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Orderly activation of human motor neurons using electrical ramp prepulses

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Abstract

Objective: Conventional electrical stimulation (rectangular pulses) recruits large before small diameter motor neurons and motor neurons close to the electrode before more distant motor neurons. The present study investigated the possibility for changing the recruitment order of electrical stimuli with sub-threshold ramp prepulses.

Methods: The median nerve was stimulated using surface electrodes at the wrist and elbow. Compound motor action potentials were recorded from abductor pollicis brevis and flexor carpi radialis. Stimulus–response curves, nerve conduction velocity and excitation thresholds of abductor pollicis brevis and flexor carpi radials, with and without ramp prepulses, were recorded in order to study the effect of ramp prepulses on axonal excitability.

Results: The conduction velocity of the initial response (10% of the maximal response) was decreased by 4.3±0.83 m/s with ramp prepulses (500 ms, 80% of the excitation threshold). The ramp prepulses also had a differential effect on the excitation thresholds of abductor pollicis brevis and flexor carpi radialis. In addition, ramp prepulses increased the threshold of 10% of the maximal response more than the threshold of 90% of the maximal response.

Conclusions: These results demonstrate that large diameter and motor neurons close to the electrode accommodate more to ramp prepulses than small diameter and distant motor neurons, which suggests that ramp prepulses may be used to change the recruitment order of rectangular pulses.

Significance: This technique of ramp prepulses allows stimulation of alternate subsets of motor nerves.

Keywords: Axonal excitability; Accommodation; Selective electrical stimulation; Compound muscle action potential

1. Introduction

Electrical stimulation is widely used for stimulating nerve fibers. However, the method is flawed with its inability for selective activation of small diameter nerve fibers without co-activation of large diameter nerve fibers. This is due to the recruitment order of conventional electrical rectangular pulses (i.e. large diameter nerve fibers are activated before small diameter nerve fibers (Blair and Erlanger, 1933)). For myelinated nerve fibers, the excitability of nerve fibers is positively related to inter-nodal distance (McNeal, 1976; Rattay, 1986), and the inter-nodal distance is positively related to nerve fiber diameter (Nilsson and Berthold, 1988). These positive relations are responsible for the higher excitability of large diameter nerve fibers to electrical stimulation. In electrodiagnostic medicine the recruitment order of rectangular pulses poses a problem when testing the integrity of small diameter nerve fibers, and in functional electrical stimulation (FES) it causes a problem for replicating the physiological recruitment order of muscle fibers (i.e. small motor units are recruited before larger units (Henneman, 1981)).

Recently, electrical sub-threshold prepulses have been proposed to invert the threshold current-to-distance (Deurloo et al., 1997; Grill and Mortimer, 1995, 1997; Poletto and Van Doren, 2002) and the threshold

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current-to-diameter relationship of rectangular pulses (Deurloo et al., 2001; van Bolhuis et al., 2001). Sub-threshold prepulses builds upon the method of differential blocking of nerve fibers by direct current, which exploits the non-linear conductance properties of the axonal membrane (Fukushima et al., 1975; Manfredi, 1970; Sassen and Zimmermann, 1973; Zimmermann, 1968). Differential blocking with direct current uses two pairs of electrodes, one for stimulation and one for blocking. Whereas in the method of sub-threshold prepulses, only one pair of stimulating electrodes are used, and the differential block is obtained by preceding a rectangular stimulation pulse with a sub-threshold prepulse. The mechanism for the latter differential block is the same as the one responsible for the recruitment order of conventional rectangular pulses (i.e. depolarization of large more than small diameter nerve fibers and depolarization of fibers close to the electrode more than distant nerve fibers). Nerve fibers have been shown to accommodate to depolarization (Kugelberg, 1944; Lucas, 1907) which increases the thresholds of the most excitable nerve fibers more than the threshold of less excitable nerve fibers. Theoretically, this enables a selective activation of previously less excitable nerve fibers (i.e. small diameter nerve fibers and distant nerve fibers). Both direct current and sub-threshold prepulses are potentially useful. However, since sub-threshold prepulses have the advantage of only requiring one pair of stimulating electrodes, it avoids the problem of positioning a second electrode along the course of the nerve. An inversion of the threshold current-to-distance relationship and an inversion of the threshold current-to-diameter relationship using sub-threshold prepulses has been shown with cuff and hook electrodes, respectively (Grill and Mortimer, 1997; van Bolhuis et al., 2001). Unfortunately, cuff and hook electrodes are not feasible for acute human use since they require surgery. Consequently, sub-threshold prepulses are only feasible in human studies if they can be used with surface or needle electrodes, and the effects of sub-threshold prepulses can be observed and verified with non-invasive measurements.

