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ORIGINAL ARTICLE

Acute and subacute effects of the ultrasonic blade and electrosurgery on nerve physiology

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Abstract

Ultrasonic blades have been shown to cause less acute electrophysiological damage when applied near nerves than monopolar electrosurgery (ES). This study was performed to determine whether the acute nerve damage observed for ES, as well as the relative lack of damage observed for ultrasonic dissection, extends through a subacute timeframe. Muscle incisions were made in rat with the Harmonic® Blade (HB) and ES at a distance of 2 mm from the sciatic nerve. Sham surgery was also performed which consisted of similar exposure of the sciatic nerve without use of an energized device. Electrophysiological function was assessed acutely over a 3-h period, and subacutely after a 7-day survival, by monitoring the sciatic nerve compound action potential (CAP), conduction velocity (CV), von Frey hair (VFH) stimulation force, leukocyte infiltration, and impaired axonal transport via β-amyloid precursor protein (β-APP) immunocytochemistry. During the acute period, ES produced significantly lower CAP and CV, and higher levels of leukocytes and β-APP than sham, whereas the ultrasonic blade was not significantly different from sham, and had significantly lower VFH force than ES. After the subacute survival, ES continued to display significantly lower CAP and CV, and higher levels of leukocytes and β-APP than sham, whereas ultrasonic blade had higher CAP and CV than sham, and lower VFH than ES. This study confirms that incisions made with an ultrasonic blade cause less acute nerve damage than monopolar ES, and are comparable to sham surgery at a distance of 2 mm from the sciatic nerve. The negative effects of electrosurgery extend through at least a 7-day survival period, whereas subacute recovery after application of the ultrasonic blade was comparable to that of sham surgery. For surgical procedures in the vicinity of vital nerves, use of the ultrasonic blade represents a lower risk than ES for both acute and subacute neural trauma.

Keywords: electrosurgery; harmonic; nerve injury; ultrasonic surgical devices

Introduction

Monopolar electrosurgery (ES) is widely used because of its ability to simultaneously cut and coagulate tissue.[1] However, its use near nerves is limited because the passage of electrical current from the device through the subject can lead to muscle contraction and potentially cause electrophysiological damage.[7]

In contrast, an ultrasonic blade can also cut and coagulate, but via a purely mechanical action, without the passage of electrical current.[2] For example, the Harmonic® Blade (HB) (Fig. 1) consists of a piezoelectric crystal that vibrates at 55.5 kHz with longitudinal displacements of the blade of 50–100 μm. The mechanical energy of the ultrasonic blade breaks hydrogen bonds between proteins, heating the tissue, while simultaneously cutting and coagulating with minimal thermal damage or smoke production.

Previously we mentioned that an ultrasonic blade caused less acute nerve injury than ES, and is equivalent to sham surgery.[5] It is unknown, however, whether the injury observed from ES was temporary with full restoration occurring a few days after surgery, or, on the other hand, if ultrasonic surgery might cause delayed electrophysiological damage during recovery even though none was observed acutely. In this study, we sought to determine whether the difference in nerve injury extends beyond the acute period, by performing similar electrophysiological evaluations both up to 3 h following surgery, and after a 7-day subacute survival period following surgery near the rat sciatic nerve with ultrasonic, ES, and sham procedures.

Methods

All surgical procedures were approved by the Institutional Animal Care and Use Committee of Wayne State University.

Fig. 1. The Harmonic SYNERGY® with Hooked Blade (inset).

The 3 treatments studied were HB, monopolar ES, and sham. The HB device (HARMONIC SYNERGY® Blade SNGHK2, Ethicon Endo-Surgery, Inc. Cincinnati OH) was used at power level of 5. The ES device (Bovie, Valleylab, Boulder CO) was used at power level of 60 Watts in "Blend 1" cut mode. This power setting has previously been shown[5] to be the lowest setting to readily cut through tissue, and produces tissue temperatures similar to those of an ultrasonic device. Each treatment consisted of an acute (3-h) and a subacute (7-day) test. A total of 49 adult male Sprague-Dawley rats (400–450 g) were used. There were 8 rats used in each of the six legs, except for the acute sham leg, which used 9 rats.

