Central Motor Conduction and Its Clinical Application

Christian W. Hess

Methodological Comments Concerning Central Motor Conduction

In clinical medicine, single-pulse TMS is primarily used to evoke motor responses in slightly activated target muscles (Fig. 6–1A). The patient is asked to exert a steady, small voluntary contraction. If the patient is not capable of contracting the target muscle, reflex activation induced by appropriately manipulating the limb or strong contraction of the homologous contralateral muscle will usually suffice. The procedure records single stimulus-induced muscle twitches called motor evoked potentials (MEP). The straightforward performance and easy interpretation of the MEPs compare favorably with the afferent evoked potentials or reflex studies and are suitable for assessing the pyramidal motor system.

For diagnostic purposes, the use of a nonfocal, large circular coil with a diameter of 10 to 12 cm is usually preferable. It is placed with its center near the vertex to make the edge of the coil to lie over the hand-arm area and to cross the precentral gyrus perpendicularly (Fig. 6–2A). When using a double coil, the point of contact must lie over the target area (see Fig. 6–2A, right panel). For exciting the facial muscles’ area, the coil has to be shifted laterally (i.e., on the scalp side contralateral to the target muscle) by few centimeters, leaving the coil orientation unchanged. There is, however, an important exception to this rule. For exciting the masseter muscle, the relevant segment of the stimulating coil must be placed parallel rather than perpendicularly to the central sulcus or precentral gyrus (see Fig. 6–2B). The reason for this probably lies in the weak (presynaptic) excitability of this cortical target area so as to require direct corticobulbar tract stimulation. The leg area is best stimulated with the big circular coil shifted a bit rostrally making the posterior segment lie over the precentral gyri so as to cross the mid-sagittal line perpendicularly (see Fig. 6–2A, lower panels).

When using a monophasic stimulator, the direction of coil current determines which hemisphere is preferentially excited, and the coil has to be turned over for exciting the other hemisphere. When using a bipolar stimulus, the current direction does not matter, and both hemispheres may be excited simultaneously. Sometimes, it is difficult to excite a lower limb muscle in an elderly person even when using high stimulus intensities and carefully searching for the optimal coil position on the scalp. In such a situation, the use of a very large double coil is advantageous, because it penetrates deeper into the brain.

A conspicuous feature of the MEP is its facilitation by voluntary background contraction, and this goes along with a shorter-onset latency by about 3 ms compared with responses from relaxed muscle (see Fig. 6–1B). In a clinical setting, it is preferable to obtain MEPs with an active target muscle for two reasons. First, lower stimulus intensities are
Figure 6-1  Influence of voluntary preactivation on motor evoked potentials (MEPs). A: MEP amplitudes related to the degree of voluntary tonic background contraction from three different target muscles in 12 and 34 normal subjects. The stimulus intensity was 1.2 times resting threshold. B: MEP onset latency related to the degree of voluntary tonic background contraction in TA and biceps brachii muscle. Notice the similar latency jump from the relaxed to the contracted state, with virtually stable values when contraction increases up to 60% of maximum force. ADM, abductor digiti minimi; TA, tibialis anterior. (Data from Kischka U, From R, Fellenberg T, et al. Facilitation of motor evoked potentials from magnetic brain stimulation in man: A comparative study of different target muscles. J Clin Neurophysiol 1993;10:505–512 and from Hess CW, Mills KR, Murray NMF. Responses in small hand muscles from magnetic stimulation of the human brain. J Physiol 1987;388:397–412.)

**Figure 6-2**  A: Approximate coil placement on scalp when using a large, round coil and a double coil (i.e., figure-of-eight coil) to excite upper and lower limb muscles. For exciting facial muscles, the coil must be moved more laterally to the target area, keeping the coil orientation (i.e., direction of the inducing current) the same. Arrows indicate the inducing current in the coil. B: Coil placement on the scalp for exciting the right masseter muscle with a double coil (left panel). A short latency peripheral response is evoked in the left masseter muscle. For comparison, the appropriate placement for upper limb muscles is shown on the right side.

required, and second, patients often have difficulty completely relaxing their muscles, producing facilitated responses. Because facilitated responses have shorter onset latencies, different sets of normal values must be used for active and relaxed muscles. In intrinsic hand muscles, the degree of facilitation is usually complete with a background force of 10% to 15% of maximum force (see Fig. 6-1A). In more proximal arm (e.g., biceps brachii) and leg muscles (e.g., tibialis anterior [TA]), the degree of facilitation rises more gradually with increasing force, but the latency remains constant above a force of about 10%. Exerting a tonic contraction of about 20% of maximal force is sufficient for clinical purposes and is easily achieved when patients are asked to make the appropriate isotonic movement without resistance. However, because in proximal muscles the amplitude depends on the degree of preactivation, amplitudes of proximal muscles cannot be used to define abnormality without
monitoring the voluntary contraction. In patients who cannot activate the target muscle, reflex activation helps. Alternatively, a strong contraction of the same muscle on the opposite side results in the same degree of latency reduction and useful amplitude increase.\(^5\) Otherwise, the procedure is done without background contraction requiring higher stimulus intensities and the corresponding normal values, because the latencies are then longer by about 2 to 3 ms.

