31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Combined Direct Current and High Frequency Nerve Block for Elimination of the Onset Response

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Abstract—**Nerve conduction in peripheral mammalian nerves can be blocked by high frequency alternating current (HFAC) waveforms. However, one of the disadvantages of HFAC block is that it produces an intense burst of firing in the nerve when the HFAC is first turned on. This is a significant obstacle to the clinical implementation of HFAC block. In this paper we present a method to produce HFAC block without the onset response, using a combination of direct current (DC) and HFAC block. This method was experimentally evaluated in an in-vivo mammalian model. Successful no-onset HFAC block was obtained using a DC block of 200 µA and an HFAC block of 30 kHz at 10 Vp-p. This may allow HFAC block to be used in clinical applications for pain relief.**

I. Introduction

High-frequency alternating current (HFAC), when applied directly to a peripheral nerve, can produce a rapid conduction block that is quickly reversible [1]-[5]. Typical parameters utilized to produce this type of block are a 5-40 kHz sinusoidal wave at 5-10 $V_{peak\text{-}peak}$ delivered through electrodes surrounding the nerve. This type of block could be useful in treating pain and spasticity. However, the HFAC induces a brief but intense burst of axonal firing when the HFAC is first delivered to the nerve. This firing is referred to as the “onset response” and is undesirable for both motor and sensory clinical applications because it is likely to produce a sensation of extreme pain [4]. Our laboratory has been studying various methods to eliminate or reduce this onset response. Our most promising method for eliminating the onset response is described in this manuscript, and utilizes a combination of HFAC and direct current (DC) block to achieve “no-onset HFAC block”.

The onset response generated by HFAC consists of a large summated twitch which is usually followed by a period of repetitive firing. There are two distinct phases of the onset response. Phase I lasts for approximately 50-100 ms and is always present regardless of the specific parameters used for HFAC block. The Phase II onset response follows directly after Phase I and has a widely variable duration from a few milliseconds to more than 30 seconds. The duration and intensity of the Phase II onset is strongly influenced by electrode design and application. We have recently shown that optimized electrode designs can significantly shorten, and in many cases eliminate, the Phase II onset. However, it is not possible to eliminate the Phase I response through adjustment to the frequency, amplitude or electrode. Therefore, we propose to allow the Phase I onset response to occur, but to block it from travelling along the nerve so that it does not reach an end organ or the central nervous system.

Direct current (DC), when delivered near a nerve at the appropriate amplitude, can produce a complete block of nerve conduction in a manner similar to HFAC block [6]. DC block, however, has two contrasting features to HFAC block. *First*, DC is inherently unsafe to the nerve (and electrode) for chronic use [7]. HFAC, which delivers a zero net charge to the tissue, is likely to be much safer for chronic use, although chronic in-vivo testing remains to be completed. *Second*, DC block can be produced without any onset response by simply ramping the DC from zero to the necessary amplitude for block over a period of ~100 ms [8]. Such amplitude ramps do not work for HFAC block, and, in fact, we demonstrated that slowly ramping the HFAC amplitude actually exacerbates the onset response [9].

Our no-onset HFAC block makes use of the contrasting features of HFAC and DC block. DC block is used for very brief periods at a very low duty cycle, so that it can be utilized safely, and HFAC is used to maintain block for long periods. We postulated that a separate electrode could be used to deliver a ramped DC for a brief period of time. During the plateau phase of the DC, the HFAC would be started so that the onset from the HFAC would be blocked by the DC electrode. The DC would be turned off as soon as the onset from the HFAC was over. The HFAC would maintain complete nerve block. Whenever it is necessary to turn the block off and back on again, the process is repeated. The goal of this study is to evaluate the possibility of utilizing this combination of AC and DC block to produce nerve block without an onset response.

II. Methods

Acute experiments were performed in adult Sprague-Dawley rats. The animals were anesthetized with intraperitoneal injections of Nembutal (Phenobarbital sodium). The left hind leg was shaved and an incision was made along the posterior aspect of the hind leg and thigh. The sciatic nerve was exposed from its most proximal aspect, just distal to the sacral plexus, to the popliteal fossa. The common peroneal and sural nerves were severed. The

Manuscript received April 7, 2009. This work was supported by the National Institute of Biomedical Imaging and Bioengineering Grant No. R01-EB-002091.

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gastrocnemius-soleus muscle complex was dissected, and the calcaneal (Achilles) tendon was severed from its distal attachment. The ipsilateral tibia was stabilized to the table via a clamp, and the calcaneal tendon was tethered to a force transducer with 1-2 N of passive tension. Figure 1 shows the experimental setup. All protocols involving animal use were approved by our institutional animal care and use committee.