Acute test surgery
Anesthesia was induced with an intraperitoneal injection of ketamine (60–80 mg/kg) and xylazine (8–13 mg/kg) and maintained with ketamine (30 mg/kg) and xylazine (2–4 mg/kg). The animal underwent a tracheotomy and, after intubation, was artificially ventilated with a small animal ventilator (Model 683, Harvard Apparatus, Holliston MA) at a tidal volume of 2.5 ml and a rate of 90–100 per minute.

A midline dorsal longitudinal incision was made over the lumbar spine. The paraspinal muscles were retracted and the L2–L5 spinous processes were removed. The L2–L5 laminectomy was performed to expose the spinal canal. The dura mater was cut to expose the nerve roots for electrophysiological neural activity recordings. The exposed left L5 dorsal spinal nerve root was kept intact with its connection to the spinal cord. The nerve roots were kept in mineral oil that was heated to 37°C. A dorsal lateral skin incision between the lateral aspect of knee joint and greater trochanter of femur bone was made to expose muscles and fascia. Conventional scissors were used to detach posterior thigh muscle from the femur bone. Forceps were used to retract posterior thigh muscle to expose the sciatic nerve. After visualizing the sciatic nerve, a miniature bipolar stimulating platinum hook electrode[6] was placed under the distal end of the sciatic nerve.

For the HB and ES treatments, using a micromanipulator, the tip of the device was placed in the lateral quadriceps muscle at the distance of 2 mm from the sciatic nerve just proximal to the popliteal fossa of the knee joint. The device was activated for 5 s and then removed. For the sham treatment, similar exposure of the sciatic nerve was carried out, but without using an energized device.

Subacute test surgery
On the day of surgery (Day 0), the left sciatic nerve was exposed using sterile techniques and was exposed to the same devices used in the acute study using the same surgical procedures. Muscle, fascia, and skin were then closed in a sterile manner using sutures. On Day 7, the distal portion of the sciatic nerve was manually exposed for placement of a bipolar stimulating electrode. A lumbar laminectomy was performed for placement of recording electrodes on the left L5 nerve roots. Nerve conduction was then assessed as described for the acute study.

Neurophysiology testing
Baseline neural discharge and evoked compound action potential (CAP) were recorded prior to using each device. To activate myelinated axons, 1, 3, and 5 V electrical stimuli with duration of 0.3 ms and a frequency of 1 Hz were applied to the sciatic nerve.[9] Neural activity was amplified with an AC preamplifier (x1000), displayed on an oscilloscope and recorded on an FM tape recorder (MR-30; TEAC, Montebello, CA). Data were digitized and recorded real time on a computer using a window-discriminating system (Enhanced Graphics Acquisition and Analysis, R.C Electronics, Goleta, CA).

After the baseline recording (−1 min time point) was completed, pancuronium bromide (2.5 mg/kg IP) was administered to block neural activity from muscles. Once the muscle twitching in response to electrical stimulation of sciatic nerve was completely abolished, a "0 min" recording was taken. The designated device was then applied at a distance of 2 mm from the nerve. For the acute study, nerve conduction monitoring was performed in an identical manner to the baseline procedure at 2, 10, 30, 60, 120, and 180 min after the device removal. For the survival study, nerve conduction was monitored at a single timepoint. After these nerve conduction studies, the sciatic nerve was harvested for the histological studies.

Hind paw probing
At the same timepoints as were used for the electrophysiological measurements, the hind paw was probed using calibrated von Frey Hair (VFH) nylon filaments (Stoelting Inc, Wood Dale, IL) to determine the minimal force required for neural response. The anesthetized rat was placed such that the hind paw lay flat on a platform with sole facing up. The tip of the nylon filament (0.5–1 mm diameter, force ranging from 12 to 80 g) was applied carefully to the hind paw until the filament buckled. Mechanical stimulation was increased in a graded manner using successively stronger nylon filaments until sensory response was evoked which was monitored by a sound monitor and EGAA histogram. The minimum force that elicited neural response was counted as the force threshold.[5]

Electrophysiological analysis
Neurophysiological recordings were evaluated for the area under the rectified CAP curve (AUC) and conduction velocity (CV). The AUC was calculated using the integrate function in the EGAA system. CV was calculated by dividing the distance between the stimulating and recording electrodes

by the latency between the onset of stimulus pulse and the onset of CAP.

