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Usefulness of cervical root magnetic stimulation in assessing proximal motor nerve conduction

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ABSTRACT

Objectives: To evaluate the reliability and utility of cervical root magnetic stimulation in exploring proximal motor conduction. *Methods*: In 20 patients with demyelinating polyneuropathy (DPN), 20 patients with amyotrophic lateral sclerosis (ALS) and 25 healthy subjects, evoked compound muscle action potentials (CMAPs) were recorded from abductor digiti minimi muscle in response to electrical stimulation up to Erb's point and magnetic stimulation up to the cervical roots. *Results*: In all healthy and ALS subjects, magnetic root stimulation confirmed the absence of conduction abnormalities, including those in whom supramaximal responses at Erb's point were not achieved. In the DPN group, conduction block and/or temporal dispersion was revealed by magnetic root stimulation in 9 out of 20 patients (45%), 3 more than those detected at Erb's point. *Conclusions*: Cervical root stimulation allowed clear distinction between motor neuronopathy and DPN. It is recommended as part of the routine evaluation of patients suspected of having DPN, especially when distal nerve studies are inconclusive.

1. Introduction

Nerve conduction studies constitute the primary examination for the evaluation of peripheral nervous system function. Conventional studies assess distal nerve segments, which are readily stimulated through the skin with surface electrical stimulator. On the other hand, proximal nerve domains and spinal roots, due to their deep location are not easily accessible and thus several alternative methods have been suggested to overcome this difficulty. Information on conduction along the entire nerve length can be obtained by F wave studies (Olney et al., 1990), while neurogenic changes of paraspinal and proximal limb muscles detected via needle electromyography provide an indirect evidence of nerve damage (Alfonsi et al., 2003). A more direct approach is electrical stimulation of the nerve root or plexus using a high voltage percutaneous stimulator or needle electrode, which however, are painful methods and often not well tolerated by some people (Vucic et al., 2006a,b). Magnetic stimulation is appropriate for activating deep located neural domains – brain cortex, spinal roots, plexuses – because the magnetic field penetrates tissues such as bones with minimal attenuation and therefore offers the advantage of a fast, non-invasive and minimal pain method with well established neuropsychiatric applications (Cros et al., 1990; Rossini et al., 2015). Specifically, previous literature on magnetic stimulation of spinal nerves at neuroforamina has shown that the evoked compound muscle action potential (CMAP) has stable latency but less reliable amplitude measurements (Ugawa et al., 1989). A recent study of healthy subjects has shown that stimulation of cervical roots with a specially designed magnetic coil produced supramaximal CMAPs, which in addition to standard latency have reproducible values of amplitude and area (Matsumoto et al., 2010).

Investigation of proximal nerve conduction is valuable in diagnosing auto-immune neuropathies and differentiating them from motor neuronopathies or anterior horn diseases. Acquired demyelinating polyneuropathies (DPN) are typically characterized by a patchy or segmental pattern with earlier and more pronounced changes in the most proximal nerve regions (Mathey and Pollard, 2013). Investigation of these segments is important for treatment related decisions, since it has been observed that secondary axonal degeneration at this level correlates better than other neurophysiological findings with clinical deficits (Menkes et al., 1998). Moreover, proximal conduction studies have also proved helpful in the evaluation of patients with suspected multifocal motor neuropathy (MMN) and in distinguishing it from amyotrophic lateral sclerosis (ALS) (Arunachalam et al., 2003). To date, methodological issues regarding proximal conductivity in pathological conditions have not been standardized. Some authors

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claimed that unlike healthy state, in chronic demyelinating pathology supramaximal stimulation of the proximal nerve segments is more difficult to achieve due to an elevated excitation threshold (Yokota et al., 1996; Meulstee et al., 1997; Inaba et al., 2001). To our knowledge, no targeted study related to the reliability of proximal magnetic stimulation in demyelinating polyneuropathies has been performed. Likewise, the absence of conduction abnormalities demonstrated by magnetic nerve stimulation in patients with suspected ALS has received very little attention (Arunachalam et al., 2003).

In the present study, motor responses to magnetic and electrical stimulation of the proximal nerve segments were studied in healthy controls, patients with DPN and ALS. We postulated that cervical root stimulation by commercially available magnetic coil could provide reliable responses increasing the diagnostic sensitivity of electrophysiology.

2. Subjects and methods

2.1. Subjects

Sixty-five subjects were prospectively enrolled in this study and were classified into the following 3 groups: I. Twenty five healthy subjects (10 men; mean age 49.2 ± 15.0 years; range 24–75 years), none of whom had symptoms of neuromuscular disease, diabetes mellitus, or other conditions known to cause polyneuropathy (including alcohol or drug abuse, chronic kidney disease and exposure to neurotoxic drugs). II. Twenty patients with ALS (10 men; mean age 59.0 ± 6.8 years; range 46–68 years). All these individuals fulfilled the revised El Escorial criteria (Brooks et al., 2000) III. Twenty patients with clinically and electrophysiologically supported diagnosis of acquired DPN (12 men, mean age 49.7 ± 18.0, range 17–73 years). This group consisted of 10 patients suffering from chronic inflammatory demyelinating polyneuropathy (CIDP), 8 patients with acute inflammatory demyelinating polyneuropathy (AIDP) and 2 patients with multifocal motor neuropathy (MMN) who all met the diagnostic criteria for each disease (Hadden et al., 1998; Olney et al., 2003; Van den Bergh et al., 2010). Written informed consent was obtained by all participates and the study was approved by the Institutional Ethics Committee of the Patras University Hospital (no of approval 434, 11.12.2013).

