Fast Optical Response to Electrical Activation in Peripheral Nerves

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ABSTRACT

Complex neuronal structures and interactions make studying fast optical signals associated with brain activation difficult, especially in non-invasive measurements that are further complicated by the filtering effect of the scalp and skull. We have chosen to study fast optical signals in the peripheral nervous system to look at a more simplified biological neuronal structure and a system that is more accessible to non-invasive optical studies. In this study, we recorded spatially resolved electrical and optical responses of the human sural nerve to electrical stimulation. A 0.1 ms electrical stimulation was used to activate the sural nerve. Electrical signals were collected by an electromyogram machine and results showed an electrical response spanning a distance of 8 mm across the nerve. Optical signals were collected by a two-wavelength (690 and 830 nm) near-infrared spectrometer and displayed a characteristic decrease in intensity at both wavelengths. Data were taken at multiple positions and then reproduced five times. The average optical data over the five trials showed an optical signal that was spatially consistent with the electrical response to sural nerve stimulation.

Keywords: Near-infrared spectroscopy, electrical stimulation, peripheral nerves, fast optical signal

INTRODUCTION

Hemodynamic response to neural activation has been studied extensively using functional magnetic resonance imaging[1] (fMRI) as well as near infrared spectroscopy[2] (NIRS). Optical methods depend on the scattering and absorption of light by the biological tissue being studied. Scattering of light is caused by the change in refractive index at the microscopic level and absorption is due to the presence of light absorbing chromophores such as hemoglobin, cytochromes, and water. The fMRI studies using blood oxygen level dependent (BOLD) signals measure hemodynamic changes but do not answer questions about the relationship between these changes and actual neural activation. Optical methods, such as NIRS, are particularly promising in functional imaging because in addition to measuring hemodynamic signals, they are sensitive to functional features at a temporal scale of 10-100 ms.

A slow hemodynamic response can be measured with NIRS a few seconds after activation as a result of an increase in blood flow at the area of activation in the brain. A separate faster optical response has been detected,[3] and associated with event related potentials,[4] about 100 ms after the brain stimulation. These fast optical signals have been studied in the brain using visual,[3] somatosensory,[5] and motor[6] stimuli. The correlation and causality between the electrical neural activation and the induced hemodynamic response is referred to as neurovascular coupling.

Currently, there is no consensus as to the physiological origin or robustness of the fast optical signals measured in the brain non-invasively[7] because the fast signal is small (~0.04% intensity change) when measured through the intact scalp and skull. The peripheral nervous system, however, has advantages such as simpler single nerve bundles that lay just millimeters below the skin, avoiding of scattering effects of the scalp and skull. The peripheral nervous system provides a potentially simpler and more robust model to study fast optical signals in response to electrical stimulation of selected nerves.[8] This study reports the spatial dependence of the optical and electrical responses associated with the electrical stimulation of the sural nerve in a human subject.

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MATERIALS AND METHODS

The electrical stimulation of 0.1 ms at a frequency of 1.5 Hz was provided by a Teca Synergy EMG monitoring system (Viasys Healthcare, Conshohocken, PA). The level of current varied with each subject but was kept constant within trials of the same subject. This current must be below the threshold of any visible motion to avoid motion-related artifacts in the optical data. The stimulating electrode was coupled to the skin over the sural nerve about 10 cm above the left ankle with conducting gel and secured with medical tape. Recording electrodes were placed distal to the stimulating electrode when recording optical data. The reference electrode was placed on the skin over the lateral malleolus and used to subtract the common signal of the unrelated tissue from the differential signal of the two recording electrodes. The placement of the recording and stimulating electrodes were switched in order to record the electrical responses spatially, due to electrode geometries. The location of the sural nerve was identified by the position of the largest sensory nerve action potential (SNAP) measured by the EMG monitor and traced distally along the nerve. Then, 16 recording positions (from 0 to 30 mm) were marked with 2 mm separation, stretching from the bottom of the lateral malleolus to the sole of the foot (see Fig. 1). For electrical data, the stimulating electrodes were placed at each previously specified position and SNAPs were recorded at each position. Figure 1 shows the experimental set up for the electrical (a) and optical (b) recordings.

