains the correlation of a greater number of voxels to the $ETCO_2$ timecourse, compared to RVT. This study demonstrates that the RVT calculated from the respiration waveform is inadequate and expired CO_2 monitoring should be employed in studies where changes in end-tidal (or arterial) CO_2 are expected to be uncoupled to respiration due to the functional task, a disease process, or a pharmacologic intervention.

References: [1] Wise et al., 2004. NIMG 21:1652-64. [2] Glover et al., 2000. MRM 44:162-67. [3] Birn et al., 2006. NIMG 31:1536-48. [4] Woolrich et al., 2004. NIMG 21:1748-61. [5] Birn et al., 2008. NIMG 40:644-54.