Published in final edited form as:

J Neural Eng. 2013 October ; 10(5): 056016. doi:10.1088/1741-2560/10/5/056016.

Different Clinical Electrodes Achieve Similar Electrical Nerve Conduction Block

Adam Boger¹, Narendra Bhadra^{1,2}, and Kenneth J. Gustafson^{1,2}

¹Case Western Reserve University Department of Biomedical Engineering, Cleveland, OH

² Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Cleveland, OH

Abstract

Objective—Evaluate the suitability of four electrodes previously used in clinical experiments for peripheral nerve electrical block applications.

Approach—We evaluated peripheral nerve electrical block using three such clinical nerve cuff electrodes (the Huntington helix, the Case self-sizing spiral and the Flat Interface Nerve Electrode) and one clinical intramuscular electrode (the Memberg electrode) in five cats. Amplitude thresholds for block using 12 or 25 kHz voltage-controlled stimulation, onset response, and stimulation thresholds before and after block testing were determined.

Main results—Complete nerve block was achieved reliably and the onset response to blocking stimulation was similar for all electrodes. Amplitude thresholds for block were lowest for the Case Spiral electrode (4 ± 1 Vpp) and lower for the nerve cuff electrodes (7 ± 3 Vpp) than for the intramuscular electrode (26 ± 10 Vpp). A minor elevation in stimulation threshold and reduction in stimulus-evoked urethral pressure was observed during testing, but the effect was temporary and did not vary between electrodes.

Significance—Multiple clinical electrodes appear suitable for neuroprostheses using peripheral nerve electrical block. The freedom to choose electrodes based on secondary criteria such as ease of implantation or cost should ease translation of electrical nerve block to clinical practice.

Keywords

Electrical Stimulation; Spinal Cord Injury; Rehabilitation; Urinary Bladder; Nerve Block

Introduction

Involuntary external urethral sphincter contractions during attempted bladder voiding often occur after neurological disease or injury (Blaivas, 1982; Litwiller, et al., 1999; Weld & Dmochowski, 2000). These contractions can prevent complete bladder voiding, resulting in recurrent urinary tract infections and upper urinary tract damage (Clayton, et al., 2010; Cardenas, et al., 2004) and impairing patient quality of life (Anderson, 2004; Hemmett, et al., 2004; Westgren & Levi, 1998).

Corresponding Address: Kenneth J. Gustafson, Ph.D. Room 309 Wickenden Building 2071, Case Western Reserve University, 10900 Euclid Avenue, Cleveland OH, USA 44106-7207 kjg@case.edu Phone: (216)-368-8626 Fax: (216)-368-4969.

Electrical conduction block of the pudendal nerve using biphasic high frequency waveforms can prevent external urethral sphincter contractions (Gaunt & Prochazka, 2009; Bhadra, et al., 2006; Tai, et al., 2004). Conduction block is rapid and reversible (Bhadra & Kilgore, 2005; Kilgore & Bhadra, 2004) and can enable acute bladder voiding in cats (Boger, et al., 2008; Tai, et al., 2007). Though bladder voiding has been reported in humans using lower stimulation frequencies than those typically associated with true nerve conduction block (Possover, et al., 2010), bladder voiding using high-frequency electrical conduction block has not been conclusively demonstrated. Bladder-voiding neuroprostheses using electrical conduction block could significantly improve the quality of life of individuals with neurological disease or injury, while reducing the cost of patient care.

A bladder-voiding neuroprosthetic will require electrodes approved for implantation in humans. Electrodes used in pre-clinical nerve block studies have not typically been approved for use in humans. Previous studies typically used electrodes made from a split silastic cuff containing de-insulated wire (Gaunt & Prochazka, 2009; Tai, et al., 2007; Williamson & Andrews, 2005) or platinum rectangles (Bhadra, et al., 2006; Bhadra & Kilgore, 2005). High frequency block has also been achieved using the Utah Slant Electrode Array (Dowden, et al., 2010), penetrating titanium wires (Ackermann, et al., 2010), and spinal cord stimulation leads (Cuellar, et al., 2012). However, the effectiveness of such non-cuff electrodes has not been systematically compared to that of cuff electrodes.