The aim of the present study was to investigate accommodation of motor neurons to ramp prepulses and the recruitment order of rectangular pulses preceded by ramp prepulses using non-invasive techniques. These techniques were stimulus–response curves, nerve conduction velocity, and determination of the excitation threshold of two muscles, representing two subsets of the motor neurons in the nerve. Stimulus–response curves were used to study accommodation of motor neurons to ramp prepulses. Nerve conduction velocities were used to test whether ramp prepulses can invert the current-to-diameter relationship of rectangular pulses. Estimation of excitation thresholds of two muscles innervated by the same nerve was used to test whether ramp prepulses can invert the recruitment order of two sets of motor neurons (i.e. inversion of the current-to-distance relationship). Motor neurons were chosen, as they are technically simpler to study than sensory neurons. Ramp prepulses were chosen instead of rectangular prepulses in order to depolarize the motor neurons more than what would be possible with rectangular prepulses. As, nerve fibers accommodate to ramp pulses the prepulse intensity may be increased with ramp prepulses as compared to rectangular prepulses without exceeding the excitation threshold. Thus, ramp prepulses may be more effective than rectangular prepulses for selective activation of small diameter motor neurons.

2. Materials and methods

2.1. Subjects

Three experiments (A, B, and C) were conducted on healthy male and female subjects. All subjects gave written informed consent to the experimental procedures. The procedures were conducted in accordance with the Helsinki Declaration of 1975 and approved by the local ethics committee. Experiment A, included 11 subjects (age 21–29 years) of whom 8 were males. Experiment B, included 13 subjects (age 23–35 years) of whom 10 were males. Experiment C, included 13 subjects (age 22–28 years) of whom 8 were males. Two subjects participated in both experiments A and C. All of the subjects had no history of wrist injuries or any known neurological disorders.

2.2. Experimental setup

Compound muscle action potentials (CMAP) were recorded from the abductor pollicis brevis (APB) and flexor carpi radialis (FCR). The active electrode was placed over the motor points and the reference electrodes over the distal tendons. The ground electrode was placed on the palm of the hand. The CMAP signals were amplified (gain 2000, bandwidth 2–5 kHz) and digitalized by a computer (Pentium PC) with a data acquisition board (PCI-MIO E Series, National Instruments). All data was sampled at a rate of 20 kHz. The CMAPs were elicited with electrical stimulation of the median nerve at the wrist and the elbow using a stimulus isolator (NoxiSTIM, JNI Biomedical A/S, Aalborg, Denmark). The stimulus isolator functioned as a voltage-controlled-current-source. The cathode at the wrist was placed between the tendons of the flexor carpi radialis and palmaris longus muscle. The cathode at the elbow was placed in the anticubital fossa by locating the brachial artery. The anodes were placed 2.5 cm proximal to their respective cathode. Standard Ag–AgCl neurology surface electrodes (720 01-K, Medicotest A/S, Ølstykke, Denmark) were used for electrical stimulation and recording of the CMAPs.

A custom written LABVIEW program controlled the recording of the CMAP and the electrical stimulator. The program generated an analogue signal that controlled the electrical stimulus, which was defined by four parameters