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A spatial and temporal comparison of hemodynamic signals measured using optical and functional magnetic resonance imaging during activation in the human primary visual cortex

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Functional near infrared spectro-imaging (fNIRSI) is potentially a very useful technique for obtaining information about the underlying physiology of the blood oxygenation level dependent (BOLD) signal used in functional magnetic resonance imaging (fMRI). In this paper the temporal and spatial statistical characteristics of fNIRSI data are compared to those of simultaneously acquired fMRI data in the human visual cortex during a variable-frequency reversing checkerboard activation paradigm. Changes in the size of activated volume caused by changes in checkerboard reversal frequency allowed a comparison of the behavior of the spatial responses measured by the two imaging methods. fNIRSI and fMRI data were each analyzed using standard correlation and fixed-effect group analyses of variance pathways. The statistical significance of fNIRSI data was found to be much lower than that of the fMRI data, due mainly to the low signal-to-noise of the measurements. Reconstructed images also showed that, while the time-course of changes in the oxy-, deoxy-, and total hemoglobin concentrations all exhibit high correlation with that of the BOLD response, the changes in the volume of tissue measured as "activated" by the BOLD response demonstrate a closer similarity to the corresponding changes in the oxy- and total hemoglobin concentrations than to that of the deoxyhemoglobin.

Keywords: Human brain; Functional activity; Near infrared imaging; fMRI

Introduction

Near-infrared spectroscopy provides a unique tool to study neurovascular coupling, with the ability to measure changes in both oxy- and deoxyhemoglobin concentrations. These measures can be related to changes in physiological parameters such as cerebral blood flow (CBF), cerebral blood volume (CBV) and the cerebral metabolic rate of oxygen ($CMRO_2$). A current search of scientific reference engines using the keywords "near infrared" and "brain" returns more than 600 references, including about 70 review papers (for the most recent reviews see Gibson et al., 2005; Gratton et al., 2005). However, the majority of these works use near infrared spectroscopy (NIRS) to study the human brain with little spatial resolution beyond the location of the optical probe (Strangman et al., 2003; Toronov et al., 2003b). A relatively small number of papers have performed surface mapping of the functional cerebral hemodynamics, i.e., the locations of the hemodynamic or neuronal changes are projected onto the surface of the head, again with a significant loss of spatial information (Franceschini et al., 2000; Sato et al., 2005; Schroeter et al., 2004; Seiyama et al., 2004).

It was realized quite early on (Arridge et al., 1986) that NIRS measurements at multiple locations combined with image reconstruction algorithms can, in principle, be used for near infrared imaging, so that cerebral hemodynamic changes could be mapped in three dimensions. However, in spite of a significant amount of theoretical work (Boas et al., 2004a,b; Boas and Dale, 2005; Guven et al., 2005; Li et al., 2005; Xu et al., 2005), the literature on practical three dimensional fNIRSI of the human brain is limited to a few papers (Bluestone et al., 2001; Boas et al., 2004b; Hintz et al., 2001; Hoshi et al., 2000; Zhang et al., 2005a,b). The reason for the modest progress in full three-dimensional fNIRS is the combination of the extremely high scattering of light in biological tissue, together with the optical heterogeneity of the human head. Improvements in image reconstruction algorithms based on the solution of the inverse problem for light transport in highly scattering media continue to attract a significant effort from many groups (Arridge, 1999; Li et al., 2005; Xu et al., 2005). It has also been shown that the problem of tissue heterogeneity can be eased somewhat by utilizing structural information provided by MRI (Boas et al., 2004a,b; Guven et al., 2005; Zhang et al., 2005a,b). Another benefit of the combination of fNIRSI with MRI is the possibility of simultaneous recording of fMRI and optical data. This allows comparisons of the spatial and temporal characteristics of the fMRI signals with optically-derived hemodynamic changes to clarify the contributions of different physiological parameters to the fMRI signals. Several studies of functional activations have

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been performed in the human motor cortex by simultaneous fMRI and NIRS (Toronov et al., 2000, 2001b, 2003a,b). In particular it was found that, in the human motor cortex, the temporal dependence of the deoxyhemoglobin concentration was the factor most closely related to the BOLD fMRI signal. In order to extend the capability to study cerebral hemodynamics to three-dimensional tomography, our group has recently developed a methodology for integrating fNIRSI with MRI (Zhang et al., 2005a), enabling simultaneous fMRI and fNIRSI data recording. Simultaneous data acquisition allows robust incorporation of spatial MRI information into the optical data reconstruction algorithm and accurate co-registration of fNIRSI and fMRI results. A similar methodology has been developed by the Photon Migration Group at Massachusetts General Hospital (Hoge et al., 2005).

