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Stimulating nerves with laser precision

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Pulsed infrared laser light provides a new method for nerve stimulation with unmatched precision, and could soon be used in medical procedures.

Our understanding of the nervous system has grown significantly over the past 20 years, triggering the emergence of many new and exiting medical procedures for the diagnosis and treatment of neurological diseases.[1] The recent growth in research and advances in scientific knowledge have allowed clinicians to specialize in this area. Unfortunately the standard method of stimulating neural tissue—with electrical current—has remained unchanged, and in some respects limited, for over a century. Shortcomings of this technique include: poor specificity that limits spatial resolution, charge build up, electrical artifacts that prevent stimulation and recording in close proximity, and damage caused by the physical contact from the electrodes themselves.

Although these limitations have encouraged neuroscientists to search for alternative means of stimulation, few techniques have been successful in clinical applications. In fact, the scientific community relies on the well-characterized behavior of electrically stimulated neural tissues to study, diagnose, and treat disorders of the nervous system. As part of a collaborative effort between Vanderbilt University's Biomedical Optics Laboratory and Department of Neurological Surgery, we recently demonstrated a fundamentally different approach to nerve stimulation that circumvents the issues described above. The basis of this work is that pulsed laser light can be used for contact-free, damage-free, artifact-free stimulation of discrete populations of neural fibers.[2,3]

Transient optical stimulation of nerves relies on pulsed infrared-laser light to elicit action potentials in neural tissue. Much of the preliminary work in optimizing this technique involved using the peripheral nerves of mammals in vivo to evoke muscle contraction. We determined safe and efficient parameters of laser stimulation based on the geometry and morphology of

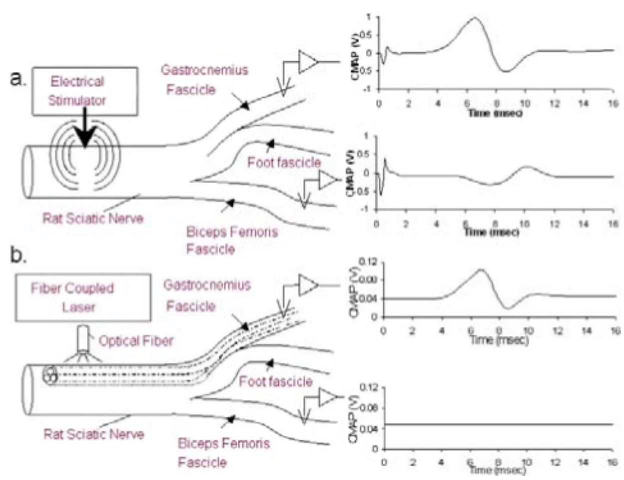

Figure 1. *Electrical and laser stimulation create different spatial selectivities in the rat sciatic-nerve bundle. (a) Electrical stimulation at threshold leads to a spread of charge to multiple motor units, which causes multiple muscles to contract. (b) Optical stimulation at threshold results in spatial selectivity and, thereby, an isolated muscle response.*

the specific tissue of interest. For instance, a collagenous sheath encases the typical peripheral nerve, surrounding and protecting the sensory and motor axons that make up a nerve bundle. Our goal was to choose a wavelength of light that would penetrate this outer layer to reach the underlying motor axons that innervate specific muscles, all the while using laser energies that do not cause nerve damage. In addition, optical fibers significantly improve the precision of stimulus delivery and, therefore, specificity of the motor response.

Initial experiments on the physiological validity of the response in nerve and muscle demonstrated that we could to excite them in a repeatable manner and generate artifact-free signals that otherwise mirror electrically stimulated recordings. We then set out to define the optimal laser parameters for safe and efficient stimulation. Noteworthy results suggest that

Continued on next page

soft-tissue absorption dictates the optimal wavelength and that the Holmium:YAG (yttrium-aluminum-garnet) laser (2.12μm) is well-suited to this technique. The threshold laser radiant exposure, or minimum laser energy necessary for motor response, was approximately 0.4J/cm^2 with this laser. Histological analysis from a neuropathologist confirmed that this technique is safe up to 2–2.5 times the threshold radiant exposures. Figure 1 demonstrates the unique advantage of spatially precise optical stimulation of nerves.

A conceptual understanding of how laser light stimulates neural tissues is crucial for the further optimization of the technique, allowing it to reach its full potential. The current hypothesis—based on a number of mechanistic experiments—is that the laser activates nerves by a transient, thermally induced mechanism. At the stimulation threshold, experiments suggest that the maximum nerve-surface temperature increase is less than 9°C, well below the 45–50°C tissue temperatures required for the onset of tissue damage. Future experiments will reveal if stimulation arises through a direct membrane interaction or an indirect effect leading to membrane depolarization.

The ultimate goal for this research is to develop a hand-held or even an implantable device for optical stimulation based on solid-state diode-laser technology operating at the optimal laser parameters to incite safe and effective peripheral- and cranial-nerve stimulation. Such a device would have utility in both basic electrophysiology studies and clinical procedures that currently rely on electrical stimulation. Recently, our group has started a collaboration with Aculight (Bothell, WA)—a commercial laser company—to explore the use of infrared-diode lasers for this purpose. Preliminary results exhibit safety thresholds and efficacy in stimulation similar to results reported with the Holmium:YAG laser. A research-grade optical stimulator is expected to be commercially available from Aculight within a year.

In summary, this article describes a new method to selectively target peripheral-nerve fibers to elicit isolated-muscle contractions. This provides higher resolution for the functional mapping of nerves. By its very nature, this optical method could easily confine the stimulation to partial segments of a nerve without requiring separation of the nerve bundles, thus facilitating partial resection. Plans for clinical trials to validate and improve this peripheral-nerve optical stimulator are in progress. We speculate that laser technology might provide a powerful interface to nerves and unlock fundamental challenges in neuroscience.

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