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Magnetic-motor-root stimulation: Review

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HIGHLIGHTS

- Magnetic-motor-root stimulation can activate spinal nerves at the neural (intervertebral) foramina, which is usually performed to measure CMAP latency.
- Recently, supramaximal stimulation has been achieved during magnetic stimulation at the neural foramina, thus contributing to the measurement of both CMAP size and latency.
- Additionally, the most proximal cauda equina can be activated, thus contributing to the measurement of cauda equina conduction time and cortico-conus motor-conduction time.

ABSTRACT

Magnetic stimulation can activate the human central and peripheral nervous systems non-invasively and virtually painlessly. Magnetic stimulation over the spinal enlargements can activate spinal nerves at the neuroforamina (magnetic-neuroforamina stimulation). This stimulation method provides us with information related to the latency of compound-muscle action potential (CMAP), which is usually interpreted as peripheral motor-conduction time (PMCT). However, this stimulation method has faced several problems in clinical applications. One is that supramaximal CMAPs were unobtainable. Another is that magnetic stimulation did not usually activate the spinal nerves in the spinal canal, i.e., the cauda equina, which prevented an evaluation of its conduction. For these reasons, magnetic-neuroforamina stimulation was rarely used to evaluate the conduction of peripheral nerves. It was mainly used to evaluate the conduction of the corticospinal tract using the parameter of central motor-conduction time (CMCT), which was calculated by subtracting PMCT from the latency of motor-evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) over the primary motor cortex. Recently, supramaximal stimulation has been achieved in magnetic-neuroforamina stimulation, and this has contributed to the measurement of both CMAP size and latency. The achievement of supramaximal stimulation is ascribed to the increase in magnetic-stimulator output and a novel coil, the magnetic augmented translumbosacral stimulation (MATS) coil. The most proximal part of the cauda equina can be reliably activated using the MATS coil (magnetic-conus stimulation), thus contributing to the measurement of cauda equina conduction time (CECT) and cortico-conus motor-conduction time (CCCT). These recent developments in magnetic-motor-root stimulation enable us to more precisely evaluate the conduction of the proximal part of peripheral nerves and that of the corticospinal tract for lower-limb muscles. In this review article, we summarise the basic mechanisms, recent topics, clinical applications, comparison to electrical stimulation, pitfalls, safety and additional issues in magnetic-motor-root stimulation.

Abbreviations: ADM, abductor digiti minimi; AH, abductor hallucis; APB, abductor pollicis brevis; BB, biceps brachii; BF, biceps femoris; C5, fifth cervical vertebra; C7, seventh cervical vertebra; CCCT, cortico-conus motor-conduction time; CECT, cauda equina conduction time; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CMAP, compound-muscle action potential; CMCT, central motor-conduction time; ECG, electrocardiography; EDB, extensor digitorum brevis; EMG, electromyography; FDI, first dorsal interosseous; L1, first lumbar vertebra; L5, fifth lumbar vertebra; M1, primary motor cortex; MAG, myelin-associated glycoprotein; MATS, magnetic augmented translumbosacral stimulation; MCV, motor-conduction velocity; MEP, motor-evoked potential; NCS, nerve-conduction study; PAC, premature atrial contraction; POEMS, polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes; PMCT, peripheral motor-conduction time; PVC, premature ventricular contraction; S1, first sacral vertebra; SEP, sensory-evoked potential; TA, tibialis anterior; TMS, transcranial magnetic stimulation; Vf, ventricular defibrillation.

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Contents

1. Introduction

Magnetic stimulation, which was developed by Barker et al. (1985), can activate the central and peripheral nervous systems. For the central nervous system, the transcranial magnetic stimulation (TMS) technique made it possible to investigate the function of the human cerebral cortex non-invasively and virtually painlessly. TMS of the primary motor cortex (M1) can move human limb muscles. Using electromyography (EMG), the muscular contraction can be recorded as muscle action potentials, which are called motor-evoked potentials (MEPs). By means of single-pulse, paired-pulse or repetitive TMS for the central nervous system, the analysis of MEPs has provided us with numerous insights (Chen et al., 2008; Groppa et al., 2012).

As distinct from nerve-conduction studies (NCS) conducted by electrical stimulation, for the peripheral nervous system, magnetic stimulation is not generally applicable to analyse the distal part of peripheral nerves. One reason for this is that supramaximal stimulation is not easily achieved, even with maximum output of the magnetic stimulator (Olney et al., 1990; Bischoff et al., 1995). Therefore, the size of compound-muscle action potentials (CMAPs) cannot always be analysed as a parameter for peripheral neuropathy. Another reason is that the site of activation is not well localised (Bischoff et al., 1995). Even though the small figure-of-eight coil with which relative focal activation is possible is used to activate peripheral nerves, the activation of several peripheral nerves causes issues such as current spread and volume conduction (Cros et al., 1990b). Moreover, when peripheral nerves are bent, the currents concentrate into the bent parts (Maccabee et al., 1993; Bischoff et al., 1995). Therefore, since the activation site is moved from peripheral nerves just beneath the edge of the coil to the unknown bent part, the CMAP latency cannot be analysed.

In contrast, magnetic stimulation at the neuroforamina (magnetic-neuroforamina stimulation) is often used in both clinical examinations and basic research. The greatest characteristic of this technique is that it permits us to activate spinal nerves at the neuroforamina and to measure the stable CMAP latency (Ugawa et al., 1989b). In this way, we can obtain information on the peripheral motor-conduction time (PMCT), which indicates the conduction time from the proximal part of peripheral nerves to the target muscle. Since TMS for M1 provides us with information on the conduction time from M1 to muscle (cortical latency), central motor-conduction time (CMCT), which is a parameter of the conduction of the corticospinal tract, can easily be calculated by subtracting

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PMCT from cortical latency. Thus, the previous main application of magnetic-neuroforamina stimulation was for calculating CMCT (Rossini et al., 1994; Terao and Ugawa, 2002). However, this technique has recently been improved and has been applied to other goals, e.g., analysis of the proximal conduction of peripheral nerves.

In this article, we review magnetic-motor-root stimulation for the upper and lower limbs, with a particular focus on recent topics. One topic is that supramaximal stimulation can be achieved in magnetic-neuroforamina stimulation (Matsumoto et al., 2009a, 2010f). Herewith, the CMAP size at the neuroforamina can be analysed similar to NCS using electrical stimulation. Another topic is that the most proximal part of the cauda equina in the vicinity of the conus medullaris can be reliably activated (magnetic-conus stimulation). In this way, it becomes possible to measure cauda equina conduction time (CECT) and cortico-conus motor-conduction time (CCCT) (Matsumoto et al., 2009b, 2010a). These recent developments in magnetic-motor-root stimulation, i.e., magnetic-neuroforamina stimulation and magnetic-conus stimulation, provide us with many novel insights. These stimulation methods were also demonstrated in a hands-on-workshop in the 29th International Congress of Clinical Neurophysiology (ICCN2010, Kobe, Japan) (Ugawa, 2010). Herein, we summarise the basic mechanisms, recent topics, clinical applications, comparison to electrical stimulation, pitfalls, safety and additional issues in magnetic-motor-root stimulation.

2. Basic mechanism of magnetic-motor-root stimulation

2.1. Principles of magnetic stimulation

A magnetic stimulator has an electrostatic capacitor with a large capacitance. The coil connected to the stimulator has a certain inductance and resistance. By flowing powerful and rapidly changing electrical currents in the winding of a coil placed on the body, in accordance with Faraday's law, changing magnetic fields are generated. The changing magnetic fields penetrate the coil vertically and produce eddy currents parallel to the coil in the body. The direction of these eddy currents is opposite to that of the coil currents (eddy currents are also called induced currents). The induced currents penetrate the membranes of the neurons or axons, generating action potentials due to the depolarisation. In the process of activating the central or peripheral nervous system, no electrical currents pass through the subject's skin. Therefore, magnetic stimulation is a non-invasive and virtually painless method (Rossini et al., 1994; Terao and Ugawa, 2002).