Simultaneously acquired spatiotemporal fNIRSI and fMRI data should ideally be analyzed using similar statistical methods. The standard pathway for fMRI data analysis typically comprises two stages: preparatory single-subject analysis followed by combined group analysis. The only paper which has applied group analysis to fNIRSI data was a study of the left-hand side of the human visual cortex by NIR topography (Schroeter et al., 2004). However, since no MRI data were acquired in that study, the optical data could not be spatially transformed to standard stereotactic space (Talairach and Tournoux, 1988). The primary goal of this paper is to present the results of a full fixed-effect group analysis of four-dimensional (space+time) fNIRSI data for different activation conditions in the human visual cortex, and to compare the statistical properties of fNIRSI with fMRI data. This study required designing an optical probe for simultaneous fMRI and fNIRSI recording from the human primary visual cortex, which was particularly difficult to implement because the subject's head must rest directly on the optical probe within the tight confines of the MRI scanner. A parallel aim was to compare fMRI and fNIRSI data for different activation conditions in the human visual cortex. In order to achieve these goals fNIRSI and fMRI data were acquired simultaneously during the presentation of a reversing checkerboard paradigm with different reversal frequencies, and analyzed by the standard group analysis of variance pathway (Cox, 1996; Friston et al., 1995a).

Materials and methods

Subjects

Nine healthy, right-handed subjects, seven males and two females, between the ages of 21 and 40 (median age 26), signed the Informed Consent form approved by the Institutional Review Board at the University of Illinois at Urbana-Champaign.

fNIRSI instrument

The optical signals were recorded using a near infrared spectrometer (Imagent, ISS, Champaign, IL). The optical sources were laser diodes (690 and 830 nm) which were amplitude modulated at 150 MHz and time-multiplexed. Light reaching the detectors was amplified by photomultiplier tubes and consequently converted into AC, DC, and phase signals for each of the source-detector combinations (channels) at each wavelength of light. Data acquisition was synchronized with the fMRI measurements using the TTL-trigger signal from the MR scanner, which also triggered the beginning of the visual stimulation paradigm.

Optical probe

The optical probe was designed with 16 pairs of 400-μm-diameter core plastic-clad multimode silica source fibers and 4 detector fiber bundles. The physical size of the MR scanner mandated the use of prisms with dielectric reflective layers for the fiber bundles (metal reflecting surfaces were found to produce significant artifacts in MR images). The optical fibers were "ferruled" using plastic tubing, and the frame of the optical probe was constructed from polyurethane which has appropriate mechanical properties and produces insignificant artifacts in the MR images. The topology of the probe was designed so that the optical channels overlapped and the distribution of source-detector distances covered the optimal range (Toronov et al., 2003a), between approximately 20 and 30 mm, as shown in Fig. 1. An MRI visible marker was attached adjacent to each of the 16 optical source fiber pairs and four detector fiber bundles so that accurate source and detector positions could be estimated from MR images (Zhang et al., 2005a,b). The thickness of the probe was less than 20 mm to ensure that it could be placed comfortably between the back of the head and the bottom of the MRI birdcage head coil. The probe was carefully tested on a tissue-mimicking phantom with homogeneous optical properties to ensure that all source-detector channels provided very similar signal amplitudes. For the experiment, the center of the optical probe was placed as close as possible to the primary visual cortex. This was achieved by initial positioning the center of the optical probe approximately 2 cm above the inion, followed by a rapid MR scan to locate the visual cortex: if necessary, the optical probe was then moved by the requisite distance.

In order to minimize the influence of hair on the optical contact between fibers and the skin, we have designed a special fabric mask with holes directly underneath the locations of the sources and detectors of the optical probe. The mask was attached to the back of the subject's head using Velcro straps overlapped on the forehead. After attaching the mask, an operator cleared the hair within the holes by pushing the hair under the mask using a cotton-tipped stick. This technique worked very well, allowing consistent signal intensities to be recorded even on subjects with dark hair.

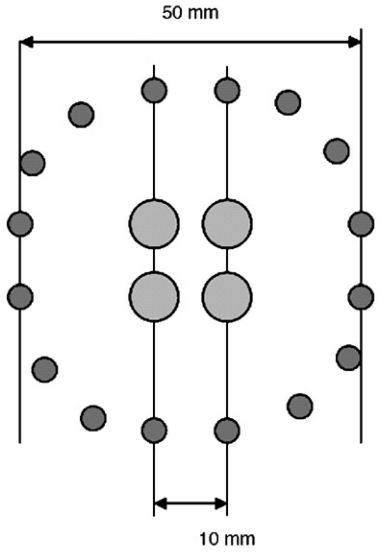

Fig. 1. Schematic of the optical probe. The probe has 16 pairs of source fibers and 4 detector fiber bundles.