Histology

After each neurophysiology experiment in the acute and subacute survival studies, the sciatic nerve was harvested and fixed immediately in 4% paraformaldehyde for 48–72 h. Paraffin sections (7–10 µm thickness) were processed with hematoxylin and eosin (H&E) staining to assess changes in vasculature and inflammatory cell content, and with β-amyloid precursor protein (β-APP) immunostaining to assess the extent of impaired axonal transport (IAT). The stained nerve sections were examined under a light microscope (Leica DMLB, Leica Microsystems Ltd., Heerbrugg, Switzerland) at 40x magnification, which is considered as high power field (HPF), to determine morphological changes. For H&E-stained sections, a score of 0 for no leukocyte infiltration and 1 for the presence of leukocytes in the blood vessels supplying the sciatic nerve were assigned to each HPF. For β-APP-stained sections, a score of 0 for no staining and 1 for positively stained abnormal axons (seen as axonal swellings) were assigned to each HPF.

β-APP immunocytochemistry

Sections of the sciatic nerve segments were deparaffinized and washed 3 times in 2% Triton X in phosphate-buffered saline. The sections were then treated with 0.6% H_2O_2 for 1 h followed by incubation in 2% normal goat serum (Vector Laboratories, Burlingame, CA). The sections were then incubated overnight in rabbit anti-β-APP antibody (1:400, Chemicon International, Inc., CA) followed by incubation in biotinylated anti-rabbit IgG produced in goat (Vector Laboratories, Burlingame, CA) for 1 h. This was followed by exposure to VECTASTAIN Elite ABC reagent and brief incubation in 3,3′-diaminobenzidine and hydrogen peroxide. Finally, the sections were washed, dehydrated, and coverslipped using Permount (Fisher Scientific, Fair Lawn, NJ). [5,19]

Statistical analysis

For CAP, CV, leukocytes, and β-APP, comparisons were made via Student's t-test between HB and sham, and between ES and sham. For VFH, the comparison was between HB and ES. For CAP, CV, and VFH on Day 1, the time-weighted post-treatment mean values were calculated and used as the comparison value. In all the statistical analyses, a p value of less than 0.05 was considered significant.

Results

Gross Findings: The ES device, operated at 60 W in "Blend 1" cut mode, produced smoke, visible tissue damage, charring, desiccation, and uncontrolled muscle contraction. The HB device produced only minimal visible muscle tissue damage.

All acute Day 1 (3 h) and subacute Day 7 results are summarized in Table I.

Compound Action Potential: Acute results are plotted in Fig. 2, showing an immediate drop in CAP of ES, and steady

Table I. Summary of results at Days 1 and 7.

Measure	Sham	HB	p-value	ES	p-value
Day 1 (3 h)					
CAP (mV ms)	1356	1858	0.107	529	0.005
CV (m/s)	63.5	60.7	0.937	35.3	0.006
VFH Force (g)	–	25.4	–	100.8	< 0.001
β-APP (%)	38.1	38.3	0.855	57.5	0.002
Leukocytes (%)	16.3	11.3	0.357	35.5	0.002
Day 7					
CAP (mV ms)	1048	1733	< 0.001	479	< 0.001
CV (m/s)	61.2	72.4	0.015	33.0	< 0.001
VFH force (g)	–	15.0	–	136.0	< 0.001
β-APP (%)	14.0	24.4	0.137	70.6	< 0.001
Leukocytes (%)	10.7	8.1	0.637	33.8	< 0.001

The p values are for comparisons between the energized device (HB or ES) and the negative control (sham), except for the case of VFH, where the comparison is between HB and ES.

values for ultrasonic and sham surgeries. CAP was significantly lower in ES than that in sham both on Days 1 and 7. The CAP of ultrasonic was not only significantly different from that of sham on Day 1, but also significantly greater than that of ES on Day 7.

Conduction Velocity: Mean acute and subacute results are shown in Fig. 3. CV of ES was significantly slower than that in sham on both Days 1 and 7. The CV of ultrasonic was not only significantly different from that of sham on Day 1, but also significantly faster than that of ES on Day 7.

Peripheral Sensory Function: The minimum VFH force required for stimulation was significantly greater for ES than that for ultrasonic on both Days 1 and 7.

