Calibrating BOLD latency with high temporal resolution precision using magnetic resonance inverse imaging

Ruo-Ning Sun[1], Ying-Hua Chu[1], Yi-Cheng Hsu[1], Wen-Jui Kuo[2], and Fa-Hsuan Lin[1]

[1]*Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan,* [2]*Institute of Neuroscience, National Yang Ming University, Taipei, Taiwan*

TARGET AUDIENCE Scientists interested in calibrating the BOLD signal to more accurately estimate timing from fMRI measurements

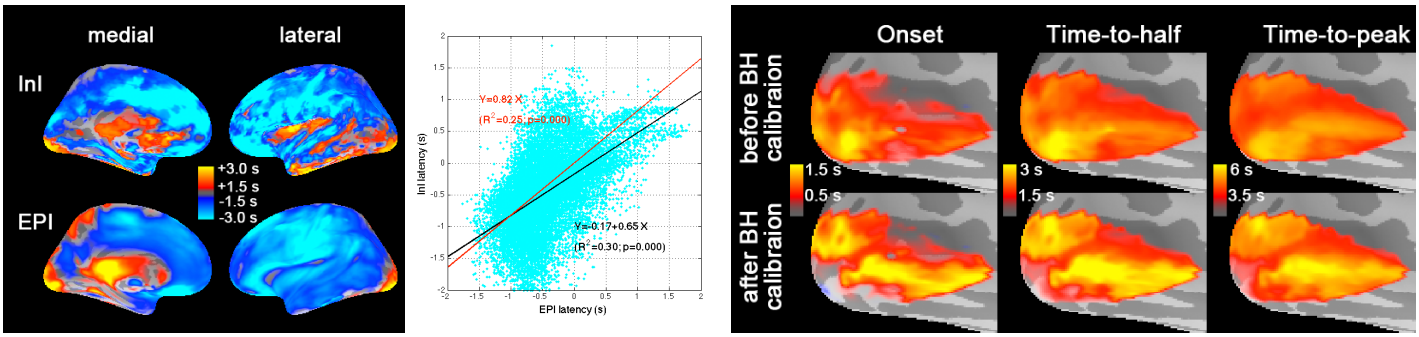
INTRODUCTION The BOLD signal [1,2] is the vascular response after neuronal activity[3]. By measuring fMRI non-invasively with the whole-brain sensitivity, it is possible to reversely infer neuronal characteristics from BOLD signal. However, inferring neuronal timing from BOLD signal has been complicated by variable vascular reactivity across areas. Previous studies suggest that such local vascular response time can be characterized by the BOLD signal elicited by a breath-holding (BH) task[4-7]. However, these studies use EPI with TR of a few seconds to obtain BOLD signal waveforms.

Here we use magnetic resonance inverse imaging (InI)[8,9], to characterize the onset of the BOLD signal across the whole brain. Without interpolating the BOLD signal from EPI with a lower temporal resolution (2 s), we hypothesize that InI can more precisely delineate BOLD onset timing. Our results delineate the distribution of relative BOLD latency with high temporal resolution precision (0.1 s). Visual cortex BOLD waveforms corrected with the estimated vascular latency show more neuronally sensible latency distributions.

METHODS Nine subjects participated the experiment were instructed to perform a breath holding task, which consisted of 25 s normal breathing and 15 s breath holding. The task was repeated for 6 times in a 4-minute run. InI data were acquired at 3T (Tim Trio, Siemens, Erlangen, Germany) using a 32-channel head coil array. The reference scan of InI was acquired from each scanner using a multi-shot echo-volumar imaging (EVI): TR=100 ms; TE=30 ms; flip angle=30o; bandwidth: 2442 Hz/px; FOV: 256 mm; image matrix: 64x64. Accelerated InI scan used the same parameters except that all partition encoding steps were left out in order to achieve TR = 100 ms. For comparison, EPI data were also collected (TR = 2 s; TE = 30 s; flip angle = 90^o, FOV 220 mm x 220 mm, slice thickness = 5 mm). High resolution anatomical MRI was also acquired for each subject using the MPRAGE sequence in order to allow morphing the analysis results onto a standard cortical surface coordinate system[10,11]. InI images were reconstructed by the minimum-norm estimate [9]. Physiological noise from cardiac and respiratory fluctuations was removed by using the DRIFTER[12] algorithm. The BOLD waveforms were first averaged across the cortex as the reference signal, which was subsequently shifted forward and backward for 4 s in 0.1 s step to calculate the correlation coefficient between this reference signal and the BOLD waveform at a chosen cortical location. The latency was estimated as the time showing the maximal correlation coefficient. This process was repeated for all locations on the cortex.

The estimated BOLD latency was used to calibrate the visual cortex BOLD signal elicited by visual hemifield stimuli. Specifically, 24 stimuli were randomly presented during a 4-min InI acquisition. Four runs of data were collected from 23 subjects. BOLD signal were analyzed by the general linear model using finite impulse responses.

RESULTS The figure below shows the spatial distributions of the relative latency of the BOLD signal estimated by the breath-holding task. Clear similarity between results estimated by InI and EPI were found at medial and lateral aspects of the frontal cortex. The visual cortex has a prominent latency longer than other parts of the brain. Different from EPI estimates, InI also found that the BOLD signal is activated later in the insular cortex compared other parts of the brain. The regression analysis on the BOLD signal latency between EPI and InI suggested that both latency estimates were significantly linearly correlated. After calibrating the BOLD latency on the visual cortex, the distributions of onset, time-to-half (TTH), and time-to-peak (TTP) timing of the BOLD signal at the visual cortex were more symmetric between upper and lower bank of the calcarine sulcus.



DISCUSSION

In this study, we used a hypercapnia challenge to estimate the timing difference in local vasculature reactivity when BOLD signal was elicited with 0.1 s precision. Compared with the previous study[13], we used InI capable of 10 Hz sampling without any interpolating the BOLD time series. The results were also presented on a standard cortical coordinate system. More symmetric BOLD timing distribution between upper and lower bank of the visual cortex after calibrating the BOLD waveforms with out latency estimates supports the validity of this approach to get physiological information closer to neuronal activity from the vascular responses.

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