

Comparison of Methods Used in Calibrated fMRI

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Introduction

One of the inherent weaknesses of functional Magnetic Resonance Imaging (fMRI) is the inability to measure direct neural activity. Numerous methods are available^{1,2} to calibrate the fMRI BOLD signal by at least partially decoupling the Cerebral Blood Flow (CBF) and the Cerebral Metabolic Rate of Oxygenation (CMRO₂), a more direct measure of neural activity. At least one of these methods³ has been shown to significantly reduce group variance in a cognitive task using a hypercapnic breath holding (BH) task. However, it remains unclear what methods are best suited for reducing variance across subjects and sites. This study investigates the voxelwise correlations among differing measures of CBF and sensorimotor (SM) task activity of a group of normal subjects. The results suggest that, of all methods, an active state CBF measurement yields the strongest voxelwise correlations with an ASL/BOLD acquisition.

Methods

An interleaved ASL/BOLD⁴ method (TR/TE=2500/50 ms, TI₁/TI₂=600/1500 ms, N_{slices}=12, TH=4 mm) was implemented using an Arterial Spin Labeling (ASL) sequence with an EPI acquisition in addition to a traditional EPI acquisition method (TR/TE=2500/50 ms, N_{slices}=12, TH=4 mm), collected for comparison on a Siemens 3T system. Using a surround subtraction between tag and control points results in a CBF measure while using a surround addition yields the T₂^{*} weighted BOLD signal⁵. Each subject was imaged twice for BH and SM task, once each using traditional EPI methods and the ASL/BOLD method (figure 1). From these data correlates included CBF-active state, CBF baseline state, BH composite maps and SM composite maps. The BH task contained a 2 min rest period and was blocked designed with 8 trials that included a 20 s normal breathing period, a 4 s transition period and a 20 s

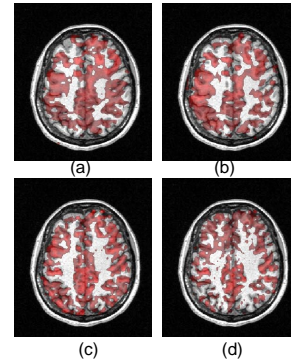


Figure 1. Composite maps of traditional bold BH (a), ASL/BOLD BH (b), Active state CBF (c), and Baseline CBF (d).

Independent	Dependent	<R>	ΔR
Comp SM	ASL/BOLD SM	0.66	0.10
Comp BH	ASL/BOLD BH	0.56	0.15
Act CBF BH	ASL/BOLD BH	0.49	0.12
Act CBF BH	Comp BH	0.36	0.03
Base CBF BH	ASL/BOLD BH	0.08	0.14
Base CBF BH	Comp BH	0.14	0.03
Base CBF BH	Comp SM	0.07	0.10
Act CBF SM	Comp SM	-0.11	0.16
Act CBF SM	ASL/BOLD SM	-0.18	0.15
Comp BH	Comp SM	0.11	0.16
Base CBF BH	Bas CBF SM	0.53	0.12
Act CBF BH	Act CBF SM	0.28	0.16

Table 1. Average group Pearson correlation coeff.

period followed by 14 on/off blocks of 16 s each. Statistical maps were calculated using the FSL processing suite. CBF active and baseline conditions were processed using in house software. Voxelwise correlations were subject to a whole brain mask for BH task and a fROI (z>2.0) in SM task. A group average and error were calculated for method comparisons.

Results

Six subjects were scanned in total, one subject needed to leave the scanner before acquiring the traditional BOLD data and one had poor slice prescription in the traditional BOLD data. Four complete comparisons of calibration between CBF measures and traditional BOLD and six of the interleaved ASL/BOLD method were made. All relevant correlations are shown in Table 1. Table 2 depicts relevant comparisons between methods accompanied by tests of significance for the accompanying hypothesis.

Correlation 1	Correlation 2	Hypothesis	P
Act CBF BH vs. ASL/BOLD	Act CBF BH vs. BOLD BH	ASL/BOLD method is superior to traditional method for calibration.	0.03
Act CBF BH vs. ASL/BOLD	Bas CBF BH vs. ASL/BOLD	Active CBF is superior to baseline CBF for calibration using the ASL/BOLD method.	0.0003
Act CBF BH vs. BOLD BH	Bas CBF BH vs. BOLD BH	Active CBF is superior to baseline CBF for calibration using the traditional method.	0.0001
Act CBF SM vs. ASL/BOLD SM	BOLD BH vs. BOLD SM	ASL/BOLD method is superior to current published methods for reducing group variance.	0.02
Act CBF BH vs. Act CBF SM	Bas CBF BH vs. Bas CBF SM	Active CBF changes for tasks, resting CBF does not.	0.01

Table 2. Hypothesis testing where correlation 1 is assumed to be greater than correlation 2 using a 2 tail normal distribution.

Discussion

Comparing BH task activation maps and baseline CBF maps with SM task activation maps resulted in weak correlations. These methods have been shown to reduce group variance in the past and any improvement in voxelwise correlations suggests that such reduction in variance can be improved upon. Active state CBF measures are shown here to be more effective than other measures at providing insight into the CBF activity involved in the BOLD signal on a voxelwise basis. This is especially true when using the interleaved ASL/BOLD method which intrinsically contains a greater amount of temporal correlation between CBF and BOLD.

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