When induced currents flow orthodromically along peripheral nerves, they are efficiently activated (Olney et al., 1990; Ruohonen et al., 1996). Maccabee et al. (1993) verified this by magnetically activating mammalian peripheral nerves immersed in Ringer's solution *in vitro* (Maccabee et al., 1993). They identified the activation site by comparing the latency of magnetic stimulation with that of electrical stimulation and found that it was at, or very near, the negative-going first spatial derivative peak of the induced electrical fields along the straight peripheral nerve (virtual cathode). In addition, they also showed that when a peripheral nerve is bent and the induced currents are directed along the peripheral nerve towards the bend, the threshold of activation is reduced at that point.

One of the aspects in which activating peripheral nerves *in vivo* differs from activating them *in vitro* is that the activation site largely depends on the local anatomical structures. When peripheral nerves are surrounded by bony structures that have a high resistance, the induced currents tend to flow along a course with a low resistance. If the bony structures form a canal with a small entrance, then the induced currents tend to concentrate around the entrance and then flow into this canal instead of penetrating the bony structures directly. This feature is also applicable to magnetic stimulation at the foramen magnum (Ugawa et al., 1994; Matsumoto et al., 2008) as well as magnetic-neuroforamina stimulation (see Section 2.2).

2.2. Principles of magnetic-neuroforamina stimulation

Ugawa et al. 1989b reported that magnetic stimulation induced by placing a round coil over the cervical or lumbosacral spinal enlargements could activate spinal nerves (magnetic-neuroforamina stimulation) (Ugawa et al., 1989b). The CMAP latency was constant regardless of the position of the coil and the direction of induced currents. The CMAP amplitude, however, was changed by these two factors. The stable CMAP latency suggested the preferred activation of the fastest motor fibres within peripheral nerves. Furthermore, judging from the CMAP latency, the activation site in magnetic stimulation seemed to be nearly identical to that in electrical stimulation using a high-voltage stimulator. The CMAP latency was always shorter than the peripheral motor-conduction time (PMCT) estimated by F-wave technique. Since the activation site in electrical stimulation using a high-voltage stimulator was considered to be around the spinal nerves traversing the intervertebral foramen (neuroforamina), that in magnetic stimulation was also considered to be the same site, i.e., the spinal nerves at the neuroforamina.

The focal activation site is explained by the concentration of induced currents into a small canal instead of penetrating the bony structures with a high resistance for electrical currents. Many papers have supported this assumption on the activation site and have demonstrated its clinical utility for cervical motor roots using a round coil (Chokroverty et al., 1991; Ugawa et al., 1990; Britton et al., 1990; Cros et al., 1990a; Schmid et al., 1990; Evans et al., 1990; Maegaki et al., 1994; Benecke, 1996; Boyaciyan et al., 1996; Öge et al., 1997; Inaba et al., 2002; Ugawa, 2004; Hitomi et al., 2007; Temuçin and Nurlu, 2011) and a figure-of-eight coil (Epstein et al., 1991; Mills et al., 1993), as well as for lumbosacral motor roots using a round coil (Chokroverty et al., 1989, 1993; Ugawa et al., 1990; Britton et al., 1990; Macdonell et al., 1992; Ertekin et al., 1994a; Benecke, 1996; Maccabee et al., 1996; Troni et al., 1996; Takada and Ravnborg, 2000; Ugawa, 2004; Souayah and Sander, 2006) and a figure-of-eight coil (Maccabee et al., 1996; Maegaki et al., 1997).

Maccabee et al. (1991) verified the assumption that the activation site is the neuroforamina *in vitro* (Maccabee et al., 1991). They measured the electrical field throughout the neuroforamina of a cervical–thoracic spine immersed in a saline volume conductor. Consistent with the *in vivo* studies, the electrical field was maximum at the neuroforamina. The activation site in magnetic stimulation over the cervical or lumbosacral spinal enlargements was thus confirmed both *in vivo* and *in vitro*.

For magnetic-neuroforamina stimulation, the optimal induced-current direction and coil position were investigated using a round coil (Ugawa et al., 1989b; Cros et al., 1990a) and a figure-of-eight coil (Epstein et al., 1991; Mills et al., 1993; Maccabee et al., 1996). Generally, at both the cervical and the lumbosacral neuroforamina, the spinal nerves were efficiently activated when the direction of induced currents in the body was from the muscles to the spinal cord. To obtain larger CMAPs, the optimal coil position was slightly shifted to the ipsilateral side of the recorded muscle. The stable CMAP latency (neuroforamina latency) was mainly used for calculating CMCT.

2.3. Principles of magnetic-conus stimulation

The cervical spinal nerves in the spinal canal are short. Their short conduction time poses few clinical problems. However, the

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lumbosacral spinal nerves in the spinal canal (i.e., cauda equina) sometimes have clinical importance because they are long and are frequently affected by various disorders. Therefore, to evaluate CECT, several methods have been proposed. For example, CECT was calculated by subtracting CMAP latency in magnetic sacral-neuroforamina stimulation from PMCT calculated by the F-wave technique (Banerjee et al., 1993), by subtracting CMAP latency in magnetic sacral-neuroforamina stimulation from PMCT calculated by the H-reflex technique (Chokroverty et al., 1993; Ertekin et al., 1996) and by subtracting CMCT for the rectus abdominis muscle from CMCT for the abductor hallucis muscle (Han et al., 2004). Alternatively, cauda equina lesions were assumed when CMCT calculated by magnetic lumbosacral-neuroforamina stimulation was prolonged and CMCT calculated by the F-wave technique was normal (Di Lazzaro et al., 2004). However, these are 'indirect' methods of determining the conduction of the cauda equina.

Maccabee et al. (1996) reported that magnetic stimulation achieved by placing a large figure-of-eight coil over the conus medullaris could activate the most proximal cauda equina (magnetic-conus stimulation) (Maccabee et al., 1996). The CMAP latency at the most proximal cauda equina was constant regardless of the CMAP size when induced currents were directed cranially. The activation site was considered to be the root-exit zone from the conus medullaris because the induced currents concentrate at the site where the electrical conductivity changes abruptly. Maegaki et al. (1997) also reported that the most proximal cauda equina could be activated in magnetic stimulation using a conventional figure-of-eight coil in normal children (Maegaki et al., 1997). Combined with lumbosacral-neuroforamina latency, the stable CMAP latency (conus latency) can be used to calculate CECT. Consequently, CECT can be calculated by subtracting lumbosacral-neuroforamina latency from conus latency. This stimulation method has one big problem, however: at both the most proximal and the most distal cauda equina, supramaximal CMAPs were unobtainable, which prevented an investigation of the proximal peripheral nerves using CMAP size.

Magnetic-neuroforamina stimulation and magnetic-conus stimulation are popularly called 'magnetic-motor-root stimulation' although the actual activation site in magnetic-neuroforamina stimulation is the trunk of the spinal nerves and not the ventral root (motor root), which is one component of the spinal nerves (Mills and Murray, 1986; Ugawa et al., 1989b; Britton et al., 1990; Epstein et al., 1991).

2.4. Magnetic stimulator

Magnetic stimulators are usually classified into two types: monophasic or biphasic stimulators. In magnetic-motor-root stimulation, a monophasic stimulator is usually used, because the direction of induced currents is very important to evoking a larger electromyography (EMG) response. Recently, thanks to advances in devices, the maximum stimulator output has increased, enabling more powerful activation of the nervous systems. To date, in magnetic-neuroforamina stimulation, supramaximal stimulation has reliably been achieved only with monophasic stimulators (Matsumoto et al., 2009a, 2010f).

2.5. Magnetic coils

There are several types of coils used for magnetic-motor-root stimulation. In general, round coils (also called circular coils) or figure-of-eight coils (also called double coils or butterfly coils) have been used. Recently, for lower-limb muscles, a powerful coil called the magnetic augmented translumbosacral stimulation (MATS) coil was developed (Matsumoto et al., 2009a,b). The stimulation method that uses a MATS coil is called the 'MATS coil stimulation method'.

