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Optical Stimulation of the Facial Nerve: A New Monitoring Technique?

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Abstract

Objectives/Hypothesis—One sequela of skull base surgery is iatrogenic damage to cranial nerves, which can be prevented if the nerve is identified. Devices that stimulate nerves with electric current assist in nerve identification. Contemporary devices have two main limitations: (1) the physical contact of the stimulating electrode and (2) the spread of the current through the tissue. In contrast to electrical stimulation, pulsed infrared optical radiation can be used to safely and selectively stimulate neural tissue and might be valuable for screening.

Methods—The gerbil facial nerve was exposed to 250 microsecond pulses of 2.12 μm radiation delivered via a 600- μm -diameter optical fiber at a repetition rate of 2 Hz. With use of 27 GA, 12-mm intradermal electrodes, muscle action potentials were recorded. Nerve samples were examined for possible tissue damage.

Results—Eight facial nerves were stimulated with radiant exposures between 0.71 and 1.77 J/cm², resulting in compound muscle action potentials (CmAPs) that were simultaneously measured at the m. orbicularis oculi, m. levator nasolabialis, and m. orbicularis oris. Resulting CmAP amplitudes were 0.3 to 0.4 mV, 0.15 to 1.4 mV, and 0.3 to 2.3 mV, respectively, depending on the radial location of the optical fiber and the radiant exposure. Individual nerve branches were also stimulated, resulting in CmAP amplitudes between 0.2 and 1.6 mV. Histology revealed tissue damage at radiant exposures of 2.2 J/cm² but no apparent damage at radiant exposures of 2.0 J/cm².

Conclusions—The experiments showed that selective muscle action potentials can be evoked optically in the gerbil facial nerve without direct physical contact.

Keywords

Facial nerve; laser; optical stimulation; monitoring; parotidectomy

INTRODUCTION

Iatrogenic injury to cranial nerves is one of the most severe sequela of head and neck surgery. In particular, tumor resections challenge the surgeon not to damage cranial nerves when normal anatomy does not exist and the nerve is difficult to identify in the tumor tissue. During parotid surgery, nerve damage often occurs after mechanical trauma or ischemia and frequently produces pain, functional disability, and cosmetic deformity.¹ It has been shown, however, that intraoperative nerve monitoring can reduce the incidence of nerve damage during procedures such as parotidectomies.¹⁻⁸ To avoid facial nerve damage, a majority of the otolaryngologists in the United States monitor the facial nerve during parotid surgery.^{9,10} The effectiveness of facial nerve monitoring, however, has been debated in previous literature. Although some studies show a good correlation between nerve monitoring and nerve preservation during surgery, other studies have failed to confirm those findings.¹¹⁻¹³

Nerve stimulation occurs by injecting current via two electrodes in the tissue and monitoring compound muscle potentials. Although electromyography is sensitive for blunt mechanical trauma, it is not sensitive to sharp transections of the nerve.¹¹ Specifically, a shortcoming of contemporary devices is the spread of electrical current in the tissue and the consequent nonselective stimulation of the nerve. With electric stimulation, the distal segment of the nerve can still be stimulated after a sharp nerve transection because the current spreads from the proximal electrode site to more distal points where the nerve and periphery connections remain intact. Electromyography responses might then be falsely interpreted as evidence of an uninjured nerve. Furthermore, the physical contact of the stimulation probe that is required in contemporary nerve monitoring devices may damage the nerve because nerve function is highly sensitive to compression and touch.²

A method, however, that would allow the surgeon to locate the nerve before it is surgically exposed and to stimulate the nerve without direct physical contact in a spatially selective manner could help to reduce the incidence of facial nerve damage. Stimulation with optical radiation from a pulsed infrared laser appears to offer these advantages¹⁴ and has the potential to significantly improve nerve mapping and monitoring during surgery. With the present experiments in gerbils, we compare the use of optical radiation for facial nerve stimulation with electric nerve stimulation.

MATERIALS AND METHODS

All animal experimental procedures were performed in accordance with the guidelines from the National Institutes of Health and were approved by the Northwestern University Animal Care and Use Committee.

Animal Surgery

Six adult gerbils (>6 wk of age) were anesthetized by an initial intraperitoneal injection of sodium pentobarbital (80 mg/kg bodyweight); maintenance doses were 17 mg/kg bodyweight. The level of anesthesia in the animal was monitored every 15 minutes by a paw withdrawal reflex, and additional sodium pentobarbital was given when necessary. To maintain the body temperature at 38°C, the animals were placed on a heating blanket (Sunbeam E12107, Rye, NY). After the animals were anesthetized, an approximate 1-inch cut was made in the skin over the parotid region, and the gland was exposed. Posterior to the parotid, the facial nerve trunk was exposed, and the facial nerve branches were dissected antegrade to their respective muscles (Fig. 1). To prevent tissues and nerves from drying, a few drops of saline, which was kept at body temperature on the heating blanket, were applied at regular time intervals.