Histology: Both the presence of β-APP-stained injured axons and infiltration of leukocytes (Fig. 4) were significantly higher for ES than that for sham on both Days 1 and 7. Ultrasonic was not different from sham for either of these injury markers at either timepoint. The leukocytes appeared to belong to the class of granulocytes or polymorphonucleocytes (PMN) that include eosinophils, basophils, and monocytes. Additionally, there were indications of PMN extravasation into the region surrounding the axons, suggesting changes in vascular permeability. In the case of ES, prominent axonal pathology was observed as evidenced by inter- and intraaxonal separations and vacuolations. Axoplasm appeared to be condensed into globules.
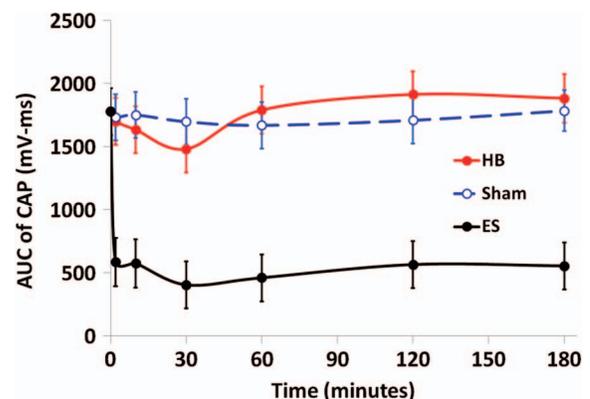

Fig. 2. CAP for the acute 3-h phase with baseline adjustment. HB: Harmonic Blade, ES: Electrosurgery.
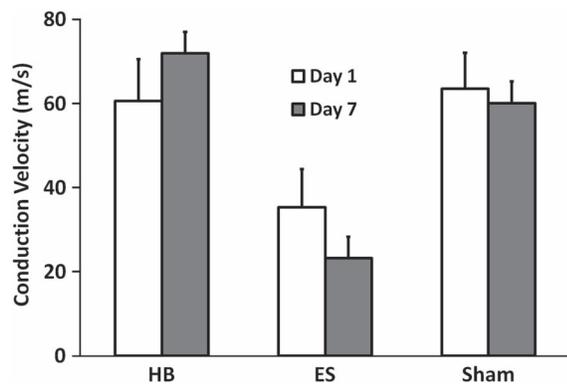
Fig. 3. Means of CV for Days 1 and 7. HB: Harmonic Blade, ES: Electrosurgery.

Fig. 4. Leukocyte inflammation measured via H&E staining. HB: Harmonic Blade, ES: Electrosurgery.

Discussion

Use of ultrasonic devices in tissues distant from vital nerves has been shown to induce less trauma than that of ES. Incisions in the tibialis cranialis muscle of rabbits with ultrasonic blade led to less acute inflammation during wound healing than that of an ES device.[18] Transections in the gastrocnemius muscle of mice with an ultrasonic blade led to less inflammation at the end of one week after surgery than ES, and to faster remodeling of fibrosis.[22] A comparison between ultrasonic and ES has even been made at the molecular level by studying gene transcript expression and protein levels after subcutaneous incisions in pig.[16] Ultrasonic incisions produced fewer differentially expressed genes and proteins than ES, especially those involved in inflammatory mediator response. The benefits observed in these studies may translate to advantages observed clinically across a wide range of procedures. In clinical trials, reduction in pain or decreased hospital stay with the use of ultrasonic devices has been demonstrated in arthroplasty,[21] cholecystectomy,[10] hemorrhoidectomy,[15] mastectomy,[13] thyroidectomy,[8] and tonsillectomy.[12]

The advantages observed for ultrasonic devices over ES in a reduction of tissue trauma may be ascribed to lower temperatures produced by the former, although in the present study these differences in temperature are not substantial. For incision near nerves, it appears to be more important in reducing the risk of electrophysiological damage, because ultrasonic devices pass no electrical current.

In an early study on acute effect of ultrasonic shears on rat femoral and sciatic nerves,[17] there was no damage to the nerve observed histologically when the device was used for less than 20 s at a distance of 3 mm from the nerve. Electrophysiological damage, as assessed by electromyography (EMG), was noted when the blade directly touched the nerve, so it was recommended to keep the device at a distance of 3 mm from sensitive structures, such as the recurrent laryngeal nerve.