The MATS coil is a flat, large, round, powerful coil that is 20 cm in diameter (The Magstim Co. Ltd., Whitland, South West Wales, UK). This coil permits us to activate the lumbosacral spinal nerves, which are located deep in the body. The distribution of magneto-electrical fields induced by magnetic stimulation depends on the size of the coil, in accordance with Faraday's law. Theoretically, the larger the coil size, the broader and deeper the distribution of magneto-electrical fields (Cohen and Cuffin, 1991; Jalinous, 1991; Maccabee et al., 1996). Hsiao and Lin (2001) simulated the electrical-field strength produced by a flat, large, round coil that was 20 cm in diameter. They verified that a flat, large, round coil can produce far stronger electrical fields that spread beneath the edge of the coil extensively and deeply (Hsiao and Lin, 2001). This is strong enough to activate deep spinal nerves at the neuroforamina (about 6–10 cm beneath the surface). Therefore, this coil is appropriate for magnetic lumbosacral motor-root stimulation (Matsumoto et al., 2009a,b, 2010a). Actually, the reproducibility in MATS coil stimulation, 'inter-examiner variability' and 'intra-examiner variability', is also sufficient for clinical application (Matsumoto et al., unpublished data). With regard to the safety, this coil should not be used for the investigation of upper-limb muscles because the subject's heart could be stimulated in magnetic cervical motor-root stimulation (see Section 11).

2.6. Clinical setting for recording

If only a TMS study is conducted, subjects can be examined while they are seated on an armchair with a large backrest (Rossini et al., 1994; Groppa et al., 2012). However, the backrest sometimes hinders us from identifying an optimal coil position for magnetic-motor-root stimulation. Therefore, subjects should be seated on a chair without a large backrest or lying on a bed in the prone position. When the target muscle is located on the front side of the body, e.g., biceps brachii (BB), abductor digiti minimi (ADM), first dorsal interosseous (FDI) or tibialis anterior (TA), the subjects should be seated on a chair or a bed. On the other hand, when the target muscle is located on the dorsal side, e.g., abductor hallucis (AH) or biceps femoris (BF), the subjects should be lying on a bed in the prone position.

To analyse the conduction of peripheral nerves, magnetic-motor-root stimulation is usually followed by electrical stimulation of the distal peripheral nerves. For electrical stimulation, the trigger in the computer to record CMAPs should be input from an electrical stimulator. For magnetic-motor-root stimulation, the trigger input should be changed to a magnetic stimulator. These preparations enable us to switch electrical stimulation to magnetic-motor-root stimulation easily.

In addition, the skin temperature should be kept at 31–34 °C for recording from upper- and lower-limb muscles, because nerve-conduction velocity decreases by approximately 2.4 m s^{-1} per 1° decrease in the skin temperature of the subject's limbs (Johnson and Olsen, 1960). The skin temperature should be measured from the distal part of extremities, i.e. forearm and/or lower leg, because the temperature of the distal part of extremities is lower than that of the proximal part of extremities. The temperature in the examination room should be around 25 °C. Extremities with a temperature of <31 °C should be warmed.

3. Magnetic cervical-neuroforamina stimulation

3.1. Recent topic

Matsumoto et al., (2010f) reported that supramaximal stimulation at the cervical neuroforamina could be reliably achieved in

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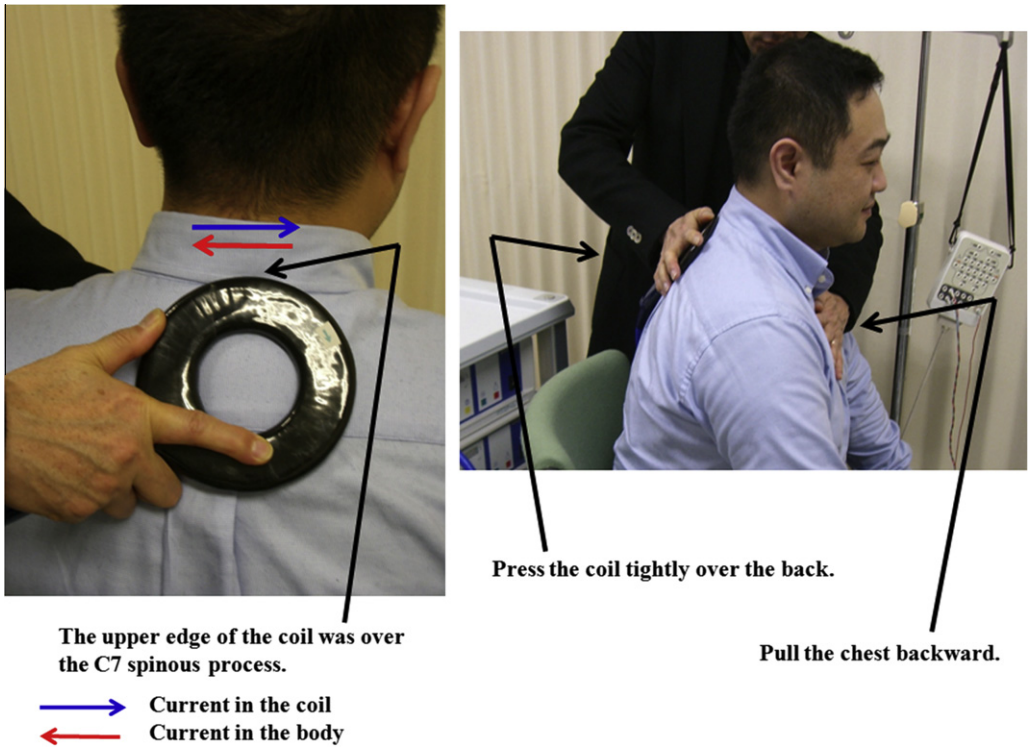

Fig. 1. Optimal round coil position for magnetic cervical motor-root stimulation. The position of a round coil is shown when CMAPs are recorded from the upper limb muscles on the right side. The coil currents are directed clockwise, as seen from behind, so that the induced currents in the body are directed from the muscle to the spinal cord at the upper edge of the coil. The examiner is pressing a round coil firmly against the back of the subject while pulling their chest backward strongly. To obtain supramaximal CMAPs, the optimal coil position is determined to be slightly to the ipsilateral side of the recorded muscle. (Cited from Matsumoto et al., 2010f, with permission.)

most normal subjects (magnetic cervical-neuroforamina stimulation) (Matsumoto et al., 2010f). The supramaximal stimulation was confirmed by electrical stimulation using a high-voltage electrical stimulator. This powerful stimulation is made possible by two main factors, namely, the increase in maximum stimulator output and the expertise of the examiner. The maximum stimulator output of a recent magnetic stimulator such as Magstim200[2] (The Magstim Co. Ltd., UK) has increased compared to that of magnetic stimulators in the 1980s or 1990s. Therefore, we can easily obtain larger CMAPs using recent magnetic stimulators. Additionally, in obtaining supramaximal CMAPs, the examiner needs to be skilled in magnetic cervical-neuroforamina stimulation, as discussed in the next section (see Section 3.2). Supramaximal stimulation contributes to measure CMAP size in addition to CMAP latency in magnetic-motor-root stimulation.

3.2. Recording for cervical-supramaximal stimulation

Muscles that are less affected by volume conduction, e.g., ADM muscle, tend to be preferentially selected for recording. During the examination, the subject sits comfortably on a chair without a large backrest (Fig. 1). When CMAPs are recorded from the right ADM muscle using a round coil, the coil currents should be directed 'clockwise' as seen from behind so that the induced currents in the body are directed along the spinal nerves from the muscles to the spinal cord. The optimal site for evoking CMAPs (i.e., the hot spot) should be searched for around the seventh cervical (C7) spinous process. At the hot spot, the stimulus intensity should be gradually increased to obtain supramaximal CMAPs (Matsumoto et al., 2010f).