Optical and Electrical Stimulation

Optical stimulation was made using a Holmium:YAG laser (Laser 1-2-3, SEO, Orlando, FL), which emitted 250-microsecond pulses of 2.1- μm radiation and were operated at a low repetition rate (2 Hz). The laser output was focused into a 600- μm -core-diameter optical fiber (P600-10-VIS/NIR, Ocean Optics, Dunedin, FL). Light-absorbing glass slabs were placed in the optical path of the beam to vary the radiant exposure of the laser. This only allowed for coarse changes in radiation energy. Consequently, the thresholds for optically evoked responses lacked fine resolution, and average values were not calculated. Instead, ranges are provided in this paper. During the measurements, the distal end of the optical fiber was positioned using a three-dimensional micromanipulator (MMW-203, Narishge, Setagaya-Ku, Japan).

Facial nerve trunks were stimulated approximately 0.5 to 1 cm from their exit from the stylomastoid foramen. Facial branches, such as the marginal and buccal branches, were stimulated 2 mm distally to the nerve's division, with the overlying facial fascia left intact (Fig. 1). In addition to optical stimulation, electrical current was injected with a handheld device. The stimulating electrode was placed either directly onto or close to the nerve. Bipolar current pulses from a current calibrator (2500 Valhalla Scientific, San Diego, CA), 0.5 milliseconds per phase, were between 30 and 150 μA . Current pulses were controlled by custom-written software.

Data Acquisition

Gross muscular responses were recorded using three 27 GA, 12-mm reusable, subdermal needle electrodes (Rochester Electromedical, Tampa, FL). The needles were inserted into different facial muscles such as the musculus orbicularis oculi, the musculus levator nasolabialis, and the musculus orbicularis oris. In some experiments, recordings were also obtained at the mandibular and buccal facial nerve branches by "hooking" silver electrode wires (75 μm in diameter) around the nerves. Although the nerve was optically or electrically stimulated, compound muscle action potentials (CmAPs) or compound nerve action potentials (CnAPs) were recorded. All measured CmAPs and CnAPs were amplified using five channels of a high-input impedance ($10^{12} \Omega$) 16-channel custom-built preamplifier set at a gain of 100. Signals were recorded with a 16 bit, 16-channel bipolar Keithley (KPCI-3116, Cleveland, OH) computer board at a 50 kHz sampling rate. Results of the measurements were analyzed off-line using IGOR (WaveMetrics version 5.0, Lake Oswego, OR).

Histology for Light Microscopy

For histologic analysis of nerves, tissue samples of irradiated nerve sections were harvested while the animals were deeply anesthetized. After fixation of the tissue with 4% paraformaldehyde in phosphate-buffered saline (PBS), some nerves were stained for 20 minutes in 1% OsO_4 . All samples were then embedded in plastic (araldite resin). Embedding followed a standard protocol: washing in PBS three times for 15 minutes, dehydration in acetone diluted with distilled water (15 min in 25%, 15 min in 50%, 15 min in 75%, 15 min in 90%, 15 min in 100%, 20 min in 100%), and infiltration in plastic for 1 hour at each step (7:1 acetone:plastic, 1:1 acetone:plastic, 1:7 acetone: plastic, 2 times in pure plastic). After curing the plastic for 12 hours in an oven at 60°C, the specimens were sectioned using an ultramicrotome (Ultratome III, LKB, Stockholm, Sweden). Three- and 5- μm thick slices were cut and placed on glass slides. The samples that had not been stained with osmium tetroxide were stained with toluidine blue. Images of nerve sections were taken using an upright light microscope (Axio ImagerA1, Zeiss, Oberkochen, Germany), which was fitted with $\times 10$, $\times 20$, and $\times 40$ Zeiss EC-Plan-Neofluar objectives. The tissue sections were

inspected for signs of damage, including edema, tissue rupture, and carbonization. Tissue sections were also viewed under crossed polarizers to detect thermal damage.

