NeuroImage 61 (2012) 1419–1427

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Concurrent fNIRS and fMRI processing allows independent visualization of the propagation of pressure waves and bulk blood flow in the cerebral vasculature

Yunjie Tong *, Blaise deB. Frederick

Brain Imaging Center, McLean Hospital, 115 Mill Street, Belmont, MA 02478, USA

ARTICLE INFO

Article history:
Accepted 5 March 2012
Available online 13 March 2012

Keywords:
fMRI
Near-infrared spectroscopy
Cerebral vasculature
Low frequency oscillation
Physiological noise
BOLD signal

ABSTRACT

Blood Oxygen Level Dependent (BOLD) functional magnetic resonance imaging (fMRI) measures changes in blood oxygenation, which is affected by physiological processes, including cardiac pulsation, breathing, and low frequency oscillations (LFO). It is challenging to identify spatial and temporal effects of these processes on the BOLD signal because the low sampling rate of BOLD leads to aliasing of higher frequency physiological signal components. In this study, we used concurrent functional near infrared spectroscopy (fNIRS) and fMRI on 6 subjects during a resting state scan. To reduce aliasing, the BOLD fMRI acquisition was repeatedly performed on a set of sequentially acquired slice stacks to lower the TR to 0.5 s while retaining high spatial resolution. Regressor interpolation at progressive time delays (RIPTiDe) method was used, in which physiological signal acquired by fNIRS (without aliasing) and its temporal shifts were used as regressors in the fMRI analysis to determine the magnitude and timing of the effects of various physiological processes on the BOLD signal. The details of the timing of the passage of the cardiac pulsation wave and of the cerebral blood itself were mapped. The result suggests that the cardiac signal affects the voxels near large blood vessels (arteries and veins) most strongly, while LFO mostly affected the drainage veins. We hypothesize that this could be the result of differences in the cerebral blood path lengths, and differences in the dynamics of the propagation of the signals. Together these results validate and extend a novel imaging technique to dynamically track the pulse-wave and bulk blood flow with concurrent fMRI and fNIRS.

Introduction

Blood Oxygen Level Dependent (BOLD) functional magnetic resonance imaging (fMRI) is the most common imaging technique utilized in the study of brain function both in response to tasks and in task-free "resting state" scans. BOLD measures changes in blood oxygenation, which can be caused by neuronal activation through neurovascular coupling. However, there are also prominent variations in cerebral hemodynamics, which arise from physiological factors affecting blood oxygenation, flow or volume that are not influenced by neuronal activations. Moreover, the temporal resolution of fMRI is relatively low, which is about 2–3 s at magnetic field strengths of 1.5–3 T. While this is sufficient for the hemodynamic effects of neuronal responses, which alter regional blood flow and volume with a slow "hemodynamic response function" (Siero et al., 2011; Tian et al., 2010), it is insufficient to measure the faster global physiological hemodynamics arising from cardiac, respiratory, and possibly other fast blood-related variations. This means that the signals from some physiological processes are aliased, which makes them unidentifiable in the detected BOLD signal, and therefore difficult to remove. These processes include respiration (0.2–0.3 Hz) and cardiac pulsation (~1 Hz). Many studies have been done to confirm the existence of these signals in the brain (Chang and Glover, 2009b; Chang et al., 2009; Shmueli et al., 2007; Triantafyllou et al., 2005) and efforts have been made to remove them (Birn et al., 2006; Chang and Glover, 2009a; Glover et al., 2000; Verstynen and Deshpande, 2011).