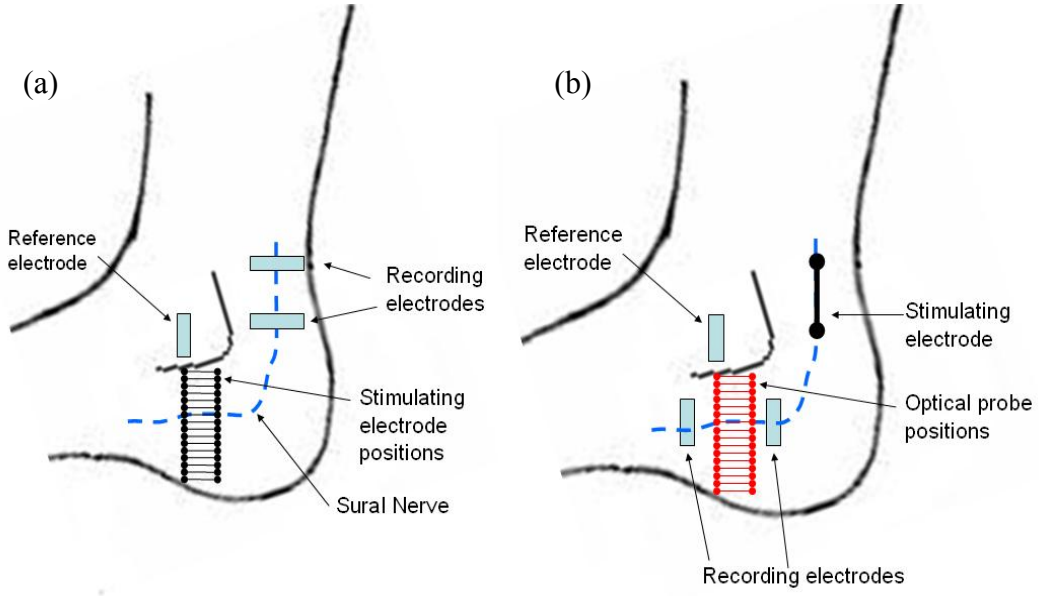

Figure 1. Experimental Setup of Electrical (a) and Optical (b) data collection

The optical spectrometer (ISS, Inc. Champaign, IL) used for the NIRS measurements featured one photomultiplier tube detector and two fiber-coupled laser diodes emitting at 690 and 830 nm. The optical probe housed the detector fiber bundle and two 400 μm source fibers, using prisms to deflect the light so that the optical fibers are parallel to the skin. The distance between the source and detector fibers was 1.5 cm. Data were acquired at a frequency of 50 Hz, corresponding to an acquisition time of 20 ms per data point. After obtaining electrical data, new recording electrodes were placed as shown in Fig. 1(b), the stimulating electrode was replaced and optical data were collected at the same previously marked 16 positions.

Synchronization between the electrical stimulation and the NIRS instrument was provided by an auxiliary input channel in the NIRS instrument. Each trial lasted 30 seconds, during which about 45 electrical pulses were administered. The optical probe position was changed after each trial from position 0-30 mm. Then the trials were repeated five times, through the entire set of 16 positions. A folding average over a 600 ms period was applied to the optical intensity data over all of the 45 stimulating pulses. The changes in intensity of the five trials were averaged and the maximum change at each position was recorded.

RESULTS AND DISCUSSION

Optical data is discussed in terms of the relative change in intensity (I), defined as $\Delta I/I_0$, where $\Delta I = I - I_0$ and I_0 represents the average intensity during the 120 ms immediately preceding the pulse of electrical stimulation. Figure 2(a) shows the response curve for trial 5 at the 14 mm position, showing $\Delta I/I_0$ for the wavelengths of 690 and 830 nm. The optical signal reaches a peak intensity change of about -0.2% at ~100 ms after the stimulation pulse is given and fully recovers after ~300 ms. We observe that this signal is one order of magnitude greater than the fast optical signal measured non-invasively in the brain. Using the modified Beer-Lambert law, the intensity changes can be translated into changes in concentrations of oxy-hemoglobin [HbO], deoxy-hemoglobin [Hb] and total hemoglobin [HbT]=[HBO]+[Hb] (Fig. 2(b)), using differential pathlength factors of 6.51 at 690 nm and 5.86 at 830 nm.