Optical Beam Profile

Radiant energy profiles at different distances from the optical fiber were determined for different media between the optical fiber and the energy sensor (J50LP-1A with a 3sigma Energy/Power Meter, Coherent, Portland, OR). For the measurements, the optical fiber was placed approximately 2 mm over the bottom of a Petri dish with a 100- μ m thick glass window at the bottom of the dish. Below the dish, the energy sensor was placed to measure the optical radiation energy (Fig. 2). During the measurements, a razor blade, which was mounted to a three-dimensional micromanipulator (MWH3, Narishige), was advanced stepwise into the optical beam (Fig. 2). For each blade position, the optical energy was measured. The incremental changes are shown in Figure 2. The results showed a gaussian beam profile. Its width was determined 6 dB below its maximum (full width). The measurements were made for three conditions: 1) air, 2) Ringer's lactate, and 3) a 1.5 mm thick tissue sample in Ringer's lactate.

RESULTS

Optical and Electric Stimulation

In six animals, eight facial nerve trunks were stimulated optically and electrically (Fig. 3). CmAP recordings of the three facial muscles (Fig. 1) were obtained using radiant exposures of 0.71 to 1.77 J/cm². Depending on the radiant exposure, recorded peak-to-peak CmAP amplitudes ranged from 0.3 to 0.4 mV for the m. orbicularis oculi, 0.15 to 1.4 mV for the m. levator nasolabialis, and 0.3 to 2.3 mV for the m. orbicularis oris. Electrical stimulation of the facial nerve trunk with current amplitudes between 30 and 150 μ A produced CmAP amplitudes of 0.2 to 2.6 mV. The peak-to-peak amplitude varied with the current applied and the muscle monitored. Moving the optical fiber across the facial nerve evoked responses from individual nerve branches (Fig. 4). This could not be replicated when electrically stimulating the nerve. For electrical stimulation, the CmAP responses were similar for different electrode positions.

Nerve potentials were measured directly from selected facial nerve branches. By optically stimulating the facial nerve trunk with 1.77 J/cm², CmAP amplitudes of the marginal and buccal branches were measured in one experiment to be 0.16 and 0.18 mV, respectively.

The responses to optical stimulation of the facial nerve trunk were compared with responses obtained during optical stimulation of the facial nerve branches. Measurements were made on eight mandibular, six buccal, and three zygomatic branches. With the facial fascia still overlying the nerves, laser radiation between 0.88 and 1.77 J/cm² was applied to the tissue. Recorded muscle responses ranged between 0.2 and 1.6 mV and were almost as large as the responses from the direct facial trunk stimulation (Fig. 5).

Histology

To determine possible tissue damage caused by optical stimulation, facial nerve trunks that were exposed to 20 laser pulses with optical stimulation as high as 4.0 J/cm² and as low as 0.11 J/cm² were examined for nerve damage. The irradiated nerve sections were then harvested and processed as described in Methods. Optical stimulation higher than 2.0 J/cm² damaged the facial nerve. An example, which was obtained for 4.0 J/cm², is shown in Figure 6. The tissue damage can be seen by the disruption of the normal tissue structure and by the decolorization. The same number of laser pulses with radiant exposures up to 2.0 J/cm² revealed no apparent tissue damage. Similar results were obtained when the tissue was

examined using crossed polarizers. Although neural tissue has been stimulated with electric current, the tissue has not been examined for subsequent damages.

Optical Beam Profile

The laser beam had a gaussian profile (Fig. 2). Media between the optical fiber can potentially change the beam profile. First, the energy transmitted to the energy sensor decreased when Ringer's lactate was placed between the optical fiber and the sensor, as compared with the optical fiber in air, and further decreased when tissue in Ringer's lactate was placed between the optical fiber and the energy sensor. The decrease in optical energy is a function of the wavelength of the laser and the type and volume of media through which the laser beam passes. For our wavelength, 2.12 μm , the optical penetration depth in water is approximately 400 μm . In other words, the optical energy decreases by 67% over this distance (data shown in Izzo et al.).¹⁵ The inclusion of a 1.5 mm thick section of muscle tissue in the experimental setup decreased the optical energy by a factor of two. In addition to the reduction of the optical energy, it is possible that the width of the beam changed. The width of the beam determined at 6 dB below the maximum is shown in Figure 7. Ringer's lactate did not change the width of the beam (Fig. 7) when compared with the beam profile in air. However, the tissue added to the Ringer's lactate widened the beam. At 1.5 mm below the Petri dish, the beam was less than 1 mm wide (Fig. 7).

DISCUSSION

The present experiments verify our hypothesis that the facial nerve can be stimulated with pulsed infrared laser radiation, thus presenting optical stimulation as a potential alternative to electrical stimulation for facial nerve monitoring and the detection and stimulation of nerve structures during surgery. This method of optical nerve stimulation, which occurs without direct contact between the stimulator and the nerve tissue, does not appear to damage the nerve when using low optical energy levels. Moreover, stimulation with optical radiation is more spatially selective than electrical stimulation.