Functional near infrared spectroscopy (fNIRS) is a promising complementary method to fMRI for the study of brain function (Gibson et al., 2005; Hillman, 2007; Hoshi, 2007; Obrig and Villringer, 2003). Like fMRI, it is sensitive to the hemodynamic changes caused by neuronal and physiological processes. Unlike fMRI, its temporal resolution is generally high enough (12.5 Hz in our study) to sample most physiological processes without aliasing, but with low spatial resolution (~1 cm) and short depth of penetration (~2 cm). A new combined method for analyzing concurrent fNIRS/fMRI data capitalizes on the strengths of both types of data (Tong et al., 2011b). The method uses the fNIRS signals to generate regressors to analyze BOLD data (based on the fact that both fMRI and fNIRS are sensitive to blood oxygenation and volume changes). The high temporal resolution offered by fNIRS allows the full sampling of the physiological processes in the fNIRS data, as well as their spectral separation. These isolated physiological signals can then be used to probe the high spatial resolution fMRI data in order to understand how physiological processes

* Corresponding author. Fax: +1 617 855 2770.
E-mail address: ytong@mclean.harvard.edu (Y. Tong).

1053-8119/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2012.03.009

unrelated to neuronal activation contribute to the BOLD signal over both time and space.

The method was first tested in a previous study (Tong et al., 2011b), in which the main goal was to study the influences of different physiological processes, such as cardiac pulsation, respiration, and low frequency oscillation (LFO) on BOLD fMRI. The method was useful to separate the physiological signals and map brain voxels affected by the cardiac and the LFO signals. In addition, the method allowed dynamic tracking of the cardiac signal through the brain. However, there were three shortcomings in the last study which this study seeks to resolve: 1) since the TR used in the last study was 1.5 s, the cardiac signals in BOLD were still heavily aliased, complicating efforts to unambiguously detect voxels with cardiac driven BOLD signal change; 2) for this reason, the dynamic map generated by time-shifting the fNIRS regressor (at the cardiac frequency) may have missed important details in the passage of the wave; 3) due to the fact that the fNIRS probe detects little to no signal at the respiration frequency, the result of using fNIRS regressors in the respiration band was not informative. In this study, we adopted two improvements. Firstly, we used a segmented whole brain fMRI acquisition, which allowed us to lower the TR to 0.5 s while maintaining the same spatial resolution ($3.5\times3.5\times3.5$ mm). Secondly, a respiration belt was used to simultaneously acquire respiration data that was used as regressor for respiration (instead of using respiration data collected with fNIRS). The main goals were: 1) to confirm and validate the new method of mapping the cerebral vasculature and dynamically assessing the passage of the cardiac wave through the brain, 2) to understand how the LFO and cardiac signals affect the BOLD signal differently in space and time, and 3) to understand how respiration directly affects the BOLD fMRI signal.

Material and methods

Protocol

Concurrent fNIRS and fMRI resting state studies were conducted on six healthy volunteers during resting state acquisitions (4 M, 2 F, average age 28 ± 4.69). The protocol was approved by the Institutional Review Board of McLean Hospital.

An MRI compatible fNIRS optical probe (as shown in Fig. 1), with three collection (detector) and two illumination (source) fibers, with source-detector distances of 1 or 3 cm, was placed over the right prefrontal area of each participant (roughly between Fp1 and F7 in the 10–20 system) and held in place by an elastic band around the head. The position of the probe was chosen due to its easy accessibility (no hair) and relatively short distance from the scalp to the cortex (11–13 mm on average) in this area (Okamoto et al., 2004). The sampling rate of fNIRS data acquisition was 12.5 Hz. fNIRS data was recorded continuously through all the fMRI acquisitions as well as for several minutes before and after the fMRI acquisition.

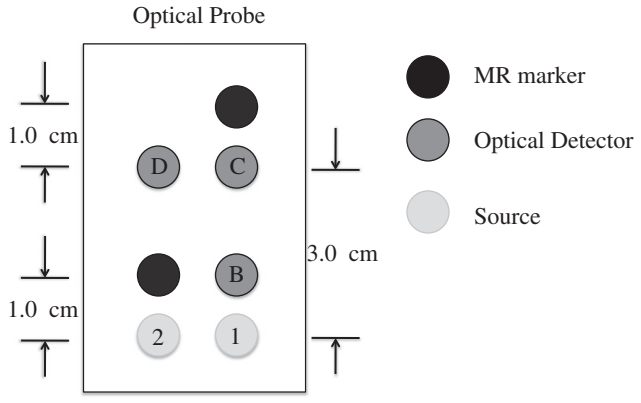

Fig. 1. Diagram of the fNIRS probe with 2 optical sources and 3 optical detectors.