This technique can be combined with NCS using conventional electrical stimulation. For the ADM muscle, magnetic cervical-neuroforamina stimulation can be followed by electrical stimulation at the wrist, elbow, axilla and Erb's point (Fig. 2). The CMAP size in

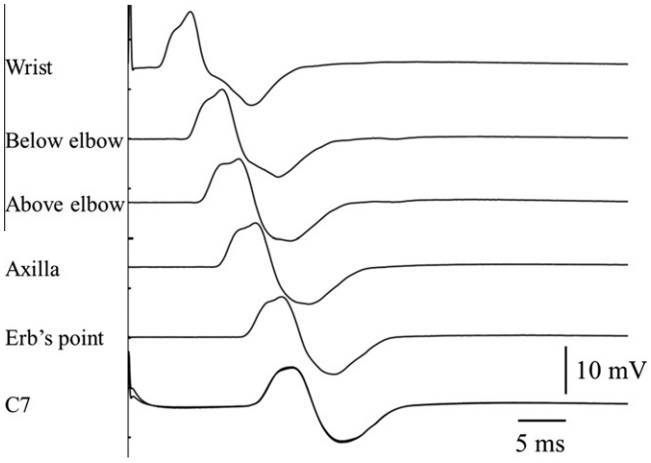

Fig. 2. CMAP waveforms in magnetic cervical motor-root stimulation. CMAPs are evoked by electrical stimulation at the wrist, elbow, axilla, and Erb's point, and they are evoked by magnetic cervical motor-root stimulation (C7), recorded from ADM muscle. Supramaximal CMAPs are obtained in all stimulations. The slight morphological change of the CMAPs evoked by magnetic-motor-root stimulation is explained by the volume conduction.

electrical stimulations at Erb's point is almost identical to that in magnetic-neuroforamina stimulation. Consequently, the focal lesions between Erb's point and neuroforamina, i.e., brachial plexus or spinal nerves just distal to neuroforamina, can also be detected using the CMAP parameters, such as amplitude, area and latency.

Similarly, if CMAPs are recorded from the BB muscle, the hot spot should be searched for around the fifth cervical (C5) spinous process (Matsumoto et al., in press). Thus, for magnetic-motor-root stimulation in particular, the optimal coil position for target muscle is very important.

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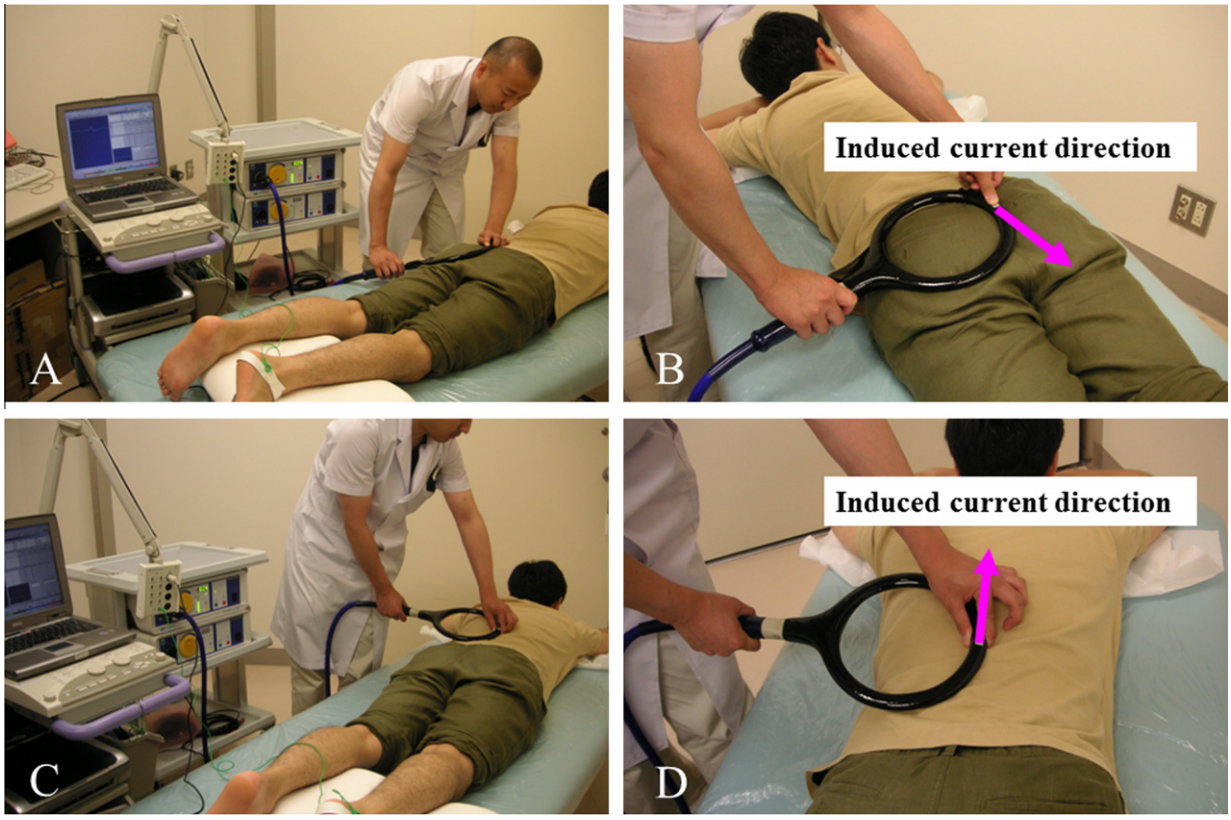

Fig. 3. MATS coil stimulation method. The positions of a MATS coil are shown when MEPs are recorded from the right AH muscle. For magnetic sacral-neuroforamina stimulation (A and B), the edge of the MATS coil is positioned over the first sacral spinous process to induce currents to flow distally along the spinal nerves. For magnetic-conus stimulation (C and D), the edge of the MATS coil is positioned over the first lumbar spinous process to induce currents to flow upward.

4. Magnetic lumbosacral-neuroforamina stimulation

4.1. Recent topic

Matsumoto et al. 2009a reported that supramaximal stimulation at the lumbosacral neuroforamina can be reliably achieved using a MATS coil in most normal subjects (magnetic lumbosacral-neuroforamina stimulation) (Matsumoto et al., 2009a). The supramaximal stimulation was confirmed by electrical stimulation using a high-voltage electrical stimulator. This powerful stimulation was accomplished mainly by a MATS coil, which is a flat, large, round coil that is 20 cm in diameter (see Section 2.5). This coil can produce very strong electrical fields that spread beneath the edge of the coil extensively and deeply. Therefore, we can easily obtain larger CMAPs using the MATS coil. To obtain supramaximal CMAPs, the examiner needs to be skilled in magnetic lumbosacral-neuroforamina stimulation, as discussed below (see Section 4.2). Supramaximal stimulation contributes to the measurement of CMAP amplitude, area and latency.

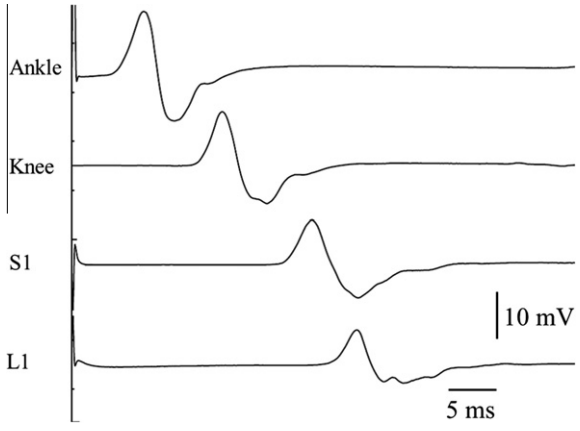

Fig. 4. CMAP waveforms in magnetic sacral motor-root stimulation. CMAPs are evoked by electrical stimulation at the ankle and knee, and they are evoked by magnetic sacral-neuroforamina stimulation (S1) and magnetic-conus stimulation (L1), recorded from AH muscle. Using a MATS coil, supramaximal CMAPs are obtained in all stimulations except for magnetic-conus stimulation. CECT is calculated by subtracting sacral-neuroforamina latency from conus latency. (Modified from Matsumoto et al., 2009b, with permission.)