Interaction of the laser radiation with the tissue determines the spatial distribution of light in the tissue. Primary light-tissue interactions fall into two broad categories, absorption and scattering, the prevalence of which is highly dependent on the wavelength of the light and the tissue characteristics.^{16,17} At first approximation, absorption dominates the light-tissue interaction in the mid-infrared wavelength range. The axial distribution of a primarily absorbed wavelength can be determined using Beer's Law, a description of the exponential decrease of laser energy over the optical path. However, scattering does play some small role in the light-tissue interaction at mid-infrared wavelengths. Spatial scatter is caused by random spatial variations in tissue density, refractive index, and dielectric constant. Although it has been reported that the scattering decreases monotonically with wavelength, a rigorous description of the multiple scattering events that occur as a collimated beam propagates through tissue is extremely difficult.¹⁷ At present, we have determined that the infrared wavelength of the radiation, which we used to stimulate the facial nerve, spreads little in air (Fig. 2). Although tissue in the radiation path increases the scatter (Fig. 2), the width of the beam is less than 1 mm at the level of the nerve. The addition of focusing optics could potentially decrease this value to the desired spot size. A more thorough study of this issue is in progress and will be published separately.

Contemporary cranial nerve monitors inject current into the tissue and thereby stimulate nerves. The physical properties of the tissue, however, result in a wide spread of the electric current and prevent the devices from being spatially selective. Moreover, the current spread can lead to "false responses." For example, a facial nerve that has been severed may still be stimulated more distally from the damage because of the current spread through the

surrounding tissue.² The neural response to the electrical stimulation could lead the surgeon to believe that the nerve is unscathed because of a positive response to electrical stimulation. However, these false recordings could be avoided with optical stimulation because a response is only evoked at the site of irradiation; the light does not spread through the tissue.

The spatial selectivity of optical nerve stimulation has been demonstrated in our experiments at the facial nerve trunk: different nerve bundles within the main nerve trunk were individually stimulated when the radial location of the stimulation site was varied. Similar spatial selectivity has been reported by Wells et al.¹⁴ for the rat sciatic nerve, in which the authors were able to individually stimulate single muscles (i.e., hamstring muscle) while scanning the small diameter optical beam over the sciatic nerve. In contrast to optical stimulation, electric stimulation evoked strong and unselective responses in all muscle groups innervated by the sciatic nerve (Fig. 4).

Moreover, we have shown for the auditory nerve that selective stimulation is possible.^{18,19} Here, the tip of the optical fiber is immersed in fluid. The optical radiation has to penetrate the fluids and the modiolar bone before it reaches the target structures, the auditory neurons. The optical stimulation has been significantly more selective when compared with electrical stimulation.²⁰ Moving the optical fiber across the opening of the round window stimulated different locations along the cochlea, thereby “scanning” the cochlea. Consequently, these data further suggest that a device using optical radiation to stimulate neurons can be used as a tool for nerve scanning. The parameter space that is useful for scanning cranial nerves, however, must first be optimized.

One might argue that stimulation with optical radiation might not be possible during difficult approaches, including approaches via the posterior fossa. The beam has to be directed toward the undersurface of acoustic neurinoma. This challenge is not necessarily a limitation because optics can be used, similar to optics in endoscopes, that are able to direct the optical beam toward the target, even in difficult to access locations.

Although the experiments confirmed our hypothesis, some shortcomings must be considered. The Holmium: YAG laser only emits 2.1 μm radiation. This wavelength corresponds to a penetration depth of approximately 400 μm , which describes the distance over which the incident optical energy is reduced by 67%. Despite this short penetration depth, we have been able to stimulate facial nerve branches through the overlying few-micrometer thick facial fascia. A longer penetration depth would appear to be beneficial when stimulating the nerve through surrounding tissue. It is not expected that thick tissue layers, on the order of several millimeters, could be penetrated with 2.1 μm radiation. Other wavelengths with longer penetration depths might be advantageous and should be tested in the future. Wells et al.¹⁴ and Izzo et al.¹⁵ showed that CmAPs and CnAPs can also be elicited with optical radiation at wavelengths from 1.844 to 1.873 μm , which corresponds to penetration depths of approximately 300 to 1,100 μm .

