Monitoring brain activity using near-infrared light

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The current techniques for diagnostic brain imaging can be broadly classified into structural and functional imaging approaches. Structural imaging of the brain aims to obtain purely anatomical information. Examples of structural imaging techniques are ultrasound imaging, X-ray computed tomography (CT), and magnetic resonance imaging (MRI). By contrast, the goal of functional imaging of the brain is to provide information on the physiological state of cerebral tissue. For example, parameters of interest in functional imaging are metabolic activity, blood flow, oxygen consumption, neuronal activity, etc. Functional imaging modalities include positron emission tomography (PET), single photon emission computed tomography (SPECT), functional MRI (fMRI), electroencephalography (EEG), and magnetoencephalography (MEG).

Near-infrared light penetrates through the intact scalp and skull to illuminate the brain, much like sunlight penetrates through the clouds to illuminate the earth.

Recently, a functional imaging approach based on visible and near-infrared light was proposed. Initial invasive studies on animal models in vivo have shown that optical methods are sensitive to the direct effects of neuronal activation[1] (occurring on a time scale of 10–100 msec), as well as to the blood flow and oxygenation changes (occurring on a time scale of seconds) induced by the neuronal activation in the cerebral cortex.[2] Following the initial invasive animal studies, noninvasive approaches have employed near-infrared light (in the wavelength range from 700 to 900 nm) to probe the human cortex through the intact scalp and skull.[3] In fact, it is now well-established that near-infrared light penetrates through the intact scalp and skull to illuminate the brain, much like sunlight penetrates through the clouds to illuminate the earth (the similarity between the two cases is that both the skull and the clouds act as stronger light scatterers than light absorbers). *Figure 1* schematically illustrates the noninvasive approach to the optical study of the brain. The main absorber for near-infrared light in brain tissue is hemoglobin (the oxygen-carrying protein in the blood) whose light absorption properties depend on its level of oxygenation. This accounts for the sensitivity of optical methods to changes in tissue perfusion and oxygenation.

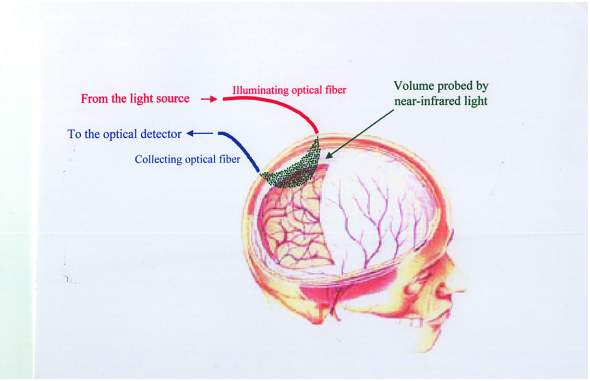

Figure 1 *Schematic representation of the noninvasive approach to the optical study of the brain. The light delivered to the skin by an optical fiber penetrates through the scalp and skull and probes the cerebral cortex before reaching the collecting optical fiber. The distance between the illuminating and collecting fibers is typically 3–4 cm. Near-infrared imaging of the brain involves the use of multiple pairs of source and detector optical fibers.*

This article presents an application of noninvasive near-infrared imaging for the optical mapping of the human cerebral cortex during a voluntary motor task (finger opposition).

Experimental

The optical instrument is a versatile, four-channel tissue spectrometer consisting of two synchronized tissue oximeter units (model 96208) (**ISS, Inc.,** Champaign, IL). One of these units is shown in *Figure 2*. The four parallel detection channels consist of four photomultiplier tube (PMT) detectors whose outputs are directed to a four-channel, 16-bit A/D acquisition card. These four independent detection channels are time-shared by 32 laser diodes that are multiplexed at a frequency of 100 Hz. In other words, the laser diodes are turned on and off in rapid succession with an on-time per diode of 10 msec. The average optical power emitted by the laser diodes during the on-time is no more than a few milliWatts. The multiplexing scheme can be selected by the user according to the particular ap-

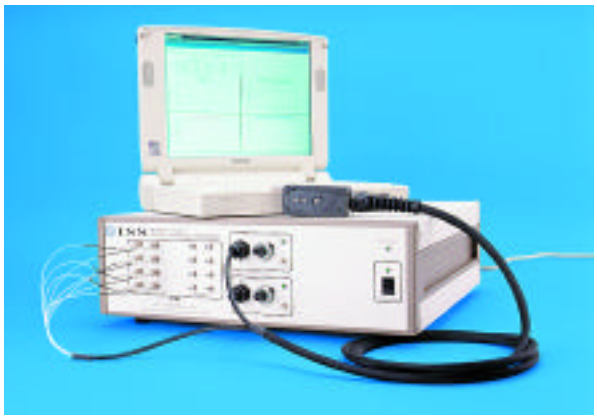

Figure 2 *Photograph of the frequency-domain tissue oximeter. Two synchronized tissue oximeter units were used (which provide a total of four parallel detection channels and 32 multiplexed light sources) for functional near-infrared imaging (fNIRI) of the brain (photograph courtesy of* ***ISS, Inc.****).*