4.2. Recording for lumbosacral–supramaximal stimulation

The AH muscle is preferentially selected because of its negligible volume conduction. During the examination, the subject lies comfortably on a bed in a prone position (Fig. 3). When CMAPs are recorded from the right AH muscle using a MATS coil, the coil currents should be directed 'anticlockwise' as seen from behind so that the induced currents in the body flow along the spinal nerves towards the distal muscle. The hot spot should be searched for around the S1 spinous process. At the hot spot, the stimulus intensity should be gradually increased to obtain supramaximal CMAPs.

This technique can be combined with NCS using conventional electrical stimulation. For the AH muscle, magnetic sacral-neuroforamina stimulation can be followed by electrical stimulation at the ankle and knee (Fig. 4). The CMAP sizes gradually and linearly decrease from the ankle stimulation to the neuroforamina stimulation. This indicates that the CMAP size at the neuroforamina can be used to detect a conduction block if the CMAP size abruptly reduces beyond expectation compared to that at the knee. Conse-

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quently, the focal lesions between the knee and neuroforamina, i.e., the sacral nerves, sacral plexus or spinal nerves just distal to neuroforamina, can also be detected using the CMAP parameters, such as amplitude, area and latency.

Similarly, if CMAPs are recorded from the BF muscle, the hot spot should be searched around the S1 spinous process (Matsumoto et al., 2013). On the other hand, to record CMAPs from the TA muscle, the hot spot should be searched around the fifth lumbar (L5) spinous process (Matsumoto et al., 2010a).

Most institutions, however, do not yet have a MATS coil. For lumbosacral–supramaximal stimulation, a round coil or a figure-of-eight coil may be useful, because supramaximal stimulation can be achieved in approximately 20% of normal subjects (Matsumoto et al., 2009a). If the subject is not a big person, magnetic lumbosacral-neuroforamina stimulation using these coils should be attempted. In these coils, the induced currents in the body should be directed from the muscles to the spinal cord to activate the spinal nerves efficiently (the direction of coil currents or induced currents are opposite to that of the MATS coil).

5. Magnetic-conus stimulation

5.1. Recent topic

Matsumoto et al., 2009b reported that the most proximal cauda equina can be reliably activated using a MATS coil in most normal subjects (magnetic-conus stimulation) (Matsumoto et al., 2009b). This reliable stimulation is attributed to the powerful stimulation produced by the MATS coil. The previous failure of magnetic-conus stimulation is explainable according to the concept that induced currents concentrate into the intervertebral foramina but do not penetrate the cauda equina in the spinal canal (Ugawa et al., 1989b; Maccabee et al., 1996). By contrast, fairly large induced currents produced by the MATS coil may penetrate further into the spinal canal and activate the cauda equina.

The CMAP latency at the most proximal cauda equina was constant regardless of the CMAP size, although the supramaximal CMAP was usually unobtainable. The activation site was considered to be the root-exit zone from the conus medullaris, similar to the findings of previous studies (Maccabee et al., 1996; Maegaki et al., 1997). The CMAP latency in magnetic stimulation was almost the same as that in electrical stimulation using a high-voltage electrical stimulator. In both electrical and magnetic stimulations, the currents may concentrate to the proximal cauda equina where the electrical conductivity changes abruptly (Maertens de Noordhout et al., 1988; Ugawa et al., 1995; Maccabee et al., 1996; Maegaki et al., 1997). Consequently, in magnetic-conus stimulation using the MATS coil, we can obtain stable CMAP latency at the most proximal cauda equina, which enables us to calculate CECT and CCCT (see Section 7).

5.2. Recording for conus stimulation

Magnetic-conus stimulation is often followed by magnetic lumbosacral-neuroforamina stimulation, because CECT can be obtained using these two stimulation methods. The MATS coil is useful for both stimulations (the MATS coil stimulation method). The recording preparations are the same as those in magnetic lumbosacral-neuroforamina stimulation (Fig. 3). When CMAPs are recorded from the right AH muscle, the coil currents should be directed 'clockwise' as seen from behind so that the induced currents flow upwards in the body. The hot spot should be searched for around the L1 spinous process. At the hot spot, the stimulus intensity should be increased gradually to obtain the minimal and reproducible CMAP latency.

This technique can be combined with NCS using conventional electrical stimulation and magnetic lumbosacral-neuroforamina stimulation (Fig. 4). CECT can be calculated by subtracting lumbosacral-neuroforamina latency from conus latency. Consequently, the focal lesions of the cauda equina in the spinal canal can be detected using the parameter of CECT. Moreover, magnetic-conus stimulation can be combined with TMS to measure CCCT, which is the most direct indicator of central motor conduction (see Section 7.5).

Even when CMAPs are recorded from other muscles such as the TA and BF muscles, the stimulation method is the same, i.e., the hot spot should be searched around the L1 spinous process (Matsumoto et al., 2010a, 2013).

A figure-of-eight coil has been reported to be able to activate the most proximal cauda equina (Maccabee et al., 1996; Maegaki et al., 1997). A conventional figure-of-eight coil is used for children, whereas a large figure-of-eight coil is required for adult subjects. In these coils, similarly, the induced currents should be directed upwards in the body.

6. Magnetic stimulation of the mid-part of the cauda equina

6.1. Recent topic

Matsumoto et al., 2009b reported that the mid-part of the cauda equina could be activated by magnetic stimulation using a MATS coil in approximately half of normal subjects (Matsumoto et al., 2009b). This can be accomplished by placing the edge of the MATS coil on the lumbar spinous process over the mid-part of the cauda equina and by flowing induced currents orthodromically along the cauda equina. However, the CMAP size is not supramaximal and the CMAP latency is not stable. To date, however, magnetic stimulation of the mid-part of the cauda equina has not been a clinically useful method because of the submaximal stimulation and the large inter-individual variability of the activation site.

7. Analysis of neurophysiological parameters

7.1. CMAP latency

CMAP latency at the cervical neuroforamina (cervical neuroforamina latency) is a parameter that reflects the overall peripheral motor conduction. The parameter does not include the conduction time of spinal nerves in the spinal canal, although the short conduction time is often negligible. On the other hand, CMAP latency at the lumbosacral neuroforamina (lumbosacral-neuroforamina latency) does not reflect the overall peripheral motor conduction, because the parameter does not include the long conduction time of spinal nerves in the spinal canal, i.e., CECT. In contrast, CMAP latency at the most proximal cauda equina (conus latency) reflects the overall peripheral motor conduction. All of these CMAP latencies are often called PMCT. It is of note that PMCT does not just reflect the conduction time of peripheral nerves but that it also includes the time of synaptic delay at the neuromuscular junction and the time of depolarisation to generate muscle action potentials.

If these CMAP latencies are prolonged, the patient can be expected to have peripheral neuropathy. The prolongation of CMAP latency should be carefully judged considering body height and age (Matsumoto et al., 2010a,f, 2013).

7.2. CMAP size

Supramaximal stimulation allows us to evaluate CMAP amplitude and area in addition to CMAP latency. Herewith, CMAP size at the neuroforamina is comparable to the CMAP size in distal

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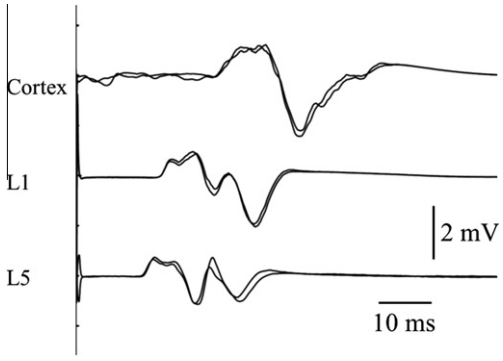

Fig. 5. MEP waveforms for the investigation for central motor conduction. MEPs are evoked by magnetic lumbar-neuroforamina stimulation (L5) by magnetic-conus stimulation (L1) and by TMS (Cortex), recorded from TA muscle. Lumbar-neuroforamina latency and conus latency are easily obtained using a MATS coil. CMCT is obtained by subtracting lumbar-neuroforamina latency from cortical latency. CCCT is obtained by subtracting conus latency from cortical latency. CECT is also available by subtracting lumbar-neuroforamina latency from conus latency. (Modified from Matsumoto et al., 2010a, with permission.)

peripheral-nerve stimulation, enabling us to judge a conduction block between a distal site and neuroforamina. For both upper and lower limbs, CMAP sizes in magnetic-neuroforamina stimulation can be evaluated (Matsumoto et al., 2009a, 2010f). On the other hand, CMAP size at the most proximal cauda equina is not a clinically useful parameter, because supramaximal stimulation cannot usually be achieved in magnetic-conus stimulation (Matsumoto et al., 2009b).