The effectiveness of a bladder-voiding neuroprosthetic could depend on the clinical electrode used in the neuroprosthetic. Both the stimulus amplitude at which nerve block is achieved and the response of the nerve to the blocking stimulation depend on electrode design (Ackermann, et al., 2010; Ackermann, et al., 2009). However, we are unaware of any study comparing the block amplitude and onset response of multiple, clinical electrodes.

This study compared conduction block amplitude-threshold and onset response among four clinical electrode designs and a research electrode intended for peripheral nerve block studies (a “J-cuff” electrode). The clinical electrodes were the self-sizing Spiral electrode (Naples, et al., 1988), the rectangular Flat Interface Nerve Electrode (FINE) (Tyler & Durand, 2002), the Huntington electrode (Tarver, et al., 1992), and the Memberg electrode (Smith, et al., 1998). The self-sizing Spiral electrode has been implanted on the human optic nerve (Veraart, et al., 1998), femoral nerve (Fisher, et al., 2009), and various upper extremity nerves (Polasek, et al., 2009). The rectangular FINE has been implanted intra-operatively on the human femoral nerve (Schiefer, et al., 2010). The Huntington electrode has been implanted on the vagal nerve for treatment of epilepsy (Tarver, et al., 1992), and the recurrent laryngeal nerve for treatment of dysphagia (Broniatowski, et al., 2001). The Memberg electrode has been used extensively as part of an upper extremity motor neuroprosthetic system (Smith, et al., 1998). The J-Cuff electrode, a split silastic cuff electrode containing platinum rectangles, has been used in multiple acute nerve block studies (Boger, et al., 2012; Foldes, et al., 2011; Ackermann, et al., 2010; Ackermann, et al., 2009; Boger, et al., 2008; Bhadra & Kilgore, 2005; Kilgore & Bhadra, 2004). This electrode is unsuitable for chronic implantation, but well-suited for acute nerve block studies because it is highly customizable, easy to manufacture, and easy to implant (Foldes, et al., 2011).

Materials and Methods

Experimental Preparation

This study was conducted on 5 intact male cats weighing 4.1 ± 0.2 kg. The Institutional Animal Care and Use Committee of Case Western Reserve University approved the experimental protocol. An anesthetic monitoring system (SurgiVet V9200 Advisor Monitor, Smiths Medical PM Inc, Wisconsin) monitored body temperature, ECG, blood oxygen saturation, blood pressure, and expired $p\text{CO}_2$. Blood pressure, heart rate, jaw tone, and withdrawal and blink reflexes were also monitored to maintain the appropriate depth of anesthesia. Respiration was maintained by a pressure-regulated respirator (ADS 1000, Engler Engineering Corporation, FL) and adjusted based on expired $p\text{CO}_2$ measurements. Animal temperature was maintained between 34 and 39 °C with a heating blanket. Saline 0.9% with 8.4 mg mL^{-1} sodium bicarbonate and 5% dextrose was administered as necessary at 3-25 ml kg hr^{-1} IV.

Anesthesia was induced with ketamine (30 mg kg^{-1} , IM) and maintained during surgery with isoflourane (0.25% – 2.5%, inhalation). Data was collected under α - chloralose anesthesia (65 mg kg^{-1} , IV) or α - chloralose in combination with isoflourane (0.25% – 0.5%, inhalation). Buprenorphine was provided for analgesia (0.01 mg kg^{-1} , subcutaneous).