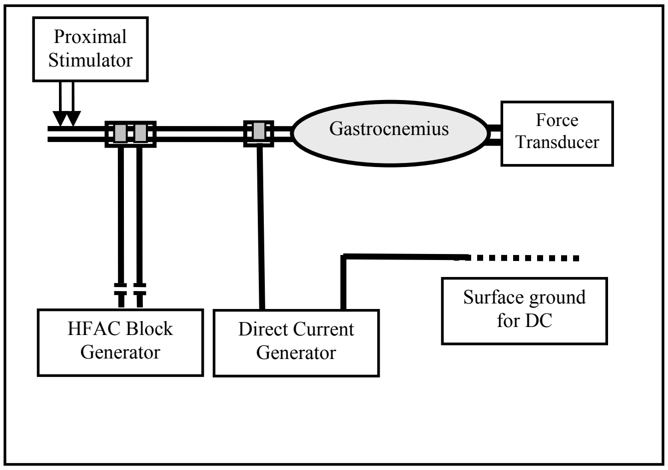

Figure 1.Experimental setup

Three nerve cuff electrodes were placed on the sciatic nerve as shown in Figure 1. The proximal and middle electrodes were bipolar nerve cuff electrodes with 3mm x 1mm rectangular platinum contacts and silicone insulation. The distal electrode, used for DC block, was a monopolar cuff electrode of similar design. A surface electrode over the shaved skin on the back was used as a return electrode for the DC. All three electrode had a J-shaped cross section, allowing the nerve to be placed in the trough of the electrode and be nearly surrounded circumferentially by the electrode contacts. The proximal electrode was used to generate gastrocnemius muscle twitches through supramaximal stimulation with a 20 µs, 300 - 500 µA cathodic pulse delivered at 1 Hz. The middle electrode was used to deliver the HFAC blocking waveform from a voltage controlled waveform generator (Wavetek, Model 395). The DC was delivered from a DC current source generator (Keithley Instruments, Model 6221). Data was collected at a sampling rate of 1000 Hz.

A typical trial demonstrating combined DC and HFAC block is shown conceptually in Figure 2. Proximal stimulation was initiated at 1Hz and continued for the duration of the trial. After three to four seconds, the DC block was turned on using an amplitude ramp to reach a plateau that produced complete nerve block. Block is indicated by the absence of muscle twitches that normally would be produced by the 1Hz proximal stimulation. Once the DC block reached a plateau, the HFAC block was turned on. After a brief plateau, the DC block was then ramped down, leaving the HFAC block on. The trial was completed when the HFAC block was turned off and the nerve resumed normal conduction, as evidenced by the return of the 1Hz muscle twitches.

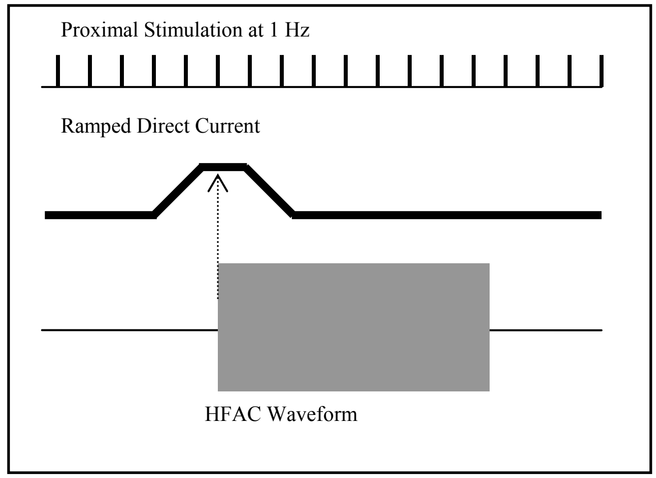

Figure 2. Experimental design to demonstrate the combination of DC and HFAC nerve conduction block.

III. Results

Demonstration of DC block without onset was verified at the beginning of each experimental session. An example of the results of DC block testing is shown in Figure 3. DC plateaus of 100 µA and 150 µA produced progressively larger partial block, as demonstrated by the decreasing peaks of the muscle twitch force. At 200 µA, a complete DC block is achieved during the plateau phase. A final trial was performed with no proximal stimulation to verify that the delivery of the DC alone did not produce any activity in the nerve. Through separate experiments, we determined the optimal ramp speed that allowed block without onset. A one second ramp was typically sufficient to prevent the onset response from the DC.

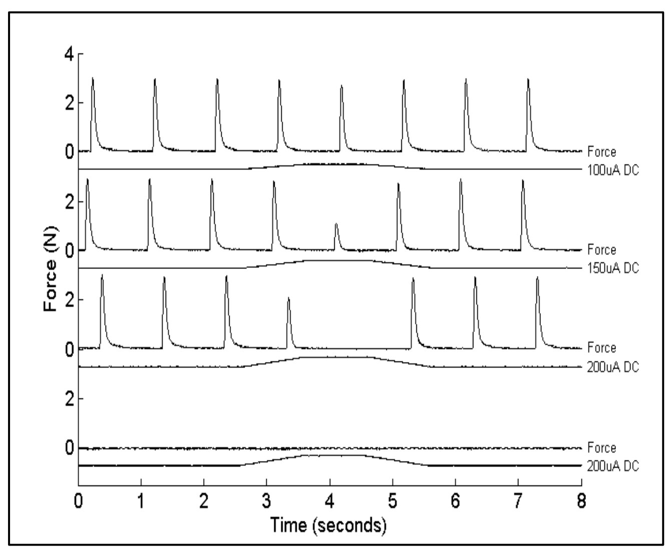

Fig. 3. Test of DC plateau level that produces conduction block without the onset response.

