Optical Response to Peripheral Nerve Activation: Possible Origins and Diagnostic Potential

Debbie K. Chen[1], Yunjie Tong[1], Jeffrey M. Martin[2], Angelo Sassaroli[1], Peter R. Bergethon[2], and Sergio Fantini[1]

[1] Tufts University, Department of Biomedical Engineering, Medford, MA
[2] Boston University School of Medicine, Department of Anatomy and Neurobiology, Boston, MA

Abstract

We report our latest findings in the study of the optical signals associated with electrical stimulation of peripheral nerves. In a pilot study, we have observed a difference in the temporal features of the optical signals measured on healthy subjects vs. subjects with diagnosed neuropathies. We have observed changes in the spectral features of the optical signals measured before and after limb venous occlusion, suggesting an influence of the baseline tissue hemodynamics. These results suggest a diagnostic potential for this electro-optical assessment of peripheral nerves.

Introduction

Optical signals on different timescales have been studied extensively in the brain. The scattering signal accompanying a nerve depolarization is usually referred to as the fast signal because it is on the order of the action potential (~2ms)[2]. The hemodynamic signal accompanying brain activation, arising 3-5 s after stimulation, is referred to as the slow signal[3]. Some studies using near-infrared spectroscopy have shown that there is an intermediate signal (~100 ms) following brain activation, but no consensus has been made on its reproducibility and its origins. We explore the peripheral nervous system because the nerve bundles are larger, more directed and easier to access than the brain.

Methods

A schematic of the experimental setup is shown in Figure 1. A surface electrode is placed on a palmar branch of the median nerve and stimulates the nerve with a 0.1 ms pulse at 1.5 Hz. Electrical stimulation was provided by an electromyogram system that administered regulated current levels below the threshold of any visible motion to avoid motion related artifacts in the optical data. An optical probe with 2 sources and 2 detectors (shown in Figure 2) is placed on the wrist. The source fibers are coupled such that each source fiber at the probe will emit both 690nm and 830nm light. The detector fibers are connected to two separate PMTs in the tissue spectrometer. The 2 source, 2 detector optical probe detects optical signals from 4 source-detector areas at one time, providing spatial information.

In the pilot study, we tested 12 healthy subjects and 3 subjects with previously diagnosed neuropathies. Each trial was 1 minute long, 90 stimulating pulses and a folding average was used to average the data. A typical intermediate optical response is shown in Figure 3 with its corresponding SNAP. Using a cubic spline, we increased the temporal resolution from 40ms per data point to 1ms per data point and calculated the average peak time and average pulse width of each subject. The results are shown in Figure 4.

In the occlusion study, 4 subjects were put under both venous (50mmHg) and arterial (150mmHg) occlusion. Each trial consisted of a 2 min baseline, 2 min stimulation with no occlusion, 5 min occlusion, and 5 min recovery. The frequency content of the raw data during the 2 minute stimulation without occlusion is shown in Figure 5. The maximum $\hat{I}\ I/I_0$ is calculated for each stimulation period (Figure 6). The bulk tissue [Hb],[HbO_2] and [HBT] are presented in Figure 7. Figures 5-7 are separated into arterial occlusion (a) and venous occlusion (b).

Figure 1. Experimental Setup

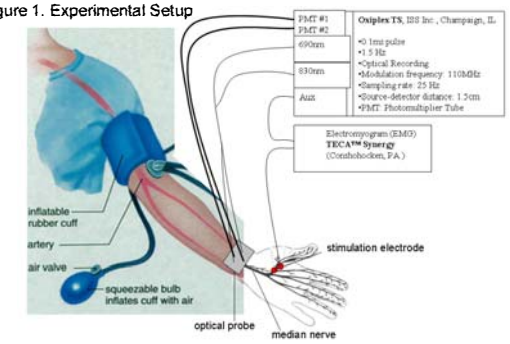


Figure 2. Schematic of 2 source × 2 detector Optical probe

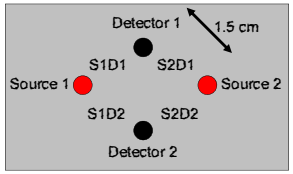


Figure 3. A typical optical response and its corresponding sensory nerve action potential (SNAP)

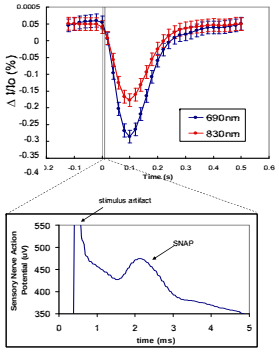
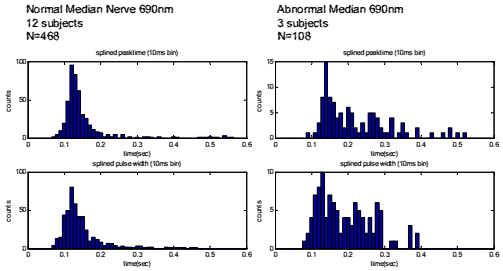


Figure 4. Histograms of peak time and pulse width of Healthy vs. Abnormal Subjects



ARTERIAL OCCLUSION

Figure 5a. Subject 1 Arterial Occlusion Frequency Content During Median Nerve Stimulation

