fMRI calibration using effective BOLD signals estimated from susceptibility-induced echo-time-shift

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Introduction:

In functional MRI (fMRI) using gradient echo blood-oxygen-level dependent (BOLD) contrast, magnetic susceptibility artifacts induced by field inhomogeneity result in geometric distortion and signal loss [1-5] near the air/tissue interface in human brain. In addition, in-plane susceptibility gradients can cause echo-time shift [5-7] resulting in BOLD signal variations, e.g. in the orbitofrontal cortex.
Effect of in-plane susceptibility gradients on echo-time-shift has been mentioned previously [6-8]. BOLD responses in neighboring gray matter are expected to exhibit similar activations during breath hold task, but non-uniformities induced by echo-time-shift exist near susceptibility interfaces. We propose a BOLD signal calibration method using effective BOLD map estimated from echo-time-shift (obtained from in-plane susceptibility gradients). We investigate if the calibration, based on magnetic field distribution, reduces variation in localized region of gray matter for breath hold task.

Methods:

We have investigated the BOLD signal changes during a breath hold task among 21 healthy subjects. The experiment was performed in a 3T Siemens head-only scanner. The breath hold task was designed as an alternation of end-inspiration breath holding and resting (each in 18 seconds blocks), repeating 7 times for each subject [9]. The scan parameters were: EPI-down scan (phase encoding direction: anterior to posterior), TR 2 seconds, TE 30 ms, matrix size 64×64, 32 slices with 4 mm slice thickness. The magnetic field inhomogeneity map (field map) acquisition was doubled resolution (128×128) in a multi-echo gradient-echo-acquisitions with echo times 10 ms and 12.46 ms. The measured BOLD sensitivity maps were converted to percent-signal-change (PSC) maps, and both the PSC maps and field maps were registered to the standard MNI space as in a typical fMRI study. The localized gray matter was in the inferior temporal lobe from z=-26 to z=-18 mm in MNI space.
We observe that the PSC is not uniform in regions of the gray matter near susceptibility interfaces. Instead, we show that echo-time shifts caused by field map gradients (especially in the phase encoding direction) significantly influence the PSC signal. We estimate an effective BOLD (eBOLD) map from an echo-time-shift map which is calculated from phase directed gradients (Y-gradient) of the imaging sequence and field map [8]. Then the measured PSC and estimated eBOLD signals across 21 subjects were compared in regions with different susceptibility-induced Y-gradient values. As shown in Fig.1, the estimated eBOLD signal shows surprisingly similar trend with the measured PSC signal. This suggests that variations of PSC signal are due to echo-time-shift resulting from Y-gradient. Therefore, we propose a calibration method normalizing the measured PSC signal by the eBOLD signal. The calibration aims to remove the indirect influence from in-plane magnetic susceptibility gradients, and thus acquire more accurate fMRI signal.

Results:

Results obtained after calibration are reported in Fig. 2, which represents an enlargement of Fig.1 for Y-gradient between -20 and 20 Hz/cm. This range was selected by observing signal cannot be sampled for Y-gradient larger than 30 Hz/cm for the current EPI sequence. In Fig.2, the PSC with calibration (PSC_Calib) by estimated eBOLD signals (eBOLD) shows a flatter trend than without calibration (PSC). The increased flatness achieved after our proposed calibration method is more consistent with our initial expectation of a uniform BOLD response in the localized gray matter for a breath hold task.
For quantitative investigation, we also analyzed the signals in two regions of interest (ROIs) in five slices near the base of the brain for each subject. The ROIs were chosen in the gray matter in regions with Y-gradient between 10 and 20 Hz/cm for ROI1 and between -20 and -10 Hz/cm for ROI2 (Fig.2). The images of ROIs (ROI1 and ROI2) for one of the subjects are shown in Fig.3. We compared the mean of the PSC signals with and without calibration in ROI1 and ROI2 separately. As shown in Table 1, the difference of PSC between two ROIs drops from 0.1501 to 0.0231 after calibration, which quantitatively shows that the PSC becomes more uniform in the gray matter with calibration.
Table 2 shows the results of a fixed-effects two-way analysis of variance (ANOVA) for PSC with ROI1 and

subjects as factors. The effect size of the ROI and subject components from ANOVA were calculated using the formula of generalized ωG2 as described in [10], treating ROI as a manipulated factor and subject as a measured factor. Results show that the p-value of ROI increases significantly indicating the difference between ROI1 and ROI2 becomes smaller after calibration. And the effect size of ROI drops from 6% to 1% suggesting the effect of ROI becomes smaller after calibration. Therefore the proposed method efficiently reduces the effects of susceptibility-induced echo-time-shift on the BOLD signal.

Conclusions:

In fMRI, magnetic susceptibility artifacts exist near air/tissue interfaces in human brain. The artifacts become more severe with higher magnetic field strength, and strongly affect BOLD signals with gradient echo acquisition. Moreover, the acquisition trajectory and echo time have varying impacts on measured BOLD signals. Thus, there is a crucial need for calibration method using susceptibility gradients in functional neuroimaging studies.

Susceptibility artifacts (geometric distortion, signal loss) have been addressed, but the effect of in-plane susceptibility gradients on BOLD signal has not been fully examined. We studied the variation of BOLD signals due to susceptibility-induced echo-time-shift in a breath hold task. We observed a high correlation between BOLD signals and in-plane susceptibility gradients. Thus, we propose a calibration method to reduce the effect of echo-time-shift on BOLD signal. Results suggest that our calibration method improves the accuracy of BOLD signal.

