Combined analysis of breath hold and post-stimulus undershoot signals

T. B. Harshbarger[1], and A. W. Song[1]
[1]BIAC, Duke University, Durham, NC, United States

Introduction The majority of functional MRI (fMRI) studies are based on measurements of the blood oxygenation level dependent (BOLD) signal response. This BOLD response is produced by changes in blood flow (CBF), blood volume (CBV), and metabolism (CMRO2) that occur with neuronal activation. A large number of studies have investigated the temporal and spatial characteristics of the BOLD response. A recent report[1] indicated that the BOLD activation could be divided into distinct regions based on the characteristics of the post-stimulus undershoot (PSU) and its response to diffusion weighting. Three distinct spatial regions were defined: first, where the undershoot magnitude did not change with increasing diffusion weighting; second, a region in which the undershoot signal decreased; and third, a region in which no significant undershoot was detected. This study added evidence to the theory that the PSU signal is metabolic in origin. Recently, there has been a great deal of interest in calibrated BOLD techniques, in which the BOLD signal is adjusted to account for regional and inter-subject variations in the hemodynamic response[2, 3]. Many of these methods depend on a breath hold task as a calibration method. This task produces wide-spread changes in CBF and CBV without changes in metabolism associated with neural activity, and thus produces a measure of the vascular response alone[4]. The PSU may reflect both metabolic demands as well as related vascular density, and thus the vascular breath hold response will show differences across the areas distinguished by undershoot characteristics. In this report, we apply a diffusion weighting approach to investigate signal changes during a breath hold task and a visual task. This will allow us to further determine if the pattern of activation based on the undershoot response is reflected within the vascular response found in the breath hold task.

Methods All images were acquired using a 4T GE system with a surface coil to enhance sensitivity within the occipital brain region. In each study, high resolution anatomical images were first acquired to determine placement of the functional images. Functional images were acquired along 8 4 mm thick slices parallel to the calcarine fissure. An inverse spiral sequence was used for these functional images, providing an in plane resolution of 64x64 voxels in a 24 cm field of view, with TE=45ms and TR=1sec. Diffusion weighting was applied at three levels, each in a separate run, with b-factors of 1, 63, and 125 s/mm2. Each b-factor was repeated twice for both breath hold and visual tasks. Three subjects participated in this study after providing informed consent. In the breath hold task, subjects breathed normally for 48 seconds, followed by a breath hold for 12 seconds. This was repeated four times within each run. Subjects were given a warning three seconds before the breath hold, and were instructed to breath out before holding their breath. The visual task had the same timing characteristics, but instead of a breath hold subjects viewed a rotating, flashing checkerboard stimulus. Data were analyzed with SPM5. Contrast maps representing signal changes were generated with an activation threshold of z=4 and used for time course analysis with custom written Matlab programs. From the visual task, areas of activation were separated based on whether the magnitude of the post-stimulus undershoot was reduced or constant under increasing diffusion weighting, or if no undershoot was detected. Within these regions, the peak breath hold signal was determined for each voxel, and a breath hold to undershoot ratio determined.

Results and Discussion All subjects showed activation in both the breath hold and visual tasks. Fig 1 is a map from a representative subject of visual activation separated into areas based on the undershoot characteristics. The average peak breath hold signal for each region (in percent change from baseline) was 1.44% in undershoot change, 0.969% in no change, and 0.738% in the no undershoot region. This relative distribution was consistent across subjects, although the difference in signal change reached significance for the no change vs no undershoot regions in all subjects and for all regions in only one subject, likely due to the small number of voxels in the undershoot change region. Previous work separating BOLD signal into regions based on the PSU characteristics suggested that this signal is largely metabolic and included the hypothesis that areas of undershoot change included larger vessels downstream from activated areas, while regions of no change were smaller vessels immediate to the activation. Based on work in calibrated BOLD techniques, the breath hold data here supports that claim. Larger breath hold signal indicates larger vessels, which would be calibrated downwards relative to smaller vessels. This indicates that the diffusion based separation of post-stimulus undershoot regions is consistent with results from breath hold tasks. These results also suggest possible uses of the post-stimulus undershoot as a means of BOLD calibration.

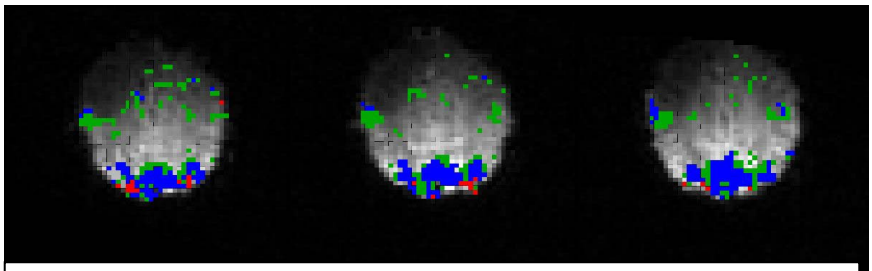

Fig 1: Red: undershoot change; blue: no change; green: no undershoot

Breath hold signal % change by subject		
change	no change	no under
1.0135	0.7944	0.5909
0.2571	0.1952	0.42799
3.0398	1.9182	1.1952

Conclusion We have shown that a breath hold task produces results consistent with previous hypotheses on the distribution of the post-stimulus undershoot, lending evidence to the nature of the origin of the undershoot.

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References:1:Harshbarger and Song PLoS One 2008; 2:Thomason et al HBM 2007; 3:Hyder et al NMR Biomed 2001; 4:Katstrup et al MRM 1999