Clinical Neurophysiology 122 (2011) 2290–2293

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

A comparison of the excitability of motor axons innervating the APB and ADM muscles

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ARTICLE INFO

Article history:
Accepted 10 April 2011
Available online 10 May 2011

Keywords:
Axonal excitability
Median
Ulnar
Peripheral nerve

HIGHLIGHTS

- Excitability indices of median and ulnar motor axons are significantly different.
- Excitability indices are specific for the nerve and muscle studied as well as the site of nerve stimulation.
- Excitability studies of the ulnar nerve at the wrist, recording from ADM, are reproducible.

ABSTRACT

Objective: Threshold tracking allows the non-invasive assessment of axonal excitability. This study aimed to determine whether axonal excitability of the motor axons of the median nerve (to APB) and ulnar nerve (to ADM) to the small muscles of the hands is sufficiently similar to be interchangeable; confirm the feasibility and reproducibility of ulnar studies and obtain control data for a young population for this site of stimulation.

Methods: Twenty normal subjects between the ages of 23–43 were studied using the TRONDF protocol of QTRACS, (©Prof Hugh Bostock, London). The median and ulnar nerves were stimulated at the wrist and the compound muscle action potentials were recorded from abductor pollicis brevis and abductor digiti minimi, respectively. Repeat studies were performed in four subjects to confirm reproducibility of the recordings.

Results: Stimulus intensity was greater and strength duration time constant was longer for the median nerve. Threshold electrotonus showed there was a greater change in threshold in the hyperpolarising direction for the median nerve compared with the ulnar nerve. There was however little difference in the recovery cycle and current threshold relationship.

Conclusions: Although recovery cycles and the current thresholds are similar for APB and ADM, there are definite differences in stimulus threshold, SDTC and threshold electrotonus which question the interchangeability of studies for these two sites.

Significance: This study demonstrates reproducibility of motor axonal excitability studies of the ulnar nerve at the wrist, provides young control data for this site of stimulation and suggests that although certain excitability indices are similar for the median nerve to APB and ulnar nerve to ADM there are definite differences making the interchangeability of the data questionable.

1. Introduction

The human hand muscles are innervated by the median and ulnar nerves. The median nerve originates from the medial and lateral cords of the brachial plexus (C6-8 and T1 roots) and in the hand supplies motor fibres to the thenar muscles (i.e. abductor pollicis brevis, flexor pollicus brevis (superficial head), opponens pollicis; and the two lateral lumbrical muscles; Wilbourn and Ferrante, 2005). The ulnar nerve arises from the medial cord (C8, T1) of the brachial plexus. The deep palmar branch of the ulnar nerve innervates the hypothenar eminence (i.e. abductor digiti minimi, flexor digiti minimi brevis and opponens digiti minimi) all the interossei, the third and fourth lumbricals, and two thenar muscles; adductor pollicis and the deep head of the flexor pollicis brevis (Wilbourn and Ferrante, 2005).

Nerve excitability studies provide an assessment of ion channel function of peripheral nerves of human subjects in vivo (Bostock et al., 1998; Kiernan et al., 2000; Burke et al., 2001). The measurements obtained from nerve excitability studies can provide insight

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doi:10.1016/j.clinph.2011.04.007

into the resting membrane potential, ion channel activity and ion channel distribution along axons, and can provide information about the pathophysiology of peripheral nerve diseases (e.g. Krishnan and Kiernan, 2005; Lin et al., 2006). Most frequently nerve excitability studies have been performed stimulating the median nerve at the wrist and recording from the thenar eminence i.e. abductor policis brevis (APB; e.g. Cappelen-Smith et al., 2002; Lin et al., 2006; Jankelowitz et al., 2007a,b). The relatively frequent incidence of carpal tunnel syndrome, especially in female patients, raises the question as to whether ulnar studies, recording from abductor digiti minimi (ADM), can be substituted for median studies. Previous studies have suggested variation in excitability between nerves, at different sites along the same nerve and recording from different muscles when stimulating one nerve at the same site (e.g. Bae et al., 2009; Jankelowitz and Burke, 2009). The differences in excitability indices for the median and ulnar nerve at the wrist have also been examined in an attempt to explain the pathophysiological basis for the "split hand" seen in motor neuron disease patients (Bae et al., 2009). The current study was designed to determine whether median studies recording from APB and ulnar nerve studies recording from ADM are interchangeable (i.e. the findings are so similar that either nerve can be studied in research studies or clinical studies) as well as whether ulnar studies are reproducible. The data will also contribute to the normal data for ulnar nerve studies (recorded from ADM) for younger subjects.