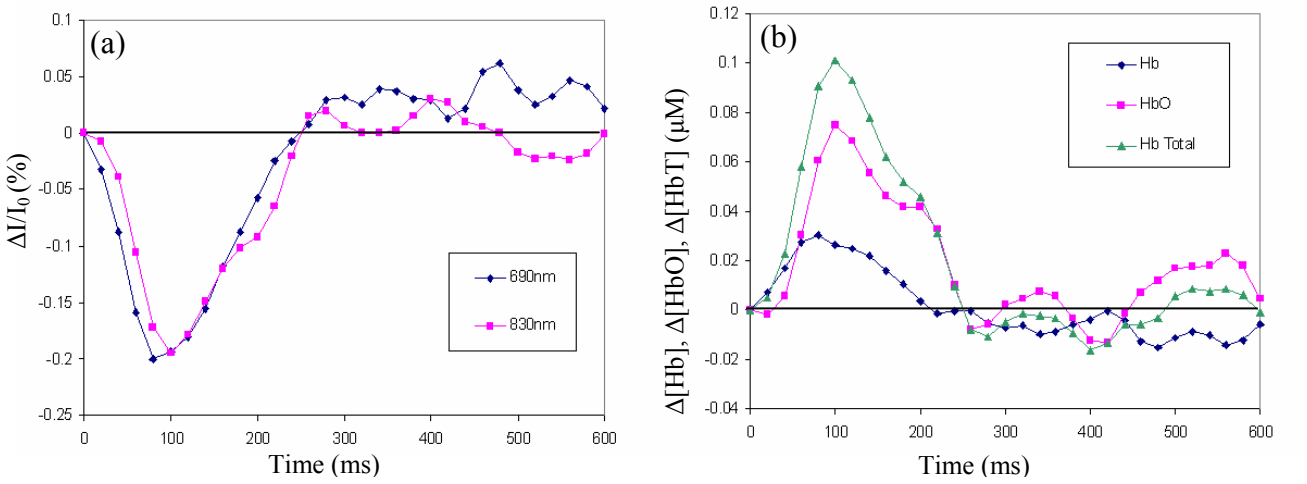

Figure 2. (a) Changes in intensity at 690 and 830 nm and (b) the corresponding changes in oxy- (HbO), deoxy- (Hb), and total (HbT) hemoglobin concentration.

The electrical measurements for the 16 different positions of the stimulation electrodes show that there is an electrical response to the stimulating pulse at coordinates 6-14 mm across the nerve (see Fig. 3(a)). All other positions result in no electrical signal recorded from the sural nerve. The maximum electrical response was recorded at 12 mm. Figure 3(a) shows a graph of the recorded electrical response at the 16 different positions. We took the average and standard deviation of the maximum change in intensity of the five trials at each of the 16 positions. The optical data in Fig. 3(b) shows that the relative intensity changes are present at coordinates 8-16 mm. A comparison between the electrical and optical data suggests that the lateral spatial extent of both signals is about 8 mm. The maximum average change in intensity was recorded at 14 mm, with $\Delta I/I_0 \sim -0.1\%$. The standard errors of the optical data show a significant difference between the signals from 8mm-16mm and those from areas away from the sural nerve. To get a sense of the optical data measured at different positions during a given trial, Fig. 4 shows the optical signals measured at 690 nm during trial 5 at each position from the ankle (0 mm) to the sole (30 mm) and shifted by arbitrary offests for clarity. Similar spatially dependent data is measured at 830 nm. We observe a trend where the signal starts from zero at positions closest to the ankle and returns to zero at positions closest to the sole.

