FACILITATIVE AND REFRACTORY PERIODS MEASURED FOR THE CAT SCIATIC NERVE FROM A NERVE CUFF ELECTRODE

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Abstract

The duration of the facilitative and the refractory periods for the cat sciatic nerve were found to be 700 and 900μsec, respectively. These values were based on the length of the facilitative and refractory periods found in 33 cases across five animals using monopolar, four-contact nerve cuff electrodes. Based on these results, the linear summation of two different stimulation configurations within the same nerve cuff electrode can be tested. The ability to produce the linear summation of two different stimulation configurations will support the hypothesis that a single self-sizing spiral cuff with multiple contacts and a single lead may be used in place of several muscle-based electrodes each with its own separate lead.

Introduction

The goal of this project was to determine the duration of the facilitative and refractory periods for the cat sciatic nerve. The answers to these questions will be used to attempt linear summation of multiple stimulus combinations in a nerve cuff electrode. The ultimate goal of this work is to support the hypothesis that a single multi-contact peripheral nerve based cuff electrode can be used in motor prostheses to replace multiple muscle-based electrodes. Multi-contact cuff electrodes on peripheral nerves are an attractive alternative to muscle base electrodes because they offer the possibility of using reduced currents, simplified surgery to implant and more compact hardware. In a multiple contact cuff electrode, however, the individual contacts are sufficiently close together that attempting to simultaneously apply multiple stimulation patterns will result in the excitatory fields summing together and result in a nonlinear addition of the evoked torque. Although a "look-up" table that relates every stimulation combination to joint torque can be created, the number of combinations can become excessively large. The problem of field summation may be avoided, if the applied stimuli are separated by a time that is long enough to allow partially depolarized fibers to recover, yet close enough in time such that fibers activated by the first stimuli are not activated by the second stimuli. Even though the two stimuli are separated in time, the delay will be small enough to effect "simultaneous" activation at the level of the muscle. This study was designed to find the duration of both the facilitative and refractory periods, from which the appropriate time interval between stimuli can be determined. Previous studies [1-4] suggest this time will be in the range of 300 to 2000 μs.

Methods

The objective of this study was to determine the time delay between pulses that was longer than the facilitative period but less than the total duration of the refractory period. For this study, the facilitative period was defined as the time immediately after a stimulus that a second stimulus of the same type and amplitude would produce a change in the resulting torque output. This change in torque output is attributed to the activation of some nerve fibers that were only partially activated by the first stimulus. The end of the refractory period was defined as the time, after the end of the facilitative period, when a second stimulus of the same type and amplitude would produce a change in the resulting torque output. The change in torque output in this case, is attributed to some of the nerve fibers activated by the first stimulus having time to reset enough to be re-activated by the second stimulus.

These experiments used self-sizing nerve cuff electrodes, each containing 4 monopolar contacts, that were implanted, for periods ranging up to 428 days, on the sciatic nerves of five adult cats (masses ranging from 3.2 - 4.3 kg). The sciatic nerve of a cat, approximately 3mm in diameter, has been used in many nerve cuff studies since it contains both smaller fascicles that serve only one or two muscles and larger fascicles that each serve multiple muscles and have sensory components. Together, these four motor nerves innervate all of the muscles controlling the ankle joint. The net resulting isometric torque about the ankle was measured as an indicator of the electrical excitation that was produced in the peripheral nerve [5].

Electrical excitation of the nerve was performed by using two pulses, identical in both pulse width and amplitude, applied from the same stimulator to the same contact set with a particular delay between the pulses. The resulting output was then recorded as a function of the delay that was used between the pulses. The range of delay times that produced the minimum amount of torque output was identified. The minimum time that produced the minimum output represented the end of the facilitative period while the maximum time that produced the minimum output represented the end of the refractory period. Previous work suggests that the delay times that would produce the minimum output would range between 300 and 2000µsec [1-4].

Results

The results of varying the delay between the applications of two identical stimuli clearly revealed two periods of heightened excitability and one period when the stimulated nerve was refractory. An example of one set of data is illustrated in Figure 1. In Figure 1, delays between 75µs and 3000µs were found to produce the least amount of torque output. The elevated torque output at delays less than 75µs indicated that these delay times were within the facilitative region, the time period when a partially depolarized nerve fiber has a heighten level of excitability and was fully activated by the second stimuli. The region of delay between 75 and 3000µsec, where the torque output was at its minimum, was when the facilitative period was over but the end of the refractory period had not yet occurred. At delays greater than 3000µs the torque output was found to increase, which indicated the refractory period for some of the activated axons had ended. In all 33 sets of data, the duration of the refractory period was greater than the duration of the facilitative period, as indicated by the region of minimum torque output.

The end of the facilitative region and the end of the refractory region from all 33 sets of data are summarized by the two cumulative histograms shown in Figure 2. Each vertical bar in Figure 2 represents the fractional number of cases in this study that were determined to have either a facilitative region (on the left side) or a refractory region (on the right side) that was less than or equal to the delay corresponding to that vertical bar. In the case of the facilitative region, only a small fraction of the cases were determined to have a facilitative region that lasted less than or equal to 100 µsec. Almost half of the cases in this study were found to have facilitative regions that lasted less than or equal to 300 µsec. There were no cases in this study where facilitative effects were found to last for more than 700 µsec. In the case of the refractory period, there were no cases that indicated the refractory period had ended before 900 µsec. About half of the cases showed evidence of the refractory period ending by about 1700 µsec. In every case in this study, there was evidence that the refractory period had ended by 2400 µsec. A region between 700 and 900 µsec delay was found to be after the end of the facilitative region but before the end of the refractory region in all cases.