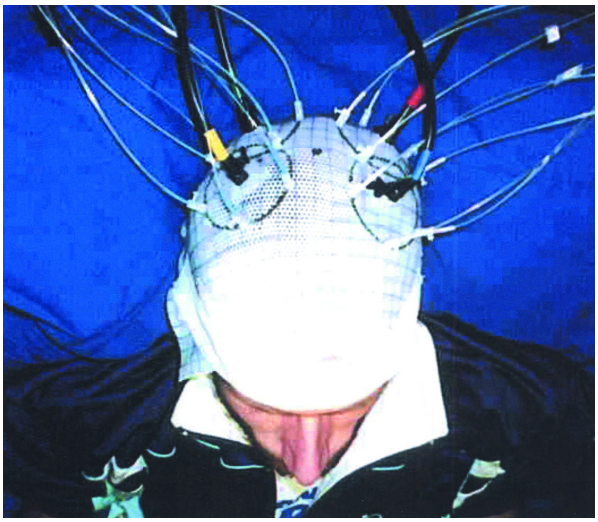

Figure 3 *Optical helmet used to arrange the 32 illuminating optical fibers and four collecting optical fibers on the head of the subject. The helmet and fiber optic cables contain no metal; thus this setup is suitable for concurrent optical and fMRI brain imaging.*

plication. In the present case, a source-detector configuration intended to map two 4×9 cm^2 cortical areas in each cerebral hemisphere was used (*Figure 3*). Therefore, the laser diodes were turned on in pairs (each pair consisting of one laser diode per brain hemisphere), after the negligible cross-talk induced by a laser diode in one hemisphere was verified to an optical detector in the other hemisphere. Because of the 10-msec on-time per laser diode, a full multiplexing cycle over the 16 pairs of laser diodes was completed every 160 msec. This is the data acquisition time per each pair of optical images. The data processing involves a computationally fast linear back-projection algorithm, so that the optical images can be displayed in real time during the examination.

The 32 laser diodes can be selected by the user according to the wavelength requirements of the particular application. The authors chose to perform measurements of the absorption coefficient at two wavelengths ($\lambda_1 = 690$ and $\lambda_2 = 830$ nm) that provide sufficient information for determining the concentration of the two species of interest (oxyhemoglobin and deoxyhemoglobin). The laser diodes and the PMT detectors are coupled to fiber optics. The 32 illuminating optical fibers (16 guiding light at 690 nm and 16 at 830 nm; core diameter: 400 µm) and the four collecting optical fiber bundles (internal diameter: 3 mm) are placed on the subject's head, as illustrated in Figure 3.

The measured intensity changes for each source-detector pair $[\Delta I(\lambda_1), \Delta I(\lambda_2)]$ were converted into changes in the cerebral absorption coefficients $[\Delta\mu_a(\lambda_1), \Delta\mu_a(\lambda_2)]$ using a modified Beer-Lambert's law approach.[4] Under the assumption that the absorption changes at λ_1 and λ_2 are solely due to changes in the cerebral concentrations of oxyhemoglobin ($\Delta[HbO_2]$) and deoxyhemoglobin ($\Delta[Hb]$), the hemoglobin concentration changes are given by:

$$\Delta[HbO_2] = \frac{\varepsilon_{Hb}(\lambda_2)\Delta\mu_a(\lambda_1) - \varepsilon_{Hb}(\lambda_1)\Delta\mu_a(\lambda_2)}{\varepsilon_{HbO2}(\lambda_1)\varepsilon_{Hb}(\lambda_2) - \varepsilon_{HbO2}(\lambda_2)\varepsilon_{Hb}(\lambda_1)}, \quad (1)$$

$$\Delta[Hb] = \frac{\varepsilon_{HbO2}(\lambda_1)\Delta\mu_a(\lambda_2) - \varepsilon_{HbO2}(\lambda_2)\Delta\mu_a(\lambda_1)}{\varepsilon_{HbO2}(\lambda_1)\varepsilon_{Hb}(\lambda_2) - \varepsilon_{HbO2}(\lambda_2)\varepsilon_{Hb}(\lambda_1)}, \quad (2)$$

where ε_{Hb} and ε_{HbO2} are the known molar extinction coefficients of Hb and HbO_2.[5] Finally, the individual source-detector readings are linearly back-projected to yield the spatial maps of the temporal changes in the cerebral concentrations of Hb and HbO_2.[6]

