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Nerve lesioning with direct current

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Abstract— **Spastic hypertonus (muscle over-activity due to exaggerated stretch reflexes) often develops in stroke and spinal cord injury (SCI) survivors and individuals who suffer from multiple sclerosis. In previous published experiments we have shown that Direct Current (DC), when used to lesion nerves, can attenuate muscle force in a gradual manner, and this attenuation can last for several months. In this paper we present initial experimental results that profile the current required to cause controlled nerve ablation.**

I. Introduction

One of the most debilitating outcomes of stroke and cervical SCI is the loss of hand and arm function, which diminishes the level of independence in activities of daily life. The reduction of upper extremity function in stroke and SCI survivors may be further complicated by spastic hypertonus, a chronic over-activity of muscle nerves. Muscle over-activity causes muscle stiffness, spasms and contractures, resulting in sensorimotor disability and discomfort [1]. The most common approaches to treating spastic hypertonus are physiotherapeutic methods such as stretching, brushing or pressure casting, these have limited efficacy and are of short duration [2, 3]. Oral antispastic drugs such as dantrolene and baclofen can cause adverse side effects such as fatigue, dizziness and sedation [4, 5], and may further increase the risk of falling [6]. Baclofen may also be delivered intrathecally via a pump, dosage is lower than oral medication but surgery is required to place the pump and complications such as infections may occur [4]. A commonly used treatment for spastic hypertonus is to block nerve conduction with phenol or botulimum toxin type A (BtA). Phenol injections often have painful side effects [7], while BtA treatment is costly, may take up to two weeks to take effect and usually lasts only a few months, necessitating repeated costly administration [8]. Recent research shows that continuous use of BtA results in muscle atrophy and loss of muscle tissue in both the target muscle and muscles elsewhere in the body [9].

Direct current (DC) has been used in the past to block the propagation of activity in nerves, but it was deemed unsuitable for clinical applications since it was shown to cause nerve damage [10]. However, it is precisely this aspect that could be of interest clinically. Recently we showed that when DC was used intentionally to ablate nerves, muscle force could be attenuated in a controlled fashion, and the attenuation could last for months [11]. This was proposed as a possible new method of treating spastic hypertonus. In this paper we present experimental data exploring the parameters of DC enabling controlled ablation of peripheral nerves.

II. Methods

The experiments were carried out on three white New Zealand rabbits. Each rabbit was anesthetized and placed in a stereotaxic frame. The tendon of the left triceps surae muscle was exposed and detached from the foot with a small part of the calcaneum. The tendon was tied to a force transducer via a strong suture. The force transducer was mounted on a muscle puller that was configured to slowly stretch and release the muscle with a triangular waveform at 0.08Hz through its full physiological range. The knee was stabilized with a clamp.

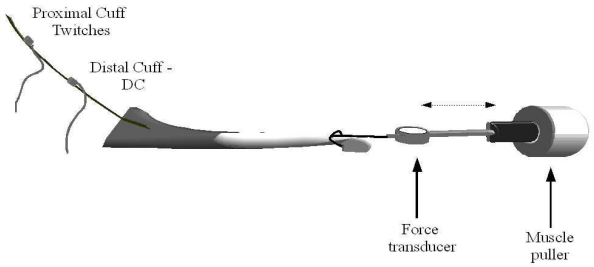

Fig.1. Experiment setup. Two cuffs were placed on the tibial nerve. The proximal cuff delivered test muscle twitches, the distal cuff delivered DC.

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Two nerve cuffs were placed on the tibial nerve (Fig. 1). The proximal cuff, comprising a silastic sleeve which held a pair of stainless steel terminals was used to deliver test muscle twitches at 2Hz throughout the experiment. The pulse amplitude was set to 1.5 times motor threshold so as to activate all alpha motoneurons in the nerve. The more distal cuff, comprising a silastic sleeve with a single Platinum-Iridium terminal, was used to deliver DC. The DC amplitudes used were 0.5mA and 0.75mA. Test muscle twitches were elicited using a custom built biphasic stimulator. DC was delivered through the monopolar terminal in the distal cuff, with the use of a surface reference electrode and a custom built constant current stimulator.

Throughout the experiment, the muscle was slowly stretched and released while test pulses were applied through the proximal cuff. A Tektronix digital oscilloscope was used to sample the force signal at a rate of 500 samples/sec for periods of 20 seconds every 1 to 5 minutes. At the beginning of each experiment the force was sampled for 5 to 15 minutes without applying DC, in order to establish a baseline. DC was then applied for short durations (2-5 minutes) to produce controlled attenuation of twitch force.

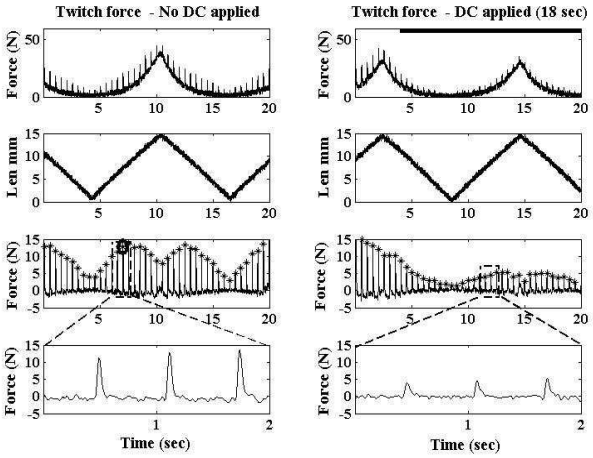

Fig.2 Top row: force transducer signal. Black bars represent the time DC was applied through the distal nerve cuff. Second row: imposed displacement. Third row: twitch forces after the passive force was removed by filtering. The peak force in each twitch, shown by asterisks, and the maximal peak force within each stretch cycle (circled asterisk) was identified by the program

The force signal had a slowly increasing and decreasing passive component upon which the test twitches were superimposed (Fig. 2). A custom Matlab program was used to remove the passive component with filtering and subtraction. The program then detected the maximal twitch force in each stretch cycle. This procedure was designed to ensure that we captured the twitch force at optimal muscle length and that any changes in twitch force were not simply the result of small changes in muscle length over time due to compliance in the apparatus or the cord attaching the tendon to the transducer.