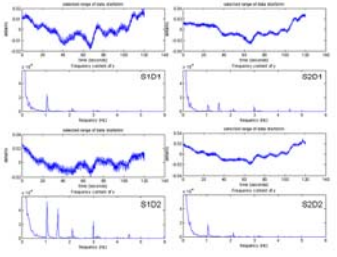


Figure 6a. Subject 1 Stimulated Max $\hat{I}\ I/I_0$ Arterial Occlusion

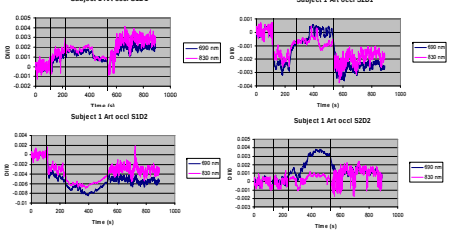
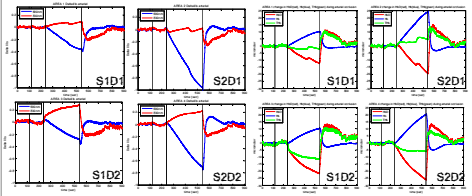


Figure 7a. Subject 1 Bulk Tissue Arterial Occlusion



VENOUS OCCLUSION

Figure 5b. Subject 1 Venous Occlusion Frequency content During Median Nerve Stimulation

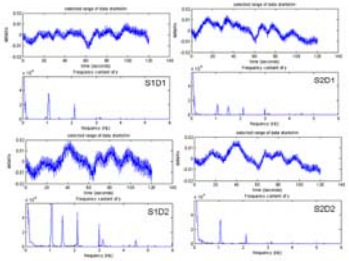


Figure 6b. Subject 1 Stimulated Max $\hat{I}\ I/I_0$ Venous Occlusion

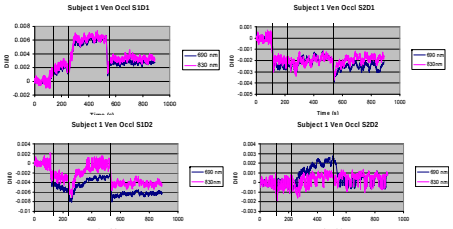
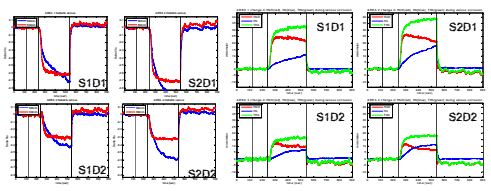


Figure 7b. Subject 1 Bulk Tissue Venous Occlusion



Discussion

- Abnormal subjects show an intermediate signal with a slower peak time and wider pulse width (Figure 3).
- The area that shows the most response to electrical stimulation (highest 1.5 Hz frequency component) is S1D2. Area S2D1 has smaller 1.5 Hz component while S1D1 and S2D2 areas shows minimal 1.5 Hz contributions. We can conclude that the optical response (1.5 Hz) is not interfered by the heart beat (1 Hz). (Figure 5 a and b)
- The areas with 1.5 Hz components are the areas most likely probing a blood vessel that responds to median nerve stimulation.
- During both venous and arterial occlusion Areas S1D2 and S2D1 show a negative max $\hat{I}\ I/I_0$~ 0.2-0.5% during the 2 min stimulation w/o occlusion, therefore we hypothesize the intermediate optical signal is due to a quick vasodilation.
- Areas S1D1 and S2D2 are most likely not probing a blood vessel (little or no 1.5 Hz component) and show either a local increase (S1D1) in max $\hat{I}\ I/I_0$ or no change (S2D2) during 2 min stimulation w/o occlusion.
- Area S1D2 during arterial occlusion suggests that the blood vessel responding to median nerve stimulation is more oxygenated (arteriole) because the 830nm max $\hat{I}\ I/I_0$ behaves opposite of bulk tissue. This also suggests intermediate optical signal is a local and separate response system than the bulk tissue.
- Area S1D2 during venous occlusion shows negative but increasing max $\hat{I}\ I/I_0$ that corresponds with the bulk tissue behavior. This may be because, if in fact we are probing an arteriole, the bulk increase in oxygen saturation during venous occlusion dominates a local vasodilation.

Conclusion

The intermediate optical signal in healthy subjects peaks and recovers faster than subjects with neuropathies. Our data suggests that the signal may originate from a quick vasodilation of local arterioles responding to electrical stimulation of the median nerve, which may be impaired in disease states, leading to damage of the vasculature and eventually nerve damage.

References:

1. Y. Tong, J. M. Martin, A. Sassaroli, P.R. Clervil, P. R. Bergethon, and S. Fantini, ÚFast optical signals in the peripheral nervous system,Ù*J. Biom. Opt.* 11, 044014-1-5 (2006).
2. R. A. Steponoski, A. LaPorta, F. Raccuia-Behling, G. E. Blonder, R. E. Slusher, and D. Kleinfeld, "Noninvasive detection of changes in membrane potential in cultured neurons by light scattering," *Proc. Natl. Acad. Sci. U.S.A.*, 88, 9382-9386 (1991).
3. E. A. Deyoe, P. Bandettini, J. Neitz, D. Miller and P. Winans, ÚFunctional magnetic resonance imaging (FMRI) of the human brain,Ù *J Neurosci Methods*, vol. 54, pp.171-187, 1994

Acknowledgements: CIMIT/U.S. Army Medical Acquisition Activity (USAMRAA) no. W81XWH-07-2-0011, NIH Grant R21-DA021817