7.3. Central motor-conduction time (CMCT)

CMCT is a parameter that reflects the conduction of the corticospinal tract (Rossini et al., 1994; Terao and Ugawa, 2002; Chen et al., 2008; Matsumoto et al., 2010e; Groppa et al., 2012). The parameter can be calculated by subtracting cortical latency from PMCT. Cortical latency can be obtained by TMS for M1, i.e., cortical latency = MEP latency in TMS. On the other hand, PMCT, the conduction time from the proximal peripheral nerves to muscle, can be measured by two methods. The first method involves magnetic-neuroforamina stimulation, i.e., PMCT = MEP latency at the neuroforamina (Fig. 5). The second method uses the F-wave technique, i.e., PMCT = (F + M − 1)/2 (F, F-wave latency; M, M-wave latency; 1, the time attributable to central delay at the level of spinal motoneurons) (Kimura, 1974; Rossini et al., 1994). CMCT using magnetic-neuroforamina stimulation is always longer than CMCT using the F-wave technique, because the former includes the conduction time of spinal nerves in the spinal canal and the latter does not include the component of peripheral nerves. Both CMCTs using these two methods are clinically useful, although in a patient with peripheral neuropathy, the prolongation of CMCT should be carefully interpreted. In such patients, CMCT can only be prolonged due to PMCT prolongation. Since the CMCT calculated by magnetic-neuroforamina stimulation includes the conduction time of spinal nerves in the spinal canal, the conduction delay of the segment may contribute to CMCT prolongation. Alternatively, if the persistence of F-waves decreases and the fastest F-waves are not evoked, PMCT may be prolonged, contributing to CMCT prolongation. Moreover, if the F-waves diminish, PMCT calculation is impossible. Therefore, in such patients, CCCT is preferable (see Section 7.5).

7.4. Cauda equina conduction time (CECT)

The CMAP latency in magnetic-conus stimulation (conus latency) is very stable despite submaximal stimulation, although CMAP size is not constant. This technique can be combined with NCS using conventional electrical stimulation and magnetic lumbosacral-neuroforamina stimulation (Fig. 4). CECT can be calculated by subtracting lumbosacral-neuroforamina latency from conus latency. Consequently, the focal lesions of the cauda equina in the spinal canal can also be detected using the CECT parameter (Matsumoto et al., 2009b). Similarly, magnetic lumbosacral motor-root stimulation and magnetic-conus stimulation can be combined with TMS to measure CMCT, CCCT and CECT (see Section 7.5). Using these combined techniques, we can assess which components contribute to CMCT prolongation, central motor conduction, peripheral motor conduction, or both (Fig. 5) (Matsumoto et al., 2010a).

7.5. Cortico-conus motor-conduction time (CCCT)

CCCT is the conduction time from M1 to the root-exit zone of the cauda equina from the conus medullaris, which is the most direct indicator of central motor conduction (Fig. 5) (Matsumoto et al., 2010a; Matsumoto and Ugawa, 2010). CCCT can be calculated by subtracting conus latency from cortical latency. This parameter gives a more accurate indication of corticospinal tract conduction than conventional CMCT because peripheral components do not contribute to CCCT. In fact, the CCCT is normal even in a patient with severe peripheral neuropathy (the patient with Charcot–Marie–Tooth disease type 1 showed severely delayed nerve conduction of $<10\ m\ s^{-1}$), indicating that the parameter is hardly affected by the conduction delay of peripheral components and that the most proximal cauda equina is certainly activated (Matsumoto et al., 2010b). CCCT is less affected by body height and age than PMCT (Matsumoto et al., 2010a, 2012).

The relative independence of CCCT from body height may be mainly explained by the disproportion between growths in the length of the spinal cord and the vertebral column (Kunitomo, 1918; Vettivel, 1991). The spinal-cord length does not elongate proportionally to body height, although the cauda equina elongates concomitantly with spinal growth proportionally to body height. On the other hand, the relative independence of CCCT from age may be mainly explained by the protection of the corticospinal tract by various structures, such as cranial bone, vertebral column, central nervous system tissue, cerebrospinal fluid and blood–brain barrier. In contrast, peripheral nerves can be directly affected by minor trauma or injuries, due to their relative lack of protection.

8. Clinical application for patients

8.1. Peripheral neuropathy

For upper limbs, Matsumoto et al., (2010f, in press) recently reported that a conduction block in the upper or the lower part of the brachial plexus is detectable via magnetic cervical motor-root stimulation in patients with neuralgic amyotrophy or tumour invasion (Matsumoto et al., 2010f, in press). In these studies, magnetic cervical motor-root stimulation clearly localised the focal lesion between Erb's point and neuroforamina.

This technique is also effective for supporting a conduction block. Even if a conduction block is suspected between the axilla and Erb's point due to the CMAP size reduction (Fig. 6), the possibility of submaximal stimulation at Erb's point cannot be easily excluded. In such cases, supramaximal stimulation at the more proximal site may be useful. If CMAP size at the cervical neuroforamina is almost identical to that at Erb's point, the conduction block rather than submaximal stimulation at Erb's point is supported.

For lower limbs, Matsumoto et al. (2010c) revealed that CECT is more frequently prolonged than the distal segment of peripheral

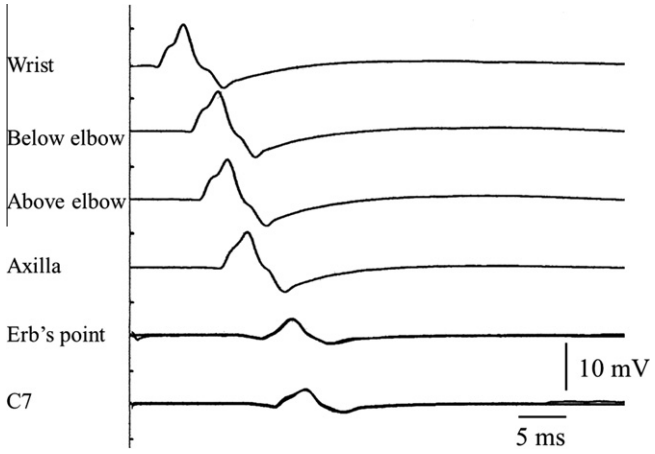

Fig. 6. A clinical application of magnetic cervical motor-root stimulation. In a patient with CIDP, similar to Fig. 2, CMAPs are evoked by electrical stimulation and magnetic stimulation, recorded from ADM muscle. CMAPs at the wrist, elbow, and axilla are normal, whereas the size of CMAPs at Erb's point is abnormally reduced. Magnetic cervical motor-root stimulation revealed that CMAP size at the neuroforamina is almost identical to that at Erb's point, supporting the fact that the CMAP reduction at Erb's point suggests the conduction block.