III. Results

Definitions:

Baseline – Test period at the beginning of each experiment prior to delivering DC. Muscle twitch forces elicited by a train of test stimuli applied through the proximal cuff were continuously monitored.
DC application – A single duration of DC applied to the nerve.
Recovery– Period following the cessation of DC delivery. Test stimuli continued to be applied through the proximal cuff and twitch force was monitored and recorded.

In the first experiment 15 applications of 0.5mA DC were carried out. Each application lasted for two minutes, and recovery periods varied from five to twenty five minutes between applications. A longer period was allowed for recovery at the end of the experiment, following the last DC application. After fifteen applications, twitch force was attenuated by about 50%.

In the subsequent two experiments, 0.75mA DC was applied for periods of two minutes. The duration of recovery varied from 5 to 10 minutes between applications with a longer duration at the end of the experiment. Conduction block was evident immediately during DC applications: the twitches disappeared almost instantly once DC was applied, and re-appeared quickly once DC was discontinued. Depending on the number of DC applications, twitch amplitudes did not always return to their pre-DC values.

As expected, the attenuation in force was more rapid with the larger DC amplitude, and the number of applications required to reach complete force ablation was smaller (15 applications of 0.5 mA produced 50% attenuation in experiment 1 while 6 and 3 applications of 0.75mA in experiments 2 and 3 correspondingly produced 100% ablation).

Figure 3 presents the results from experiment 2 in which 0.75mA DC was applied 6 times.

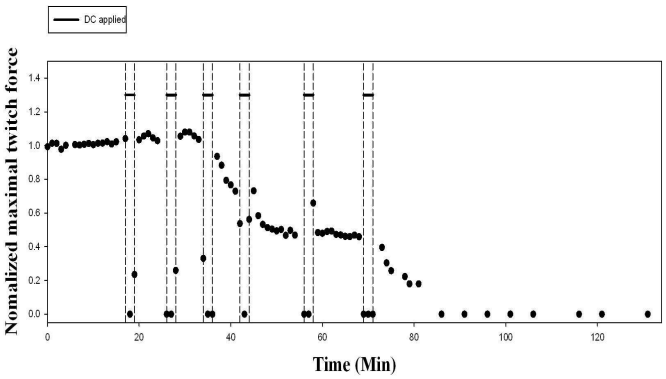

Fig.3. Twitch forces over a single 2-hour experiment during which 0.75mA DC was applied 6 times (top horizontal bars). Twitch forces were measured at intervals of 1 to 10 minutes throughout the experiment and were normalized to the mean value of the first 5 peak twitch forces of baseline. Twitch force diminished to zero during each DC application and rebounded to progressively lower values after each application, finally remaining at zero after the last application.

IV. Discussion

Our previously published data [11] and the present experiments show that repeated applications of DC to peripheral nerves for short durations result in attenuation in muscle force due to nerve ablation. We propose that controlled nerve ablation with DC might provide an alternative treatment to chemo-denervation to reduce spastic hypertonus.

DC could be delivered to a nerve by an implanted device. When the desired muscle force attenuation is achieved and the extremity is more relaxed, the same device could be used as a neuroprosthesis, using a stimulator to deliver pulses to the nerve to control muscles in functional movements such as hand grasp. In this way, the device would serve two functions: that of an ablation device, and that of an assistive device for activities of daily life. A well-known disadvantage of chemo-denervation is the reduction in functionality due to muscle weakness [5, 6]. Using the implanted device as a neuroprosthesis after ablation could mitigate this problem.

When the method is applied in humans, it will be possible to measure muscle force before, during and after DC delivery so that the amount of ablation can be controlled. Partial ablation is the desired outcome. If recovery due to regeneration occurs after some months, the process can be easily repeated. After the desired partial ablation, conventional pulsatile stimulation of the remaining intact axons may be used to achieve functional movements of the previously hypertonic muscles.

In the first chronic animal implant [11] technical difficulties prevented us from repeating DC ablation following regeneration. Repeated ablation is the subject of further chronic animal studies now underway.

In a previous study in rabbits, Neurofilament H staining of nerves some weeks after DC application confirmed that the nerves had indeed been partially ablated [11]. This has not yet been confirmed in animals implanted chronically with nerve cuffs. Osmium tetroxide staining is currently being added to provide more information on the histological effect of DC.

The mechanism of DC ablation may involve irreversible reactions occurring at the electrode-tissue interface[12]. Initial testing of electrodes through which DC was applied in saline solution showed no visible corrosion after 10 hours of DC application. Further testing is required to ensure that chronically implanted electrodes remain intact after repeated DC applications.

Peripheral nerve injury sometimes causes mechanical allodynia and hyperalgesia and DC ablation could have this effect in some cases. Before DC ablation can be seriously considered as a clinical modality, this must be clarified. In one previous experiment, 0.4 mA DC was delivered to an awake cat for 1.5 minutes. The cat showed no sign of discomfort during or after the treatment. Further experiments of this type are currently underway with the use of larger DC currents causing complete nerve ablation.

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