Results and discussion

The following results are from a study conducted on a healthy, left-handed, 54-year-old male subject. After placing the optical helmet as shown in Figure 3, the subject was asked to perform a protocol consisting of a 3-min baseline (while he was comfortably resting in a supine position), followed by 10 15-sec finger-opposition tasks performed alternatively with either the right or left hand. The time evolution of this protocol is illustrated in *Figure 4*. *Figure 5* shows the aver-

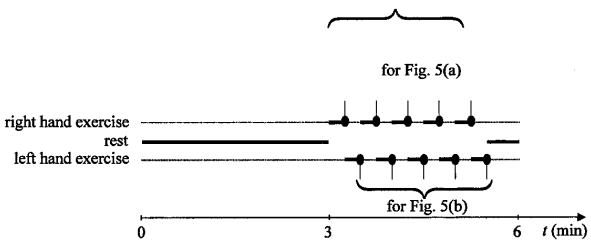

Figure 4 *Motor activation protocol consisting of alternating periods of right- and left-hand finger-opposition tasks. The average of the Δ[Hb] images recorded at the end of each right-hand (left-hand) motor task (collected at the times indicated by the circles) is shown in* Figure 5.

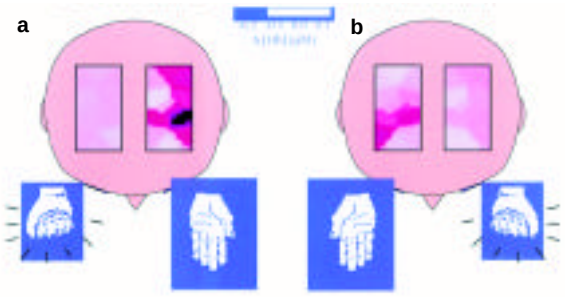

Figure 5 *Average image of the changes in cerebral deoxyhemoglobin concentration (Δ[Hb]) recorded at the end of each of the five periods of a) right-hand and b) left-hand finger-opposition tasks. Note the activation-induced decrease in the deoxyhemoglobin concentration at the motor cortex contralateral to the exercising hand.*

age images of Δ[Hb] recorded at the end of each right- and left-hand task, respectively (as shown pictorially in Figure 4). The cerebral activation is represented by a localized decrease in cerebral [Hb], which is determined by the increased wash-out of deoxyhemoglobin resulting from the local increase in blood flow.[3] It must be noted that the quantitative values of the gray-scale palette for the changes in cerebral [Hb] may not be accurate because of the approximate model used (modified Beer-Lambert's law and linear back-projection). However, it is believed that the direction (increase vs decrease) and the spatial distribution of the observed [Hb] changes are accurate. Figure 5 shows the expected contralateral cerebral response to the finger-opposition task (namely, the left motor cortex is activated by the right-hand motor task and vice versa). The spatial resolution of the optical images can be improved by using a finer distribution of illuminating and collecting optical fibers.

The spatial resolution of the optical images can be improved by using a finer distribution of illuminating and collecting optical fibers.

Functional near-infrared imaging (fNIRI) of the brain is a practical approach. It involves a compact instrumentation that is suitable for bedside or portable operation, and it is not hindered by the presence of the protective tissue layers of skin, scalp, skull, cerebrospinal fluid, dura, etc. Even the presence of hair does not prevent the application of noninvasive optical imaging of the brain, because the optical fibers can be placed in close proximity to the skin through the hair. While the lack of optical penetration beyond the cortical gray matter is a drawback, a significant amount of functional brain activity occurs at the level of superficial brain layers that are optically accessible. A more significant limitation is the relatively poor spatial resolution, on the order of 5 mm, of optical brain imaging. However, this limitation is balanced by a high temporal resolution (currently on the order of 10–100 msec, but potentially even better than that) and by the relative insensitivity of optical imaging to the subject's motion (which significantly deteriorates the quality of fMRI, PET, and SPECT images). Furthermore, it has recently been reported that noninvasive near-infrared techniques can directly monitor the fast neuronal activation in humans,[7,8] in addition to the activation-induced hemodynamic response illustrated in this article (Figure 5). The sensitivity of near-infrared brain imaging to both ends of the neurovascular coupling, together with the low sensitivity to the subject's motion, makes optical imaging a unique method for functional studies of the brain that may open new opportunities in the field of brain research.

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