Urethral pressure was measured using a 4F microtransducer catheter (CTC/4F – 2, Gaeltech LTD, Dunvegan, UK) inserted into the urethra. The urethral pressure signal was input to a strain gauge signal-conditioning module including an instrumentation amplifier and 1.6 kHz lowpass filter (NI SCC-SG24, National Instruments Corporation, TX). The output of the instrumentation amplifier was routed to a data acquisition card (NI PCI-6221, National Instruments Corporation, TX, sampling rate 99 Hz or 1 kHz) through a configurable feed-through module (SCC-FT01, National Instruments Corporation, TX) contained in an NI terminal block (NI SC-2345, National Instruments Corporation, TX) and digitized. The digitized signal was processed using a customized interface (Labview 8.0, National Instruments Corporation, TX). Data were also recorded on a strip chart (TA-11, Gould Inc., AZ).

The pudendal nerves were mobilized (bilaterally in 4 animals and unilaterally in 1 animal), enabling the implantation of the proximal stimulating and distal blocking electrodes (Bhadra, et al., 2006). To implant the Memberg electrode, the pudendal nerve was elevated and the Memberg electrode was placed between the nerve and the underlying muscle. The proximal stimulating electrode was implanted at the beginning of the experiment and remained in place for the duration of the experiment.

Prior to testing, the microtransducer catheter was inserted in the urethra and the EUS located using the evoked response to pudendal nerve stimulation. The microtransducer catheter was rotated to minimize the baseline EUS pressure and an external support was used to fix the catheter location and orientation during testing.

In two animals, a resistor was placed in series with the blocking electrode (Figure 1) and the voltage drop across the resistor was measured using an oscilloscope (TDS 2004B,

Tektronix, Inc., OR). Cuff impedance was calculated as one half the peak-to-peak voltage measured across the cuff divided by the current through the resistor.

Contact spacing for the nerve cuff electrodes ranged from 1 – 2 mm (Table 1). This contact spacing range was chosen to minimize the block amplitude-threshold and onset response (Ackermann, et al., 2009). Contact size was determined by the manner of cuff fabrication.

Matlab (Mathworks, Inc., Natick, MA) was used to extract and process features from the recorded urethral pressure traces. Statistical comparisons were conducted using Minitab (Minitab Inc, PA).

Experimental Design

Each blocking electrode was sequentially implanted, evaluated, and explanted. The order in which the FINE, Spiral, and Huntington Helical electrodes were implanted varied between experiments. The J-Cuff was always implanted fourth and the Memberg electrode last. In the animals implanted bilaterally, block testing typically alternated between nerves (31 of 36 testing sessions).

Evaluation of each blocking nerve cuff electrode comprised determining: 1) the stimulation threshold for urethral sphincter activation before and after conduction block testing, 2) the amplitude threshold for high-frequency nerve conduction block, and 3) the onset response to blocking waveforms with amplitudes greater than 125% of the block amplitude-threshold.

Stimulation Thresholds

Stimulation thresholds for urethral sphincter activation were determined for each nerve cuff electrode before and after testing conduction block using recruitment curves consisting of twitch or tetanic stimulation at varying amplitudes (twitch: rectangular biphasic pulses, voltage-controlled, 100 μ s pulse width; tetanic: 20 Hz train of rectangular biphasic pulses, 100 μ s pulse width). Evoked pressures for multiple trials (range: 1-6) at the same stimulus amplitudes were averaged. From each recruitment curve the maximum evoked pressure, full recruitment amplitude, and stimulation threshold were extracted. The stimulation threshold was defined as the lowest stimulus amplitude in a recruitment curve evoking a pressure greater than 10% of the maximum evoked pressure (or greater than 5 cmH₂O in two experiments, a threshold chosen to distinguish evoked pressures from artifacts in the measured urethral pressure). The full recruitment amplitude was defined as the stimulation amplitude evoking 90% of the maximum evoked pressure.