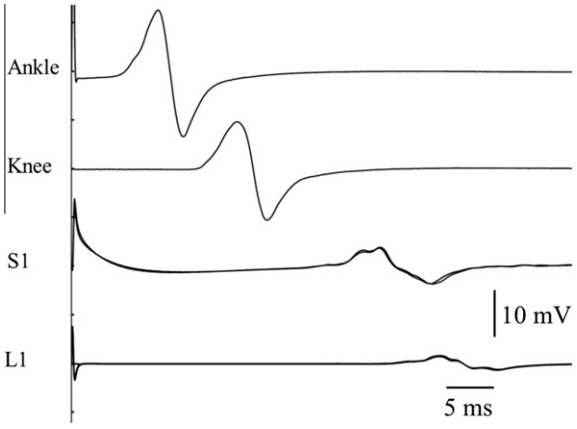

Fig. 7. A clinical application of magnetic sacral motor-root stimulation. In a patient with CIDP, similar to Fig. 4, CMAPs are evoked by electrical stimulation and magnetic stimulation, recorded from AH muscle. CMAPs at the ankle and knee are normal, although a conduction block is observed between the knee and the neuroforamina and CECT is abnormally prolonged to 6.9 ms (normal values: 3.7 ± 0.8 ms). In this patient, abnormal nerve conduction is concretely confirmed only in the proximal segments. (Modified from Matsumoto et al., 2010c, with permission.)

nerves in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) (Matsumoto et al., 2010c). In a patient with CIDP (Fig. 7), although motor-conduction velocity (MCV) between the ankle and the knee was normal (50.0 m s^{-1}), a conduction block between the knee and the sacral neuroforamina was present and CECT was abnormally prolonged to 6.9 ms (normal values matched in age and body height: 3.7 ± 0.8 ms, mean ± standard deviation). CECT was prolonged in 9 out of 11 CIDP patients (81.8%), whereas MCV between the ankle and the knee was delayed in only four patients (36.4%). The cauda equina in the spinal canal lacks blood–nerve barriers and are directly exposed to cerebrospinal fluid (Haller and Low, 1971). These anatomical structures may allow unknown antibodies or other circulating factors to gain direct access to the spinal nerves, including the cauda equina. Maccabee et al. (2011) reported similar CECT prolongation in CIDP patients (Maccabee et al., 2011).

In patients with other peripheral neuropathies, CECT prolongation has been reported, e.g., the demyelinating type of Guillain–

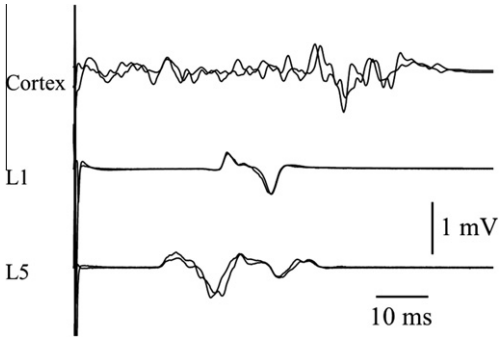

Fig. 8. A clinical application of CCCT. In a patient with spastic paraplegia, similar to Fig. 5, MEPs are evoked by magnetic stimulation, recorded from TA muscle. Lumbar-neuroforamina latency (L5) is 15.8 ms, conus latency (L1) is 27.0 ms (normal values: 14.0 ± 1.4 ms), and cortical latency is 43.7 ms. CCCT is 16.7 ms (normal values: 12.3 ± 1.2 ms). Consequently, the MATS coil stimulation method can objectively demonstrate the involvement of the corticospinal tract in spite of CECT prolongation.

Barré syndrome (Matsumoto et al., 2010d; Maccabee et al., 2011), polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome (Maccabee et al., 2011; Matsumoto et al., 2013), anti-myelin-associated glycoprotein (MAG) polyneuropathy (Maccabee et al., 2011; Matsumoto et al., unpublished data), Charcot–Marie–Tooth disease type 1 (Maccabee et al., 2011), tumour invasion (Matsumoto et al., 2009b) and lumbar spinal stenosis (Senocak et al., 2009).

8.2. Corticospinal tract involvement with peripheral neuropathy

Tokushige et al. (in press) investigated the central and peripheral motor conductions using a MATS coil stimulation method in a patient with adult-onset Krabbe disease (Tokushige et al., in press). In this disorder, both central and peripheral motor systems are usually involved (Matsumoto et al., 1995). Therefore, conventional CMCT is not effective as a parameter showing the conduction of the corticospinal tract because the involvement of the corticospinal tract can be masked by the CMCT prolongation due to peripheral neuropathy. In their study, both CCCT and conus latency were prolonged. Thus, the corticospinal-tract involvement is accurately evaluable using CCCT, even in patients with peripheral neuropathy.

This technique, the MATS coil stimulation method, is also applicable to any neurological disorders affecting the central and peripheral nervous systems, e.g., for patients with spastic paraplegia (Fig. 8). In the patient, lumbar-neuroforamina latency is 15.8 ms, conus latency is 27.0 ms (normal values matched in age and body height: 14.0 ± 1.4 ms), and cortical latency is 43.7 ms. CCCT is 16.7 ms (normal values: 12.3 ± 1.2 ms). Consequently, the MATS coil stimulation method can objectively demonstrate the involvement of the corticospinal tract in spite of CECT prolongation, as shown in other neurological disorders (Matsumoto et al., 2011).

9. Comparison to electrical motor-root stimulations

9.1. Electrical motor-root stimulation using a high-voltage electrical stimulator

Five years before the development of magnetic stimulation, Merton and Morton (1980) reported the electrical-stimulation method using a high-voltage electrical stimulator to activate the central and peripheral nervous systems (Merton and Morton, 1980). This stimulator has a high-voltage capacitance that discharges a single electrical current rather than a train of smaller

Table 1
Comparison of magnetic and electrical motor-root stimulations.

	Magnetic stimulation	Electrical stimulation (high-voltage stimulator)	Electrical stimulation (needle electrodes)
Invasiveness	Non-invasive	Non-invasive	Invasive
Skin preparation	Unnecessary	Necessary	Necessary
Clothing removal	Unnecessary	Necessary	Necessary
Pain	Small	Not small	Not small
Supramaximal stimulation			
Neuroforamina	Possible	Possible	Possible
Proximal cauda equina	Impossible	Possible	Possible
Device (Cost)	Expensive	Expensive	Not expensive
Device (Size)	Large	Small	Small

Underline: disadvantage.

shocks, allowing penetration of electrical currents into the brain structure with a relatively small electrical current flowing through the scalp. For electrical motor-root stimulation, the cathode stimulus electrode is placed on the spinous process over the target spinal nerves and the anode stimulus electrode on the spinous process rostral to the cathode or the iliac crest contralateral to the target muscle. Electrical stimulation has also been applied to cervical motor roots (Rossini et al., 1985; Mills and Murray, 1986; Ugawa et al., 1988a,b,1989a,b, 1990, 1995; Plassman and Gandevia, 1989; Schmid et al., 1990, 1991; Thomas et al., 1996; Troni et al., 1996, 2011; Lo and Mills, 1999; Watson et al., 2001; Arunachalam et al., 2003; Lo and Tan, 2004; Matsumoto et al., 2010f) and lumbosacral motor roots (Rossini et al., 1985; Swash and Snooks, 1986; Maertens de Noordhout et al., 1988; Ugawa et al., 1988a,b,1989a,b, 1990, 1995; Tabaraud et al., 1989; Troni et al., 1996, 2011; Ogura et al., 2003; Osawa et al., 2003; Matsumoto et al., 2009a,b; Akaza et al., 2011). In this technique, supramaximal stimulation can be achieved at the cervical and lumbosacral neuroforamina and even at the most proximal cauda equina. Moreover, even at the mid-part of the cauda equina, supramaximal CMAPs can be obtained although the CMAP latency is unstable (Matsumoto et al., 2009b). On the other hand, the pain accompanying stimulation is not always minimal.

9.2. Electrical motor-root stimulation using needle electrodes

By inserting needle electrodes into the tissues around the intervertebral foramen, the spinal nerves at the neuroforamina can be activated using a conventional electrical stimulator. Similarly, by inserting needle electrodes into the tissues around the conus medullaris, the most proximal cauda equina can be activated. Electrical stimulation has also been applied to cervical motor roots (Berger et al., 1987; Cros et al., 1990a; Evans et al., 1990; Menkes et al., 1998; Vucic et al., 2006a,b) and lumbosacral motor roots (Chang and Lien, 1990; Pease et al., 1990; Macdonell et al., 1992; Ertekin et al., 1994a,b; Menkes et al., 1998; Zileli et al., 2002; Seçil et al., 2012). In this technique, supramaximal stimulation can be achieved at both the neuroforamina and the most proximal cauda equina. The invasiveness and pain involved in this stimulation method are not always minimal.