2.2. Neurophysiological technique

All studies were performed on a two-channel Keypoint ver. 3.25 electromyographic apparatus (Medtronic-Dantec Electronics, Sakovlunde, Denmark) and a Magstim 200 stimulator (The Magstim Company, Whitland, Dyfed, U.K.) equipped with a commercially available figure-of-eight double coil (each loop 70 mm in diameter), that generates a maximum field strength, at the center of the coil, of 2.2 T. Subjects were instructed to remain relaxed and the limb temperature was maintained at 33 °C ± 0.5 °C throughout the recording procedure. At first, conventional nerve conduction studies and needle EMG was performed to confirm the diagnosis in the patient groups. Motor and sensory conduction of the ulnar nerve were also studied in all healthy subjects to exclude subclinical abnormalities.

For the purpose of this study, CMAPs were recorded by a surface bar electrode (2 × 10 mm stainless steel discs fixed in a plastic mount with a 30 mm center-to-center distance) placed over the motor point of the Abductor Digiti Minimi (ADM) muscle, on the side of weaker muscle strength or on the left side if normal or similar strength on both sides. Electrical stimulation of the ulnar nerve was delivered through a bipolar saline-soaked felt pad electrode (6 mm-diameter cathode, 23 mm distal to the 6 mm diameter anode). The nerve was stimulated just above the elbow and Erb's point using a constant current stimulator that delivers square waves. In order to achieve supramaximal activation at Erb's point, single shocks of 0.5 ms duration and 100 mA were applied. For magnetic nerve stimulation, the point of maximal current at the intersection of the two round components was placed over the same sites as with electrical stimulation, i.e. above the elbow while the subject maintained the arm in abduction flexing the forearm and at the Erb's point with the subject's neck laterally flexed 30 degrees to the opposite side. For magnetic root simulation the point of maximal current was positioned over the C7 spinous process with the induced current in an orthodromic direction and the coil firmly held against the spine with the subjects head bent slightly forward (Mills et al., 1993). The handle of the coil was parallel to the nerve at each stimulation site (Fig. 1). The magnetic stimulation level for all positions was set at 100% output. In all subjects CMAP amplitudes were saturated with intensity lower than 90% of the maximal stimulator output. The stimulus intensity was increased gradually and CMAP latency monitored to avoid possible current spreading, which would be recorded as an abrupt shortening of CMAP latency (Matsumoto et al., 2013). Each magnetically evoked CMAP was repeated 3–5 times to ensure reproducibility. Moreover, in a subgroup of 10 healthy subjects a circular coil of 90 mm diameter was additionally used to deliver magnetic stimulation at root level. Optimal recordings were obtained from the left ADM when the center of the circular coil was placed slightly to the ipsilateral side of the C7 spinal process and the coil current traveled anti-clockwise and vice versa for the right ADM. All potentials were recorded with band-pass filtering between 20 Hz and 10 kHz using a display sensitivity of 0.5–5 mV/division 16 bits A/D conversion, sampling at 5 kHz, input impedance >1000 MOhm/25pF, common mode rejection ratio >100 dB, noise level (RMS) <1 μV and acquisition sweep speed 5 ms/division.

At each site of stimulation the following parameters of CMAP were measured: latency (stimulus artefact to the onset of negative phase), amplitude (from baseline to negative peak), area (under the

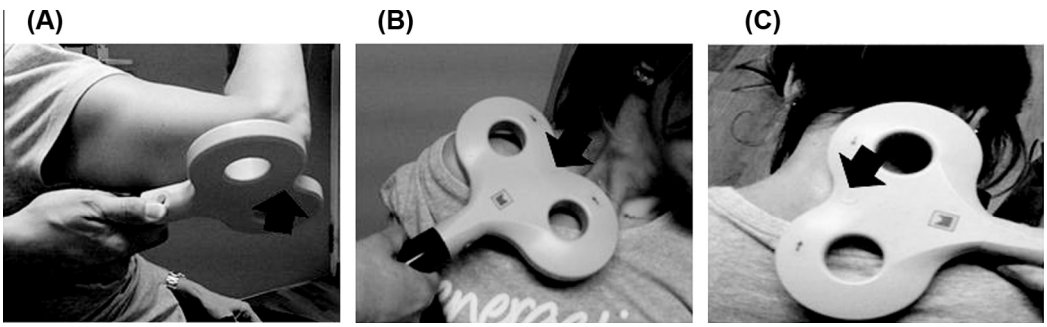

Fig. 1. Optimal coil position for magnetic stimulation above the elbow (A), at Erb's point (B) and at the cervical root level (C). The point of stimulation at each site is indicated by the arrows.