Nerve Conduction Block Trials

Multiple nerve conduction block trials were conducted to determine the block amplitude-threshold for each blocking electrode on each nerve in each experiment. Each of these individual nerve conduction block trials was conducted at a fixed blocking waveform amplitude and frequency. These trials included proximal stimulation and distal block (Figure 2: Conduction Block Trial Description). Proximal stimulation consisted of 16 s of 20 Hz stimulation (voltage-controlled rectangular biphasic, pulse width 100 μ s). The distal blocking waveform consisted of a biphasic voltage-controlled square wave and was applied

for 10 s, beginning 3 s after the initiation of proximal stimulation. If conduction block could not be achieved with a blocking electrode using a 12 kHz waveform then block trials were repeated for that blocking electrode using a 25 kHz blocking waveform (except on one nerve in one experiment). Peripheral nerve conduction block has been demonstrated at 2-40 kHz. Lower onset responses are obtained at higher stimulation frequencies (Bhadra & Kilgore, 2005); however higher stimulation frequencies may require higher stimulation amplitudes to achieve block (Bhadra, et al., 2006). The 12 and 25 kHz block waveform frequencies were chosen as a balance between these competing factors.

The completeness of nerve conduction block and the onset response to blocking stimulation were measured in each block trial. To quantify the completeness of block, the minimum evoked urethral pressure during block (Min Pressure) was measured. The 10 s following the application of the blocking waveform were divided into ten one-second intervals. The average urethral pressure for each one-second interval was calculated and Min Pressure was defined as the lowest of these pressures. Min Pressure approached zero for complete pudendal nerve conduction block. Unblocked proximally-evoked action potentials or action potentials evoked by the blocking waveform increased Min Pressure by increasing the urethral pressure during blocking stimulation.

To quantify the onset response, the average evoked urethral pressure during blocking stimulation was measured. Measurement of the onset response was necessary because block completeness does not imply a minimal onset response. Electrical block of the feline pudendal nerve may evoke a steady decrease in the measured urethral pressure to a low minimum value over several seconds (Bhadra, et al., 2006). An electrode exhibiting such a prolonged onset response might not be suitable for clinical use. The average evoked urethral pressure over the period of blocking stimulation provides a straightforward measure of this onset response.

The average evoked pressure during proximal stimulation prior to the initiation of blocking stimulation was recorded to identify trends in the proximally-evoked urethral pressure over the course of the experiment. All pressures were measured with respect to the average pressure over the second before the trial began.

Nerve Conduction Block Amplitude-Thresholds

The nerve conduction block amplitude-threshold was defined as the blocking waveform amplitude for which Min Pressure was closest to a threshold pressure of 10 cmH₂O. A three-step process was used to calculate this block amplitude-threshold for each combination of nerve, electrode, and block waveform frequency. First, Min Pressures for block trials using the same block waveform amplitude were averaged. Second, the lowest blocking waveform amplitude for which the averaged Min Pressure was less than 10 cmH₂O was determined. Of that amplitude and the next lowest amplitude, the amplitude minimizing the difference between the average Min Pressure and 10 cmH₂O was chosen as the conduction block amplitude-threshold (See Figure 2: Block Amplitude-Threshold Determination).

Inter-Electrode Comparisons

Stimulation Threshold and Full Recruitment Amplitude—The general linear model tool in Minitab (Minitab, State College PA) was used to test the dependence on the experiment and the type of blocking electrode of the stimulation threshold and the full recruitment amplitude prior to conduction block testing. A logarithmic transformation was used to equalize variances; the statistical tests were conducted on the transformed data.

The Kruskal-Wallis test was used to evaluate the dependence of the difference in stimulation threshold before and after conduction block testing on the type of electrode used to provide blocking stimulation. The change in stimulation threshold, pooled across all cuffs, was compared to zero using the Wilcoxon one-sample test.

Conduction Block Amplitude-Threshold—The dependence of the conduction block amplitude-threshold on the type of blocking electrode was investigated using an analysis of variance. A logarithmic transformation equalized the variances for each electrode type and an ANOVA was performed on the transformed data. If block amplitude-thresholds were found for both 12 and 25 kHz, only the lower conduction block amplitude-threshold was included in the analysis of variance.

