Simultaneous fMRI and event-related near infrared tomography for studying hemodynamic and neuronal responses in human visual cortex

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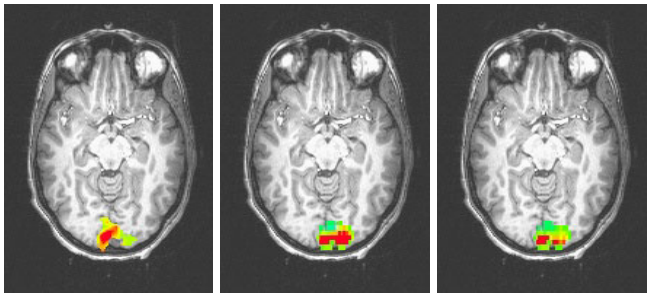
INTRODUCTION In spite of its central role in neuroimaging, BOLD fMRI is an indirect measurement of cerebral hemodynamics, and has a relatively low temporal resolution dictated by the hemodynamic response. In contrast, near infrared optical spectroscopy (NIRS) is a localized direct measurement of oxy- and deoxyhemoglobin concentrations with a response time on the order of milliseconds, which enables it to study the "fast" neuronal responses, such as the event-related optical signals (EROS). NIRS can also be used to study slower hemodynamic changes. Our previous studies have demonstrated that combined fMRI and NIRS can uncouple the contributions due to blood flow deoxyhemoglobin concentrations to the BOLD signals, as well as study the "fast" optical neuronal responses [1], [2]. However, the NIRS method is inferior to fMRI in localizing functional responses. When only a limited number of measurements are available in a highly inhomogeneous structure, such as the human head, optical image reconstruction represents a non-trivial inverse problem. In this work, we performed optical tomography by adapting the method of diffuse optical tomography (DOT) using a perturbation approach of the diffusion equation [3]. To compute the spatially dependent sensitivity point-spread function of the diffusion equation, we used Monte Carlo simulations [4] of light transport in a segmented head model from the high-resolution MR anatomical image. In order to demonstrate the capabilities of our bi-modality imaging technique, we acquired BOLD fMRI and near infrared optical data during functional stimulation on the primary visual cortex of humans. The reconstructed optical image of changes in oxy- and deoxyhemoglobin was compared with the BOLD fMRI study using EPI on a 3-Tesla MR head-scanner. The results show the promising feasibility of measuring hemodynamic and "fast" neuronal responses simultaneously.

COMPUTATIONAL Algorithms have been developed to identify MRI markers on the optical probe and consequently reconstruct the positions of the optical sources and detectors. This information is used for Monte Carlo simulations and co-registration of optical and fMRI results. A Monte Carlo simulation software package is used to simulate the integration kernel (the product of photon density and the Green's function) in the diffusion equation, which in turn can be written as a set of linear equations after discretization. The computation is based on stimulation induced changes in the absorption coefficient in this preliminary investigation. A simultaneous iterative reconstructive technique (SIRT) is used to reconstruct the image of absorption coefficient from the optical signal. The optical image reconstruction is performed with a resolution of $(4\ \text{mm})^3$. The solution to the inverse problem is constrained to voxels within the illuminated region of brain, which correspond to values of the integration kernel > 0.01.

EXPERIMENTAL The BOLD fMRI studies were performed on a 3-Tesla MR head-scanner (Allegra, Siemens) using a standard EPI pulse sequence (FOV 240 mm, resolution 64x64, slice thickness 4 mm, gap 10%, voxel size 3.75x3.75x4.0 mm^3, TR 2000 ms, TE 25 ms, and flip angle 60^o). A full-head high-resolution T_1-weighted 3-D anatomical MR image (MPRAGE) was taken for image co-registration and for the reconstruction of optical source-/detector-positions. It was also used to generate the segmented head model for optical simulations and image reconstruction. A flashing checkerboard was used as visual stimulation with different flashing frequencies (1, 2, 4, 6, and 8 Hz). We designed and constructed an optical probe specifically for this work which gave negligible MR image distortion. It consists of 16 pairs of optical fibers as light sources, and 4 detector optical fiber bundles. The near infrared light sources (690 and 830 nm laser-diodes) are amplitude modulated at 150 MHz. Optical data acquisition at a sampling rate of 16 ms was triggered by the MR scanner signal.

RESULTS The figures show functional maps for oxyhemoglobin, deoxyhemoglobin and BOLD fMRI signals, from left to right, respectively. Note that the deoxyhemoglobin map is displayed as a negative change for clearer visualization. While the BOLD map is similar to that of deoxyhemoglobin, the oxyhemoglobin map is not the same, indicating that the overall topology of the functional hemodynamic changes can be more complicated than that reproduced in the BOLD maps. The NIRS data had a signal-to-noise ratio sufficiently high to image hemodynamic responses on the single-subject level by averaging data over four stimulation blocks. By averaging optical data over several hundreds of checkerboard reversing stimulations, we have also been able to obtain the time course of the neuronal response, which occurred in the 50 ms time range (data not shown).

CONCLUSION Simultaneous fMRI and near infrared optical tomography on adult human heads has been demonstrated. Besides its fast response time, the optical method also provides a spatial resolution close to our BOLD fMRI measurement. It also better localizes the hemodynamic response compared with the traditional NIRS method. Near infrared optical tomography reveals not only the deoxyhemoglobin response as does BOLD fMRI, but also the oxyhemoglobin response and the fast signal due to neuronal activity. Therefore, it provides critical clues of physiological mechanisms of BOLD fMRI signals. Further study is underway into improving image reconstruction algorithms by incorporating scattering and using fMRI and optical data to further develop physiological models of the response to cognitive function.



BOLD fMRI | **Oxyhemoglobin change** | **Deoxyhemoglobin change (negative)**

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