Discussion

The goal of the delayed stimulation experiment was to find out how long the facilitative and refractory periods lasted in the cat sciatic nerve. These tests were dependent on both the actual values of the facilitative and refractory periods and also the geometric configuration of the nerve fibers within the nerve trunk. The range of 700-900 µsec was chosen as a worst case scenario to account for geometric arrangements in the nerve trunk that might result in values of facilitative periods that are shorter than actual, or refractory periods that are longer than actual. An example of a case where

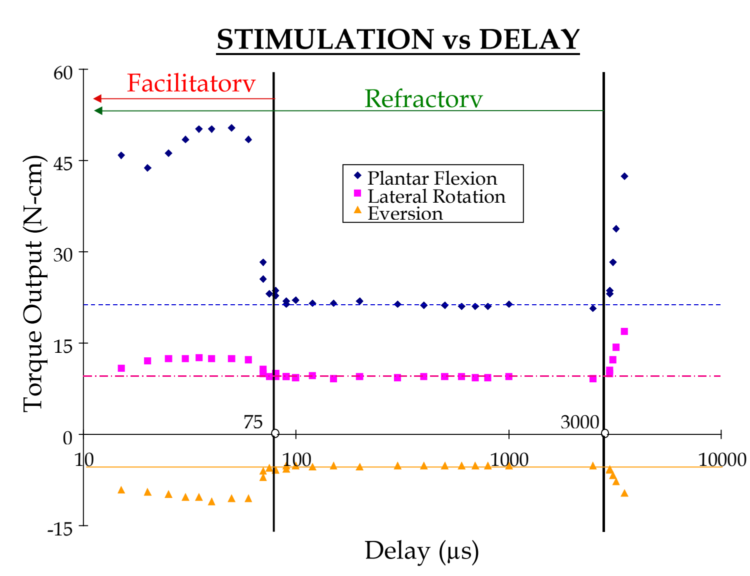

Figure 1 – The torque output produced by two identical stimulation pulses applied through the same electrode contact is shown versus the delay between the two pulses. The facilitative period, the time during which nerve fibers partially depolarized by the first pulse were fully activated by the second pulse, was found to last up to 75µs in this case. The refractory period, the time during which the second pulse could not activate nerve fibers that were fully activated by the first pulse, was found to last up to 3000µs in this case. After the end of the refractory period, some nerve fibers were fully activated by both stimuli resulting in those nerve fibers delivering two action potentials to their corresponding muscles and producing additional torque output.

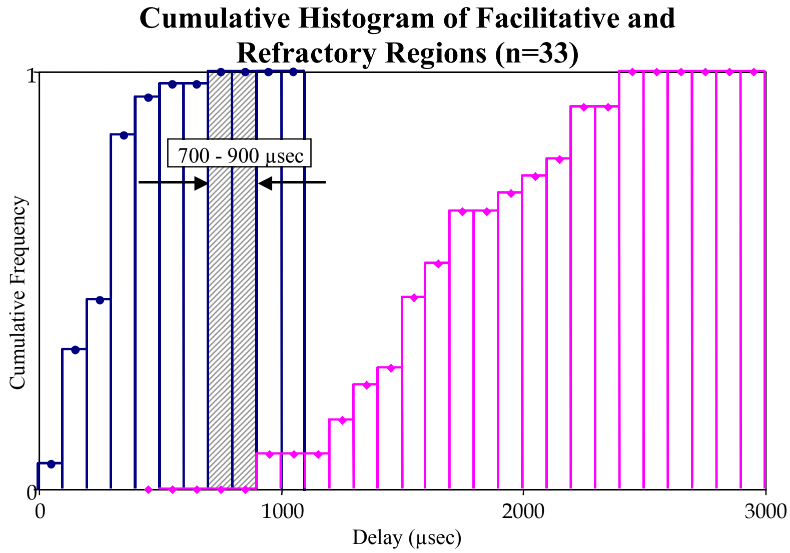

Figure 2 – A cumulative histogram of the delays that indicate the end of the facilitative region and the end of the refractory region in 33 data sets acquired across four animals. The region between 700 and 900 µsec delay was after the facilitative region but before the end of the refractory region in all cases.

the facilitative region would appear to end sooner than the actual value would be if the region of the nerve that was stimulated just below threshold contained either all sensory fibers or interstitial tissue. Since the region that is stimulated to just below threshold will take the longest time to return to baseline, this is the region that would exhibit the longest (or closest to the actual) value for the facilitative period. If that region was either sensory fibers or interstitial tissue, no response would be recorded and the facilitative period would appear to have ended at a shorter duration.

The actual facilitative and refractory periods are dependent on properties of the ion channels in the nerve membrane. Although these results only quantify the facilitative and refractory periods for the cat sciatic nerve, these results should and were found to correspond well with other nerves in the cat and other species. In particular, the range 700-900 µsec, found in this study, is within the ranges found by Peckham [1] using intramuscular electrodes in rats and humans and Liang et al. [2], Rutten et al. [3], and Yoshida and Horch [4] using intrafascicular electrodes in cat nerves.

Although any delay between 700 and 900µsec should be usable to produce independent stimulation from two different stimulation configurations within the same nerve cuff electrode, a delay of 900µsec is recommended. This recommendation of a 900µsec delay based on the location of the two stimulation sites being two different locations around the nerve trunk. Since the end of the refractory period will affect the region closest to the nerve first, non-linear affects due to the end of the refractory period are less likely. Since the facilitative period will have the most affect on a region of the nerve away from the contact, an affect due to an overlap of the facilitative region is much more likely to occur. Using a 900µsec delay will provide the delay with the least likelihood of producing non-linear field effects.

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