Onset Response—The dependence of onset response on nerve cuff design was examined using the Kruskal-Wallis test. Block onset response decreases slightly with increasing amplitude (Bhadra & Kilgore, 2005). Therefore this analysis of onset response included only trials using nerve cuff electrodes and blocking stimulation with amplitude greater than 125% of the block amplitude-threshold. The Mann-Whitney test was used to compare the conduction block onset response between trials using the Memberg electrode and trials using the nerve cuff electrodes.

Results

Stimulation Threshold and Full Recruitment Amplitude

Stimulation thresholds were measured in all five animals. In a single animal the evoked sphincter pressures were not digitally stored, so only the presence or absence of an evoked response was recorded. Stimulation thresholds (Table 1) depended on the choice of electrodes and the experiment (electrode: $P < 0.001$, experiment: $P < 0.05$, $n = 41$ conduction block testing sessions). Among the nerve cuff electrodes, the Spiral electrode had the lowest threshold, significantly lower than the threshold for the FINE electrode ($P < 0.05$). The stimulation amplitude required to fully recruit the nerve (FINE: 2.0 ± 1.7 Vpp; Huntington: 1.0 ± 0.51 Vpp; J-Cuff: 1.3 ± 0.8 Vpp; Spiral: 0.8 ± 0.7 Vpp; Memberg: 5.1 ± 4.2 Vpp) depended on type of electrode and the experiment (electrode: $P < 0.001$, experiment: $P < 0.05$, $n = 36$ conduction block testing sessions). The Memberg electrode required higher amplitude stimulation to fully recruit the EUS than the nerve cuff electrodes ($P < 0.001$). The evoked maximum urethral pressures during blocking stimulation did not depend on the choice of blocking electrode (FINE: 122 ± 73 cmH₂O; Huntington: 124 ± 53 cmH₂O; J-Cuff: 117 ± 53 cmH₂O; Spiral: 103 ± 49 cmH₂O; Memberg: 105 ± 42 cmH₂O; $P = 0.91$).

Stimulation thresholds in nerve cuff electrodes increased following conduction block testing ($P < 0.001$). The median increase in thresholds was 0.08 Vpp. This increase did not depend on the type of nerve cuff electrode used to provide blocking stimulation (FINE: 0.23 ± 0.27 Vpp; Huntington: 0.06 ± 0.09 Vpp; J-Cuff: 0.11 ± 0.11 Vpp; Spiral: 0.17 ± 0.11 Vpp; $P = 0.16$, $n = 35$ conduction block testing sessions).

The proximally-evoked pressure before blocking stimulation averaged 95 ± 42 cmH₂O ($n = 380$ individual conduction block trials). This pressure steadily decreased during testing. In each conduction block testing session, the average proximally-evoked pressure was $13\% \pm 23\%$ lower in the last recorded conduction block trial than in the first recorded conduction block trial at the same proximal stimulus amplitude ($n = 37$ testing sessions, pressures not recorded in a single experiment). However, the average proximally-evoked pressure typically recovered by the time the next cuff was tested (decrease of $5\% \pm 27\%$ between successive testing sessions on the same nerve, $n = 29$ testing sessions).

Electrode impedances ranged from $518 \pm 130 \Omega$ for the Memberg electrode ($n = 3$ nerves) to $4305 \pm 4512 \Omega$ for the FINE electrode ($n = 4$ nerves, range: 1052 to 10715 Ω).

Conduction Block Amplitude-Threshold

Conduction block amplitude-thresholds were determined in 45 conduction block testing sessions using five different blocking electrodes on nine nerves in five animals. In three conduction block testing sessions the cuff came off the nerve or the stimulator was incorrectly configured. Block was achieved in 40 of the remaining 42 testing sessions using either 12 or 25 kHz stimulation (95%). Twelve kilohertz stimulation achieved block in 36 of 41 testing sessions (88%), while 25 kHz stimulation achieved block in 5 of 5 testing sessions. The evoked sphincter pressures were not digitally stored in a single animal. Consequently only the presence or absence of conduction block was recorded in this animal.