All MRI data were acquired on a Siemens TIM Trio 3 T scanner (Siemens Medical Systems, Malvern, PA) using a 12-channel phased array head matrix coil. To reduce the aliasing of the cardiac signal (~1 Hz) on the BOLD data, the TR has to be smaller than 0.5 s to sample a cardiac frequency of 1 Hz (or bigger) based on the Nyquist theorem (five out of six of our subjects had heart rate greater than 1 Hz). However, reducing the TR lowers the number of slices that can be obtained, reducing either the spatial resolution or coverage of the fMRI data. To work around this trade-off, we employed a segmented fMRI acquisition, which allowed us to lower the TR to 0.5 s while maintaining the same spatial resolution ($3.5\times3.5\times3.5$ mm). We serially imaged multiple, adjacent subvolumes (segments) of brain. Each segment consisted of a stack of consecutive slices. Segments were acquired from the bottom of the cerebellum to top of the head, and each acquisition was a full resting state scan lasting about 6 min and 30 s with the following parameters: 240 time points, TR/TE = 500/30 ms, flip angle 48°, matrix = 64×64 on a 224×224 mm FOV, 9 3.5 mm slices with no gap parallel to the AC–PC line extending down from the top of the brain with a brief pause (~10 s) between each consecutive stack scan. The total number of segments needed depended on the size of the brain; for this group of subjects, 5 or 6 segments were needed to cover the whole brain. Fig. 2(a) illustrates the procedure on one subject. For the depicted subject, five segmental scans were needed for full brain coverage. Physiological waveforms (pulse oximetry, and respiratory timing and depth) were recorded using the scanner's built-in wireless fingertip pulse oximeter and respiratory belt at a rate of 50 Hz throughout the entire set of acquisitions. This segmented acquisition is possible because the quantity of interest is the correlation between the fNIRS and fMRI data, which is consistent between task free acquisitions, rather than the actual time courses, which vary. Under these circumstances, data from multiple resting state acquisitions can be combined seamlessly.

Combined data analysis

Regular preprocessing steps in FSL (Smith et al., 2004), including motion correction, slice timing correction and spatial smoothing were applied on fMRI data. Then the data analysis procedure (RIPTiDe), similar to the one we presented in the previous work (Tong et al., 2011b) with some important modifications, was used. As in the previous analysis, bandpass filtration was used to spectrally isolate signals of different physiological processes from simultaneously recorded data of oxy-hemoglobin concentration change (Δ[HbO]) from fNIRS, which had high temporal resolution (12.5 Hz). The Δ[HbO] is used due to its high sensitivity to global physiological fluctuations, such as cardiac pulsations. For each spectral band, a set of time-shifted versions of the signal was generated. These signals were then down-sampled to create a set of regressors at the sample rate of the fMRI data (2 Hz). A set of GLM analyses of the fMRI data was performed to determine the relationship between time shift and fit strength in each voxel. The results of this group of analyses were combined temporally to assess the spatial variation in this relationship as it evolved over time, and allowing visualization of the dynamic wave of correlation passing through the brain.

Several modifications in the data analysis procedure were introduced in this study. Firstly and most importantly, due to the fact that the fMRI data was acquired in sequential segments of slices, combined data analyses were carried out in three steps: first, each segment was processed individually, then the segments were merged, and lastly the results were registered onto the anatomical brain and concatenated over time. This procedure is shown for the cardiac signal in Fig. 2(b). In Step 1, for each set of slices, or segment, Δ[HbO] from the fNIRS signal in the cardiac band is successively time shifted and used as a regressor in the GLM based fMRI analysis. For each segment shown