9.3. Advantage and disadvantage of magnetic-motor-root stimulation

Table 1 shows a comparison of magnetic-motor-root stimulation and electrical motor-root stimulations. The most important advantages of magnetic stimulation are the non-invasiveness and the minimal pain. Further, no skin preparation to reduce the impedance of stimulus electrodes is required. These advantages are especially notable in patients with skin disorders. We reported one patient with proximal demyelinating neuropathy who had severe skin lesions caused by chronic graft-versus-host disease (Matsumoto et al., 2005). Electrical motor-root stimulation using a high-voltage electrical stimulator was not applicable, because the skin was scaled with the stimulus surface electrodes. In such cases, magnetic stimulation that obviates electrode fixation is the sole method that can be used to investigate proximal peripheral nerves.

Another advantage is that magnetic stimulation can be applied to a dressed subject. In electrical stimulations studying the lower-limb muscles, the stimulus electrodes should be placed or inserted at the lumbosacral spinous process level. Therefore, the subject must undress partially. This may present problems, especially when there is a gender difference between the examiner and the subject.

The most important disadvantage of magnetic stimulation is that it is impossible to obtain supramaximal CMAPs at the most proximal cauda equina, which prevents us from judging if there is a conduction block within the cauda equina. In this regard, electrical motor-root stimulation is superior to magnetic-motor-root stimulation. Another disadvantage is the large size and high price of a magnetic stimulator. Electrical stimulation using needle electrodes is the cheapest method and it does not require a specialised device, even though it is quite invasive.

10. Pitfalls

10.1. Volume conduction

When selecting the target muscle, the volume conduction should always be taken into consideration. For ADM, FDI, BB or AH muscle, the volume conduction from the muscles innervated by the spinal nerves other than the target spinal nerves is relatively negligible, whereas for the abductor pollicis brevis (APB) or extensor digitorum brevis (EDB) muscle, the volume conduction is not negligible (Matsumoto et al., 2009a,b, 2010f). When electrical stimulation of the distal peripheral nerves and magnetic-motor-root stimulation were performed simultaneously (collision technique), the volume conduction was <9% in FDI and 4% in ADM. However, in APB, it was substantially greater (approximately 30%) than those in the other two muscles (Matsumoto et al., 2010f). For foot muscles, the volume conduction was <2% in AH, whereas it was >100% in EDB (Matsumoto et al., unpublished data). Therefore, when CMAPs are recorded from APB or EDB muscle, the collision technique is necessary to abolish volume conduction (Kimura, 1976). In any muscle, if atrophy of the target muscle is severe, the volume conduction from non-target muscles affects the CMAPs recorded from the target muscle. In this case, the collision technique should be considered to apply to magnetic-motor-root stimulation: in this technique, electrical stimulation of the distal peripheral nerves and magnetic-motor-root stimulation are conducted simultaneously.

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10.2. Conduction block or pathological-nerve inexcitability

In judging whether a conduction block is present, pathological-nerve inexcitability is always a problem. The presence of decreased excitability may give rise to a seemingly low CMAP, which may erroneously lead to the conclusion of a conduction block (Meulstee et al., 1997; Matsumoto et al., 2010f). However, no clinical-stimulation methods can completely exclude this possibility. Even electrical stimulation using a high-voltage electrical stimulator or needle electrodes may not activate such inexcitable parts with high stimulus intensity. For this reason, supramaximal stimulation is clinically determined to be the point at which CMAPs are not increased by 1.2–1.5 times the stimulation of the lowest stimulus intensity that produced a supramaximal CMAP, even though some very high threshold groups of axons would not be able to be activated.

To judge a conduction block, stimulation at the more proximal parts of peripheral nerves might be useful, as shown in clinical application (Fig. 6). If the size of CMAPs evoked by the stimulation at the more proximal parts were almost the same as the reduced size of CMAPs suspected of a conduction block, the findings showing the same CMAP sizes would support the presence of a conduction block. Other methods such as electrical stimulation using a high-voltage electrical stimulator or needle electrodes, needle EMG, conventional NCS and sensory-evoked potentials (SEPs) may also be useful to support the presence of a conduction block.

10.3. Current spread to distal peripheral nerves

Care must be taken to prevent the current from spreading to a distal part away from the expected stimulation point (the neuroforamina or most proximal cauda equina) when stimulation is conducted at very high stimulus intensities, such as stimulation with 95% or 100% maximum stimulator output (Cros et al., 1990a; Schmid et al., 1990, 1991; Macdonell et al., 1992; Matsumoto et al., 2010f), because the induced magneto-electrical fields are distributed widely and deeply. In this case, the conduction block may be missed because the activation site may jump to a more distal position beyond the point of the conduction block. To overcome this weak point, the stimulus intensity should be increased gradually to check for the abrupt shortening of CMAP latency.

11. Safety

Despite the long history of single-pulse magnetic stimulation, no severe side effects have been reported (Rossi et al., 2009). Therefore, magnetic-motor-root stimulation can be considered very safe if attention is paid to safety. As in the preparation of a TMS study, the major contraindication is the presence of metallic hardware in close contact with the coil (such as an internal pulse generator or a medication pump). Magnetic cervical motor-root stimulation in particular is best avoided by patients with heart diseases who have a high risk of arrhythmia. Yamaguchi et al. (1994) investigated how magnetic stimulation affects the heartbeat in dogs (Yamaguchi et al., 1994). A very strong magnetic coil (9.2 T) was tightly attached to the heart of an open-chest dog, while stimulus effects were detected by electrocardiography (ECG). As a result of magnetic stimulation, single, premature atrial contraction (PAC) or premature ventricular contraction (PVC) was observed, although ventricular defibrillation (Vf) was never generated. Despite the safety of the magnetic stimulation of normal hearts in their animal study, there is no similar study on abnormal or diseased hearts. As such, it must be recognised that the safety of the magnetic stimulation of the heart has not yet been completely established.

Magnetic lumbosacral motor-root stimulation must not be performed in pregnant subjects, because the safety for the unborn baby is unknown. When using a MATS coil in particular, we must be very careful about adverse effects in patients with heart failure or those who are pregnant because of the broad and deep induced currents. In accordance with its name (i.e., magnetic augmented translumbosacral stimulation coil), the MATS coil should only be used for lumbosacral stimulation – it should not be employed for cervical stimulation because the heart might be stimulated. The risk of heart stimulation is also present in magnetic-conus stimulation.

12. Issues in the future

For each disorder having the focal lesions of the proximal part of peripheral nerves, the sensitivity or specificity of magnetic-motor-root stimulation is unknown. If the sensitivity and specificity in magnetic-motor-root stimulation could be compared to those in other neurophysiological examinations such as F-waves, H-reflexes and SEP, the data must be useful to make a diagnosis.

Previous guidelines or reviews related to conduction blocks have not recommended the use of magnetic stimulation to detect conduction blocks, because it is considered difficult to achieve supramaximal stimulation through magnetic-neuroforamina stimulation (Olney, 1999; Nobile-Orazio et al., 2005). Based on our review article, however, we propose that magnetic-neuroforamina stimulation is sufficient to detect a conduction block. We expect that the guidelines and reviews on conduction blocks will be revised in the future. For this purpose, the additional clinical utilities of magnetic-motor-root stimulation must be demonstrated.

13. Conclusions

The proximal peripheral nerves are frequently involved in peripheral neuropathies, such as demyelinating neuropathies, nerve compressions or tumours. However, conventional nerve-conduction studies are insufficient for detecting the proximal lesions of peripheral nerves. The F-wave technique is, however, one method that can be employed to study the proximal peripheral nerves, but it cannot provide any information on the lesion site. Magnetic-motor-root stimulation has already enabled us to evaluate the CMAP amplitude, area and latency up to the neuroforamina. Moreover, this stimulation method can also provide us with information on the cauda equina and corticospinal tract by measuring each conduction time. We propose that magnetic-motor-root stimulation is a clinically useful tool for detecting abnormalities of the proximal peripheral nerves and for evaluating the abnormal conduction of the corticospinal tract more precisely. These stimulation methods are expected to make a breakthrough in the diagnosis, pathophysiology and judgement of therapeutic efficacy, especially when combined with other neurophysiological techniques such as NCS, needle EMG, F-waves, H-reflexes and SEP. In the future, with the use of these updated and innovative methodologies, we look forward to many discoveries related to neurological disorders.

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