Block amplitude-thresholds depended on the type of blocking electrode ($P < 0.001$, $n = 40$ thresholds, 12 or 25 kHz blocking stimulation, Table 1) and were significantly lower for all nerve cuff electrodes than for the Memberg electrode ($P < 0.05$). Such thresholds were also lower for the Spiral electrode than the Huntington or FINE electrode ($P < 0.05$). Block amplitude-thresholds did not differ significantly between the J-Cuff electrode and the Spiral, FINE, or Huntington electrodes. For 12 kHz blocking stimulation, the median block amplitude-threshold was approximately 10 times the stimulation threshold (25th percentile = 7.6; Median = 9.8; 75th percentile = 12.8; $n = 34$ block amplitude-thresholds using 12 kHz blocking stimulation). As discussed below, this relationship might permit estimation of block amplitude-thresholds in clinical experiments lacking proximal stimulation electrodes.

Stimulation currents at the nerve conduction block amplitude-threshold averaged 3.1 ± 2.3 mA for the cuff electrodes ($n=16$ nerves) and 20.7 ± 5.1 mA ($n = 3$ nerves) for the Memberg electrode.

Onset Response

The onset response, as measured by the average evoked urethral pressure during blocking stimulation, did not depend on the choice of blocking electrode. This pressure did not differ

among the nerve cuff electrodes (FINE: 16 ± 14 cmH₂O, n= 36; Huntington: 27 ± 23 cmH₂O, n= 20; J-Cuff: 24 ± 23 cmH₂O, n= 35; Spiral: 25 ± 27 cmH₂O, n= 65; P = 0.33, n=156 individual blocking trials). Furthermore, while few trials using the Memberg electrode were conducted above 125% of the block amplitude-threshold, the median of the average evoked urethral pressures was similar in these trials and in the trials using nerve cuff electrodes (Memberg: 25 ± 15 cmH₂O, n = 7; Nerve cuff electrodes: 23 ± 20 cmH₂O, n = 156, P = 0.22).

When using Spiral electrodes, incomplete block or prolonged onset response was sometimes witnessed in individual nerve conduction block trials, even at high blocking stimulation amplitudes. This effect was observed in 11 of the 65 conduction blocks trials that used Spiral electrodes and included blocking stimulation with an amplitude exceeding 125% of the block amplitude-threshold. In some experiments this effect was only observed intermittently or at certain amplitudes (allowing complete block at higher and lower amplitudes). These effects were not observed with other electrodes.

Discussion

We achieved complete, rapid, and reversible pudendal nerve block using five very different electrode designs, four of which have been used clinically. Block was reliably achievable with all electrodes. Block onset response did not vary between electrodes and differences in conduction block amplitude-threshold between cuff electrodes were small, though significant. These results suggest that either the FINE, self-sizing Spiral, or Huntington helical electrode could be used in a clinical conduction block neuroprosthetic. Secondary criteria such as ease of implantation, safety and durability, or intellectual property status could guide the final choice of electrode design, increasing the likelihood of successful clinical translation.

As measured by the onset response to stimulation, the quality of nerve block achieved using the cuff and non-cuff electrodes were comparable. Stimulation and block amplitude-thresholds were lowest for the self-sizing Spiral electrode and successful block with the Spiral electrode was always achieved. However, incomplete nerve block or a prolonged onset response was observed in certain individual nerve conduction block trials when using the Spiral electrode, even when the blocking stimulation amplitude exceeding the block amplitude-threshold. This effect was limited in duration and often specific to certain blocking stimulation amplitudes.

Our results support further research into non-cuff electrodes for pudendal nerve block. Non-cuff electrodes may be percutaneously implantable, enabling a class of bladder-voiding neuroprosthesis significantly less invasive than those requiring surgical implantation of cuff electrodes on the pudendal nerves. Reducing the invasiveness of bladder-voiding therapies or other conduction block therapies would increase the viability of translational research efforts by increasing the patient populations suitable for such therapies. Unfortunately, in the present study the Memberg electrode required impractically high-amplitude blocking waveforms. However, other researchers have reported significantly lower block amplitude-thresholds using non-cuff electrode designs (Dowden, et al., 2010). HFAC applied through

spinal cord stimulator leads and hemi-cuff leads has suppressed and blocked the response of wide dynamic range dorsal horn neurons (Cuellar, et al., 2012). Refinements in electrode design or placement may enable pudendal nerve conduction block using non-cuff electrode with lower block amplitude-thresholds than were achieved in this study.