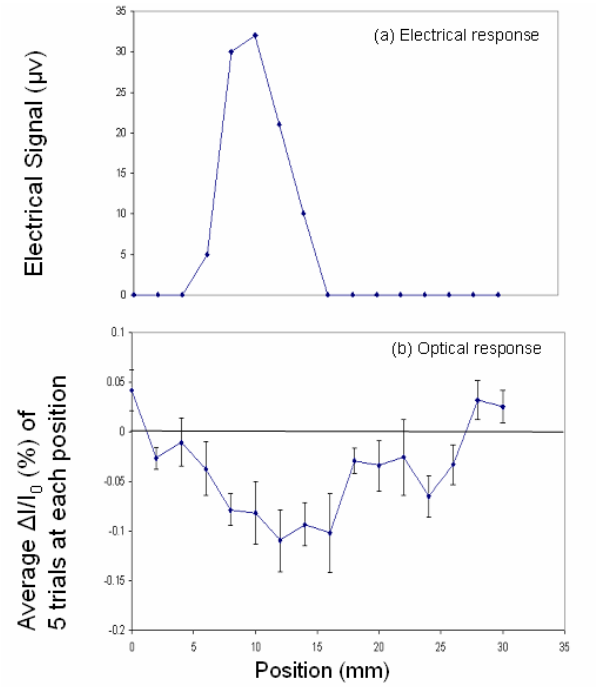

Figure 3. Electrical (a) and averaged optical (b) signals at the 16 positions shown in figure 1.

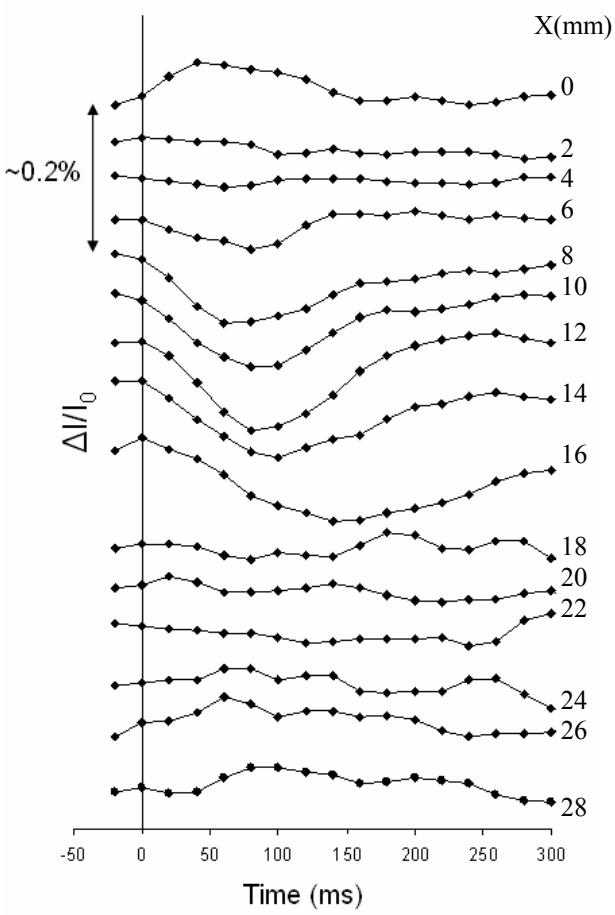

Figure 4. Fast optical signals measured at 690 nm, positions at 0 mm (top) to 28 mm (bottom).

CONCLUSION

We have reported spatially resolved measurements of optical and electrical signals associated with electrical stimulation of the sural nerve in a human subject. While the central and peripheral nervous systems present unique physiological and functional features, we hypothesize that there may be similarities in the relationship between electrical and optical signals in the brain and peripheral nerves. Under this hypothesis, peripheral nerves, which are more accessible than the brain to non-invasive optical studies, can provide an effective system to investigate neurovascular coupling. Even beyond this hypothesis, an understanding of the relationship between the fast (ms) electrical signals and slower (~100 ms) optical signals associated with peripheral nerve stimulation may have important physiological and diagnostic implications.

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