The threshold of optical stimulation was approximately 0.71 J/cm² for the facial nerve trunk and approximately 0.88 J/cm² for the facial nerve branches, with both being stimulated through the facial fascia, which corresponds in the gerbil to several micrometers. After the histologic examination of the nerve samples, the nerve-damage threshold was determined to be above 2.0 J/cm²; above this threshold, one saw carbonization and disruption within the nerve tissue, as shown in Figure 6. The ratio between the ablation threshold and stimulation threshold revealed a safety ratio of approximately 2.6 for optical stimulation with the Ho:YAG laser radiation. Wells et al.¹⁴ determined a safety ratio of 6.25 using the Ho:YAG laser. Note that no difference exists between the damaging threshold in the two experiments: the radiant exposure for both sets of experiments was 2.0 J/cm². However, a difference

exists in the stimulation threshold: 0.71 J/cm² versus 0.32 J/cm² in the experiment by Wells et al.¹⁴

CONCLUSIONS

With the present experiments, we were able to verify that the gerbil facial nerve can be stimulated with low-energy pulsed optical radiation. The threshold radiant exposure was 0.71 J/cm² with 2.1 μ m radiation. Qualitatively and quantitatively, the action potentials recorded in response to optical stimulation were similar to those in response to electrical stimulation and could be evoked without causing histologically identifiable damage to the nerve tissue. The no-touch technique and spatial selectivity attributed to optical stimulation may prove to be of great value to nerve monitoring in the field of otolaryngology as well as a wide range of other specialties.

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Fig. 1.

(A) Laterofacial view of a gerbil head after cutis and subcutaneous fat and parotid gland are removed. Facial nerve is exposed, and its trunk and branches are labeled as shown. Round dots (counted from top) mark insertion site for muscle electrodes m. orbicularis oculi, m. levator nasolabialis, and m. orbicularis oris, respectively. Rectangles represent nerve recording positions for the buccal and mandibular branches of the facial nerve. Arrows point to the region of optical and electric stimulation at the facial nerve. (B) Preparation of gerbil for optical stimulation. Facial nerve trunk is exposed, and optical fiber is lowered to the nerve. Recording electrodes are in place (as explained in A). During stimulation, twitching of the gerbil's whiskers could be seen while recording compound muscle action potentials from m. levator nasolabialis.

Fig. 2.

Measurements of laser beam profile. Optical fiber, which is coupled to the laser, is placed approximately 2 mm away from the bottom of the Petri dish (right column). The Petri dish contains a thin glass window below the tip of the optical fiber. Radiation energy is measured with an energy sensor below the dish. During measurements, a razor blade is moved in 50- μm increments into the optical path, thereby blocking radiation to the energy sensor. The razor blade is moved along traces with increasing distance from the dish. Resulting plots show incremental energy change for each advancement of the razor blade. Results reveal a gaussian laser beam profile. Measurements were made while the dish was filled with air (upper left), with Ringer's lactate (middle left), and with a 1.5-mm thick slice of muscle tissue immersed in Ringer's lactate placed below the optical fiber (lower left). The width of the laser beam becomes wider when tissue is placed between the optical fiber and the energy sensor.

Fig. 3. Compound muscle action potentials recorded in m. levator nasolabialis after facial trunk stimulation with $70 \mu\text{A}$ electric and 1.13 J/cm^2 optical stimulation. Note optical radiation and electrical current generated similar response amplitudes.

Fig. 4.

Compound muscle action potentials (CmAPs) measured in three facial muscles. CmAP response evoked by an electrical stimulus ($70 \mu\text{A}$) on facial nerve trunk (left column). CmAP responses after optical radiation (0.88 J/cm^2) at the same stimulation site for electrical stimulation (4 right columns). Both CmAPs are an average of 10 recordings. After the first recording (nerve center), the optical fiber was moved by $50 \mu\text{m}$ steps radially away from the nerve center. After each step, additional measurements were performed. Note the isolated maximal response of the m. levator nasolabialis after moving the fiber $50 \mu\text{m}$ from the initial nerve center.

Fig. 5.

Compound muscle action potential responses generated by optical radiation of the facial nerve trunk (top row) and facial nerve branches (bottom row). The facial nerve trunk was stimulated at 0.88 J/cm^2 , and branches were stimulated at 1.13 J/cm^2 . The fascia overlying nerve branches, which is not present on nerve trunk, might explain the difference in radiant exposure to evoke similar responses.

Fig. 6.

Light microscopy photograph of facial nerve cross section after optical stimulation with 20 pulses of 2.1- μm radiation at 4.0 J/cm² (left). Enlarged section reveals obvious disruption and carbonization of neural tissue. Light microscopy photograph of facial nerve after stimulation with 2.0 J/cm² (right). Visible damage caused by optical radiation is not observed.

Fig. 7.

Traces show the width of the laser beam for different conditions described in Figure 6. The width of the beam was determined as the full width at 6 dB below the maximum optical energy for each of the traces. The width is very similar for the beam in air and in Ringer's lactate. Tissue in the optical path, however, widens the beam.