Furthermore, the Memberg and Huntington electrodes sometimes required 25 kHz waveforms to block nerve conduction. In these instances, the application of 12 kHz stimulation may have caused excitation of the pudendal nerve distal to the blocking electrode. The application of blocking stimulation at amplitudes insufficient to achieve nerve block will cause the nerve to generate action potentials repetitively (Bhadra, et al., 2007). When using these electrodes, the nerve may have been exposed to such sub-blocking threshold stimulation. Properly fitting cuff electrodes would confine current (Navarro, et al., 2005), but the Memberg electrode is a non-cuff electrode and the Huntington electrode contacts were sometimes exposed because the Huntington electrode fit loosely around the nerves. Successful nerve block using Memberg or Huntington electrodes and 25 kHz stimulation, in circumstances when 12 kHz stimulation could not achieve nerve block, may have been the result of greater spatial selectivity of 25 kHz stimulation. Higher frequency block waveforms have shorter pulse widths. The increased spatial selectivity of shorter pulse width stimulation has been demonstrated in computer simulations (Bhadra, et al., 2007; Grill & Mortimer, 1996) and chronic experiments (Grill & Mortimer, 1996).

Blocking stimulation did not appear to damage the nerves in this study. Previous studies have identified changing stimulation thresholds with nerve damage (Agnew & McCreery, 1990). While stimulation thresholds increased and proximally-evoked pressures decreased between the beginning and end of each conduction block testing session, nerves typically recovered between testing sessions. Furthermore, for experiments in which stimulus currents were recorded, stimulus charge per phase and charge density per phase were within the safe limits described by Shannon and Rose (Shannon, 1992; Rose & Robblee, 1990). However, the duration of our experiments was limited.

We observed a predictable relationship between stimulation threshold and block amplitude-threshold. Evaluated over all 12 kHz trials, the conduction block amplitude-threshold was typically between 7 and 12.5 times the stimulation threshold. Simulation studies have shown conduction block at similar multiples of the stimulation threshold (Kilgore & Bhadra, 2006). This relationship appears robust and could be used to evaluate block amplitude-threshold in situations where block testing using a proximal electrode is impractical, for example during implantation of a clinical neuroprosthetic.

Complete pudendal nerve block was reliably achieved for all electrodes evaluated, including the Memberg intramuscular electrode. Our results suggest that the clinical nerve cuff electrodes tested could be used in clinical conduction block studies. Though the block amplitude-thresholds for the Memberg electrode were impractically high, further investigation of non-cuff block is justified. Development of non-cuff electrodes could significantly expand the set of conduction block therapies by reducing their invasiveness.

Acknowledgements

This work was supported by the Coulter-Case Translation & Innovation Partnership, Department of Veteran Affairs RR&D B6685R, NIH DK077089, the Cleveland VA FES Center and the Cleveland VA APT Center. Dr. Boger and Case Western Reserve University have ownership interest in a company related to this research. Drs. Bhadra and Gustafson are inventors on patents owned by Case Western Reserve University that are licensed to a company related to this research. A COI management plan is in place to manage this conflict. The authors thank Jaime McCoin, Manfred Franke, Timothy Bruns, Tina Goetz, and Timothy Mariano for their experimental assistance.

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Figure 1.

Pudendal nerve conduction block was evaluated for five distinct blocking electrode designs. In the absence of pudendal nerve block, electrical stimulation at the proximal electrode evoked an increase in urethral pressure. During proximal stimulation, a biphasic 12 or 25 kHz square wave was applied to the blocking electrode, potentially creating a local nerve conduction block under the blocking electrode and reducing the measured urethral pressure. The urethral pressure was recorded with a microtransducer catheter. In two experiments an oscilloscope measured the voltage across resistor R_{sense} to determine the current through the blocking electrode. Figure shows a cuff electrode. When testing a Memberg electrode, the pudendal nerve was elevated and the electrode placed between the pudendal nerve and the underlying muscle. A needle inserted into the animal was used as a return electrode.