Another acute electromyographic study [3] showed that when dissecting at a distance of 1 mm from the rat sciatic nerve, ES caused significantly greater reduction in EMG potential than an ultrasonic device, in agreement with histological assessment. A later study by the same group
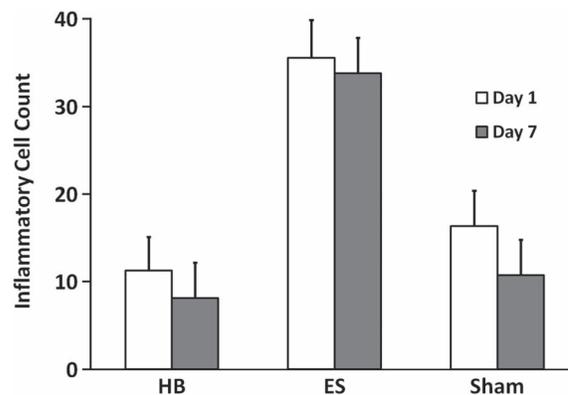
using similar dissection procedures [4] showed significantly higher temperatures for bipolar ES than ultrasonic, more histological damage for monopolar ES, and the least EMG functional loss for the ultrasonic device.

In an electromyographic study of sciatic nerve function in rat, ultrasonic and ES devices were applied at a distance of 2 mm from the nerve. The ES device caused a significant decrease in the CAP without any signs of recovery, while the ultrasonic blade had no perceptible effect on EMG, similar to a control.[20]

Evoked EMG of vocal muscles has been monitored acutely after using an ultrasonic device at varying distances from the recurrent laryngeal nerve (RLN) in a rabbit model.[11] No functional loss was observed when the ultrasonic tip was maintained at a distance of 2 mm or greater from the RLN for up to 3 s. Another acute study in rabbits[23] confirmed that there were no changes of amplitude or latency in RLN electrophysiology when the ultrasonic device was used 3 mm away for up to 2 s. In an acute canine model, [14] no histological changes or vocal cord abnormalities, as assessed by laryngoscopy, were observed when the ultrasonic device was used 3 mm or farther from the RLN.

Our previous study[5] also compared ultrasonic with ES, but only examined the acute (3-h) effects. In the current study, we have confirmed the acute effects and extended the observation period to 7 days to determine whether the advantage of ultrasonic use continues as the tissue heals. In contrast to the first study, in which incisions were made at 1, 2, 3, and 4 mm distances from the nerve, in this study incisions were made only at 2 mm from the sciatic nerve. It was thought that this is the closest approach to a vital nerve that could be carried out reasonably and safely during the actual surgery. Device activation time for both studies was 5 s.

In the acute phase of this study, ES produced significantly lower CAPs, slower CVs, increased leukocyte infiltration, and greater accumulation of β-APP than sham surgery. All these are indicators of injury either directly to the nerve or the surrounding tissue. In contrast, the ultrasonic device was not negatively different from sham in any of these measures, and additionally required lower von Frey stimulation forces than ES.

In the subacute survival study, ES again showed significantly lower CAPs, slower CVs, increased leukocyte

infiltration, and greater accumulation of β-APP than that of sham surgery with no sign of recovery during the 7-day period. Results for the ultrasonic blade were similar to the acute phase, that is, no difference between ultrasonic and sham for leukocyte infiltration or β-APP levels, and lower von Frey stimulation than ES. Moreover, ultrasonic appeared to have slightly better recovery from surgery, showing increased CAPs and faster CVs than sham. This study provides initial evidence for clinical use of ultrasonic blade in place of manual cutting devices to achieve hemostasis in spine, orthopedics, or other surgery performed in the vicinity of vital nerves.

Based on this study, as well as the large body of published evidence, it appears that use of an ultrasonic device within 2 mm of a vital nerve for up to 5 s causes no more electrophysiological injury than sham surgery, whereas similar use of an ES device produces substantial trauma to the nerve both acutely and subacutely. Since the tissue temperatures produced by the different devices are similar, the mode of tissue heating (mechanical vs. electrical) is more critical to nerve injury than the temperature reached by the device itself. Previous acute studies have repeatedly shown that ultrasonic devices cause less electrophysiological trauma than ES when used over the range of 1–3 mm from a vital nerve for about 3–5s. This is the first study to show that the superiority of ultrasonic over ES extends to at least 7 days, and that incisions with an ultrasonic blade at 2 mm from a nerve are no more likely to cause long-term neural damage than surgery without use of an energized device. In any case, surgeons should not touch the nerve following activation, as would be advised with any energy-based technology since that can lead to inadvertent injury.

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