2. Methods

Nerve Excitability studies were conducted on the non-dominant hand of 20 healthy subjects who had no previous history of neurological disease (10 male, 10 female, mean age 29.9, range 20–43). In four subjects three ulnar motor studies were performed on three different days to determine reproducibility of the study. Approval for the study was obtained from the Human Research Ethics Committee of the University of Sydney, with each subject providing written informed consent prior to participating in the study. Skin temperature was closely monitored at the site of stimulation and maintained at or above 32 °C.

The median nerve was stimulated just proximal to the wrist crease using a button electrode custom-made with a 4 cm interelectrode distance. The anode (Cleartrace REF 1700-030, CONMED Corp, New York, USA) was located on the radial aspect of the arm approximately 10 cm more proximal positioned over muscle. The ulnar nerve was stimulated at the wrist crease with the anode positioned 10 cm more proximal over muscle on the ulnar aspect of the forearm. The order of stimulation of the median and ulnar nerves was randomised between the subjects. Surface recordings were made using 1 cm diameter disposable Ag–AgCl electrodes (Cleartrace REF 1700-030, CONMED Corp, New York, USA) from abductor pollicus brevis (APB) for the median studies and adductor digiti minimi (ADM) for the ulnar studies. The recording electrode was placed over the muscle belly and the reference electrode was placed on the first metacarpophalangeal joint or fifth metacarpophalangeal joint, respectively. The studies were performed with the arm in a neutral position, slightly flexed at the elbow, resting on a bench.

Excitability was assessed using the TRONDF protocol of QTRACS, (version 25/6/2009 ©Professor Hugh Bostock, Institute of Neurology, London), a computerised protocol for studies of nerve excitability. An isolated linear bipolar constant current stimulator with a maximal output of 50 mA (Digitimer DS5 stimulator, UK) was used. The signal was amplified (ICP511 AC amplifier, Grass Technologies, West Warwick, USA) and filtered (3–3 kHz plus Hum Bug 50/60 Hz Noise Eliminator, Quest Scientific Instruments, North Vancouver, Canada). The TRONDF protocol cycles through five subroutines; the stimulus–response curve, determination of strength-duration time constant, threshold electrotonus, the current-threshold relationship and the recovery cycle.

2.1. Stimulus–response curve

The stimulus–response curve was measured using stimuli of 1 ms. The stimulus was manually increased to obtain a CMAP of maximal amplitude. The curve was then repeated in smaller increments of stimulus by the computer. The target potential was set to be approximately 40% of the maximal CMAP, on the fast rising phase of the stimulus–response curve. The current necessary to produce this 40% CMAP is referred to as the "threshold" for the CMAP.

2.2. Strength-duration time constant

The total "energy" of a stimulus is related to the duration and intensity of the stimulus. The strength-duration time constant for the motor axons of the median and ulnar nerves was calculated using five different stimulus durations from 0.2 to 1.0 ms and assessing the change in stimulus current necessary to produce the test CMAP (~40% of maximum). Stimulus charge was plotted against stimulus duration and Weiss' law was used to calculate the strength-duration time constant (SDTC).

2.3. Threshold-electrotonus

Prolonged subthreshold currents were used to alter the potential difference across the nodal and internodal membrane for the third and fourth subroutines. The term threshold electrotonus refers to the changes in threshold associated with the electrotonic changes in membrane potential of the axon. Threshold was tested at different intervals following subthreshold currents of 100 ms duration that had been set at +40% and +20% (depolarising) and −40% and −20% (hyperpolarising) of the "threshold current". The change in threshold at the various time intervals was plotted with the depolarising directions above the baseline and the hyperpolarising direction below the base line (Fig. 1C).

2.4. The current-threshold relationship

The current-threshold (IV) relationship is dependent on the rectifying properties of the internodal membrane of the axon and is analagous to the current–voltage relationship. The change in threshold was determined 200 ms after the onset of a 220 ms subthreshold polarising current. The strength of the polarising conditioning current was altered in 10% increments, from +50% (depolarising) to −100% (hyperpolarising) of the control threshold.

2.5. Recovery cycle

The last subroutine measured by the protocol recorded the recovery cycle i.e. changes in axonal excitability following a supramaximal conditioning stimulus. The recovery cycle examines the changes in axonal excitability as the axons pass through the relative refractory period (at short interstimulus intervals), superexcitable period (when the nerve is easier to excite) and subexcitable period (when the nerve is less excitable). Eighteen conditioning-test intervals from 200 to 2 ms were used to record the changes in threshold current. In order to calculate the response to the test stimulus, the CMAP produced by the supramaximal conditioning stimulus was subtracted from the conditioning stimulus to eliminate contamination by the maximal CMAP due to the conditioning stimulus.