Demonstration of successful no-onset block with the combined DC/HFAC approach is shown in Figure 4. Three successive trials are shown. In the top trial, an HFAC block consisting of a 30 kHz, 10Vp-p sinusoid is turned on without DC block or proximal stimulation, showing the phase I onset response that occurs when HFAC is turned on (occurs at 4 seconds). The onset response lasts about 100 ms in this case. In the middle trial, proximal stimulation is delivered, producing muscle twitches at 1Hz. At 2.5 s, the DC ramp begins, reaching a plateau of 200 μA at 3.5 s. Complete block is indicated by the absence of muscle twitches once the plateau is reached. At 4 s, the HFAC is turned on. The DC is able to block the onset that would normally have occurred when the HFAC was turned on. The DC is ramped off by 6 s and HFAC block is maintained until 9 s. The quick reversibility of HFAC block is demonstrated by the return of the muscle twitch force to the original peak force within 2 s of cessation of block. The bottom trial confirms that the HFAC block continues to produce the expected onset response after the previous demonstration of no-onset block.

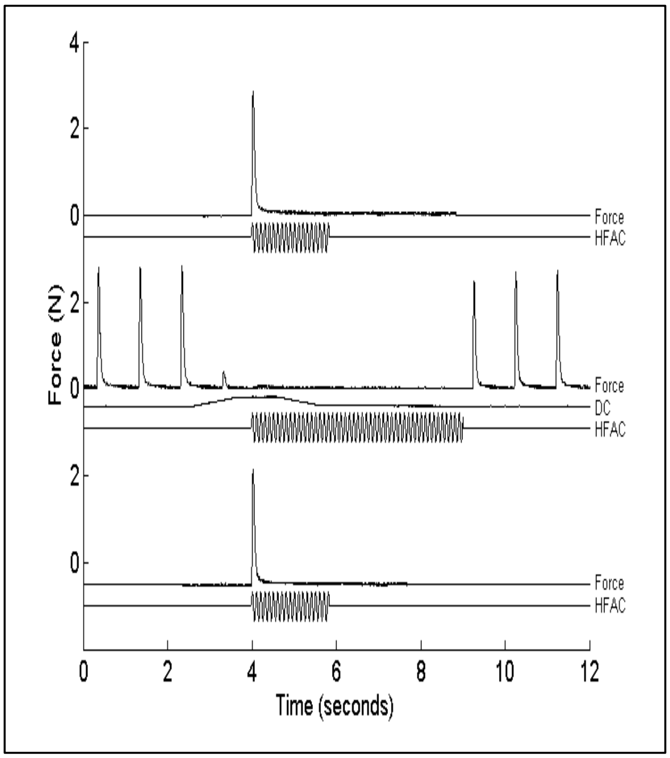

Fig. 4. Demonstration of DC/HFAC no-onset block.

IV. Discussion

We have developed a novel approach to producing HFAC block without the unwanted onset response by using a combination of HFAC and DC electrodes. This method uses a direct current (DC) block to prevent the HFAC onset response from traveling past the electrode assembly. DC block can be achieved without an onset response, but it cannot be maintained for more than a few seconds before it begins to produce damaging electrochemical effects on both the electrode and nerve. However, since the onset response from the HFAC can be limited to a few hundred milliseconds, it is possible to deliver the DC block long enough to block the entire onset response. Once the onset is complete, the DC block is turned off while the HFAC block is maintained for the desired period.

One anticipated application of HFAC block is the relief of spasmodic peripheral nerve pain. In this application, the block is likely to be turned on a few times a day for periods of many minutes each. Thus, the duty cycle of DC block will be extremely low. In some cases, the HFAC block may be maintained for many hours to provide continuous pain relief and the need for the DC block might only be once per day. At present, it is not clear what a safe duty cycle will be for DC block. The nerve and surrounding tissue has been shown to be capable of buffering the chronic continuous delivery of approximately 10 μA delivered through electrodes on the spinal cord [10]. In our application, we will require an order of magnitude higher current. It will be necessary to evaluate the safety of this method through chronic in-vivo animal testing.

It is expected that most applications utilizing the combined HFAC and DC block will require DC electrodes on both the proximal and distal side of the HFAC electrode. The proximal DC electrode prevents the onset response from producing any unwanted sensation and the distal DC electrode prevents the onset response from producing an unwanted muscle twitch. It may be possible to combine these three electrodes into a single assembly that can be placed on the nerve for block.

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