Figure 2.

The results of individual block trials (left panel) were used to determine block amplitude-thresholds for each cuff (right panel). **Conduction Block Trial Description:** Individual block trials included proximal stimulation to evoke a urethral pressure response. Proximal stimulation was applied immediately following the start of the trial (0 – 16 s). A blocking waveform was applied to the distal cuff on the pudendal nerve beginning 3 s after the start of the trial (3 – 13 s). Effective block resulted in a reduction of the evoked sphincter pressure. **A)** The average urethral pressure before the trial provided a baseline for measuring evoked pressures. **B)** The average pressure evoked by proximal stimulation before the blocking waveform was applied was measured. This pressure was monitored throughout the experiment as a measure of urethral sphincter fatigue. **C)** The average evoked urethral pressure during block provided a measure of the onset response to blocking stimulation. **D)** The average urethral pressure was calculated for each one-second interval during block; Min Pressure was the lowest of these averages. Min Pressure measured the completeness of block and was used to determine the Block Amplitude-Threshold. **Block Amplitude-Threshold Determination:** Min Pressure was compared for multiple trials conducted on the same nerve with the same electrode at the same blocking waveform frequency. First, Min Pressure was averaged for all trials conducted at the same amplitude. Next, the lowest blocking waveform amplitude for which the average Min Pressure was less than 10 cmH₂O was determined (5 Vpp in figure). Of this blocking waveform amplitude and the next lowest blocking waveform amplitude (4.5 Vpp in figure) the block amplitude-threshold was the amplitude minimizing the difference between the average Min Pressure and 10 cmH₂O (5 Vpp in figure).

Table 1

Block was achieved reliably at 12 or 25 kHz for all blocking electrode designs.

Electrode	Clinical Use	Description	Contact Separation (mm)	Exposed Contact Area (mm ²)	Stimulus Threshold (V _{pp})	Block Amplitude Threshold (V _{pp})	Block Achieved (Success / Attempts)
J-Cuff	Preclinical Use Only	Tripolar Length: 6–9 mm Diameter: 1½–1¾ mm Platinum Contacts	1–2	1½–3	0.60 ± 0.30	5±2	9/9
Huntington	Vagal N. Recurrent Laryngeal N.	Bipolar Length: 8–9 mm Diameter: 2 mm Platinum Contacts	1	8	0.50 ± 0.11	10±4	7/8
FINE[†]	Femoral N.	Tripolar Length: 7 mm Diameter: 1 mm Thickness: 1 mm Platinum Contacts	1	¾	0.85 ± 0.50	8±3	9/9
Case Spiral	Optic N. Femoral N. Upper Extremity	Tripolar Length: 9 mm Diameter: 1 mm Platinum Contacts	2	¾	0.31 ± 0.13	4±1	8/8
Memberg	Upper Extremity	Monopolar Length: 2 mm Diameter: 1 mm Stainless Steel Contact	Not Applicable	6¼	2.29 ± 1.33	26 ± 10	7/8

Stimulation and block amplitude-thresholds varied between electrode designs and were significantly higher for the Memberg intramuscular electrode than for the nerve cuff electrodes. The Spiral electrode had significantly lower stimulation thresholds than the Memberg or FINE electrodes. Block amplitude-thresholds for Spiral electrode were significantly lower than the thresholds for all remaining electrodes except the J-Cuff electrode. With the exception of the J-Cuff electrode, all of the electrodes have been used clinically. For all comparisons $\alpha = 0.05$.

[†] FINE electrode length, width, and thickness refer to the channel through which the nerve passes. Stimulus Threshold and Block Amplitude-Threshold are reported as mean and standard deviation.