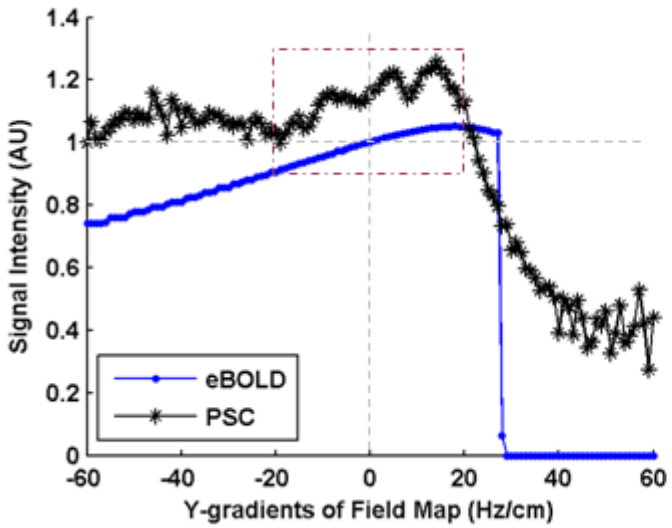

Fig.1. Average percent signal changes (PSC) and estimated effective BOLD (eBOLD) signals for different Y-gradients of the field map in a breath hold task (signal intensity averaged over 21 subjects). The plot suggests that the measured average PSC and the estimated eBOLD signals are highly correlated when plotted with respect to the susceptibility gradients in the phase-encode direction (Y-gradients of Field map).

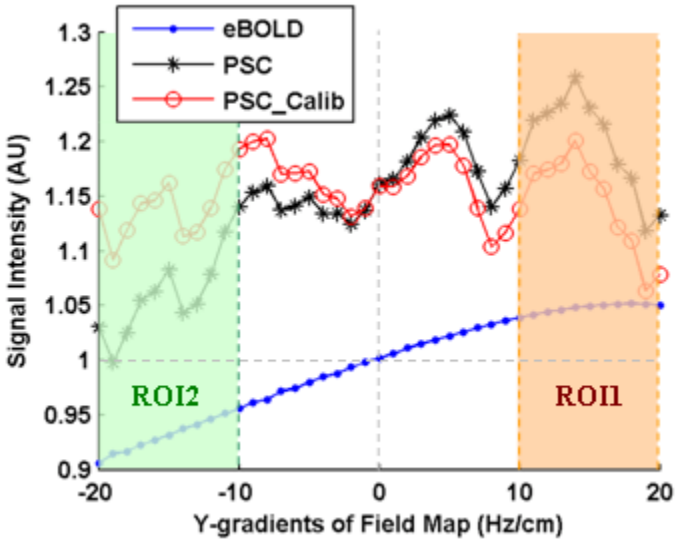

Fig.2. Results of the proposed calibration method for BOLD fMRI signals in the range of Y-gradients from -20 Hz/cm to 20 Hz/cm. The measured percent signal changes without calibration (PSC) and with calibration (PSC_Calib) by the estimated effective BOLD (eBOLD) signals are shown. The curves show that the measured PSC become more uniform after calibration in a breath hold task in BOLD fMRI.

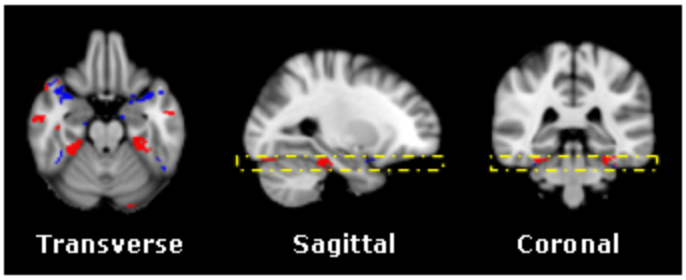

Fig.3. The images represent the region of interests (ROIs) in gray matter according to the susceptibility-induced gradients in phase encode direction (Y-gradients) in the standard Montreal neurological Institute (MNI) space for one of the subjects. ROI1 (10—20 Hz/cm) and ROI2 (-20—-10 Hz/cm) are marked in blue and red, respectively. As shown in the yellow dashed boxes, we restricted our statistical analysis to 5 slices in the inferior temporal lobe from z=-26 to z=-18 mm in MNI space.

Table1. Average signal percent change in ROI1 and ROI2 for 21 subjects (The data is corresponding to Fig. 2)

	ROI1 (10 — 20 Hz/cm)	ROI2 (-20 — -10 Hz/cm)	Difference
Without calibration	1.0660	1.2161	**0.1501**
With calibration	1.1386	1.1617	**0.0231**

Table2. Analysis of variance (ANOVA) for signal percent change in ROI1 and ROI2 for 21 subjects

	P-value		Effect size	
	ROI	Subject	ROI	Subject
Without calibration	**0.0003**	1.5413×10^{-9}	**0.0631**	0.5131
With calibration	**0.0327**	1.1353×10^{-9}	**0.0180**	0.5636

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Categories

- Functional MRI (Imaging Techniques and Contrast Mechanism)
- Bold fMRI (Modeling and Analysis)