The small hand muscles are particularly convenient for studies of central motor conduction (CMC), because large responses are readily obtained and the peripheral nerve component of the motor pathway to the hand muscles is easily accessible. Other than MEPs from proximal muscles, MEPs from hand muscles do not much depend in size on the level of voluntary pre-innervation, making the amplitude a usable parameter.\(^4\) Responses from lower limb muscles are at higher stimulus intensity and are proportionately smaller and of longer duration than those obtained in the hand muscles. However, in neurologic diseases, abnormality tends to be more common in lower limb muscles.\(^6\)

In contrast to peripherally elicited supramaximal motor responses, MEPs show a considerable inherent variability under constant stimulation and recording conditions. The variability in onset latency is best dealt with by taking the shortest latency from a series of four stimuli, because the shortest of four is similar to the shortest of 15.\(^7\) This procedure has the practical advantage that a single response may suffice, provided its latency is comfortably within normal limits. Analogously, the greatest amplitude encountered in a given number of trials can be taken.\(^8,9\) Given the greater variability of conventionally assessed MEP amplitudes, a single large response could, however, be an unrepresentative estimate of the amplitude. Measurement of several individual trials and then taking the mean or median of these values may be preferred.\(^10\) However, McDonnell and coworkers\(^9\) did not find a significant difference between various methods of assessing conventional MEP amplitudes of first dorsal interosseous muscle, when comparing mean values, the greatest potential, and averaging of 20 responses considering peak-to-peak measure and area. Averaging is rarely needed to make visible a possible MEP, when a patient is not capable of activating only slightly and steadily, producing a large, irregular electromyographic (EMG) pattern that may obscure a small response. Otherwise, averaging does not seem to offer an advantage over other methods to assess MEP amplitudes.\(^9\) In any case, it is important to assess patients and normal values using the same procedure.

To reduce confounding factors of peripheral pathology when measuring MEP amplitudes, the examiner preferably uses the ratio of the compound motor action potential (CMAP) from cortical stimulation to that from maximal peripheral (distal) nerve stimulation. In principle, these relative MEP amplitudes should reflect the number of conducting central motoneurons. However, MEP amplitudes are usually much smaller than those of motor responses to maximal peripheral nerve stimulation, although virtually all motoneurons supplying a target muscle have been shown to be excited by TMS in normal subjects.\(^11\) The MEPs show marked amplitude variation between normal subjects and from one stimulus to another. The MEP amplitudes are primarily degraded by the great dispersion of the descending volley over the long motor route from brain to muscle with intercalated synapses, ensuing phase cancellation phenomena of the biphasic CMAP. The maximum relative MEPs from active small hand muscle were found to be as small as 18% of the distally evoked muscle response in some normal subjects.\(^8\) For the reasons mentioned previously, amplitudes of more proximal muscle cannot be reliably quantified.

Some recording devices automatically provide the area under the curve, which can reflect the number of excited motoneurons more faithfully than the amplitude, compensating partially for the temporal dispersion. However, cancellation phenomena are not made up for by taking the area. Measuring the area instead of amplitude may be inaccurate for other reasons. With strong cortical stimuli and high voluntary background contraction, some motoneurons tend to fire more than once in response to a stimulus induced
corticospinal volley, and this enlarges the measured MEP area. Multiple firing of motoneurons particularly occurs in some lower limb MEPs, where it has been shown to significantly affect the measured MEP area.12

The limited utility of MEP amplitudes is a major drawback of the method. A much more accurate estimate of the proportion of excited motoneurons is possible using the triple-stimulation technique.13 This technique uses a double-collision paradigm to resynchronize the corticomuscular volley, making it possible to directly quantify the upper motoneuron loss (Fig. 6–3C). The TMS on the scalp is followed by two successive maximal electrical stimuli, one to the ulnar nerve at the wrist and one to the brachial plexus at Erb's point, with appropriate delays to make the induced volleys collide in the ulnar nerve (TSTtest: cortex-wrist-Erb). A first collision takes place when the distal stimulus at the wrist sets up an antidromic volley to meet the descending impulses from cortical stimulation, letting through only the ascending impulses that are traveling in a motor axon the motoneuron of which has not fired in response to the cortical shock. Subsequently, the brachial plexus stimulus sends a volley down to meet the remaining uncollided antidromic impulses, of which there are virtually none in a normal subject. The resulting test potential is compared with the control response obtained from a similar triple-stimulation procedure in which the initial stimulus is applied at the brachial plexus instead of the scalp (TSTcontrol: Erb-wrist-Erb). The ratio of TSTTest/TSTcontrol reflects the percentage of cortically activated spinal motoneurons. This method has been shown to enhance diagnostic sensitivity greatly in multiple sclerosis (MS), spinal cord disorders, and amyotrophic lateral sclerosis (ALS).13-14 However, the method can be used only in distal limb muscles and complicates the procedure.

The latency of MEPs has a considerable peripheral component that is strongly influenced by body stature or limb length and possible abnormality of peripheral nerve conduction. To minimize influence from arm or leg length, body stature, and possible peripheral conduction slowing as a confounding factor, the central motor conduction time (CMCT), defined as time from the motor cortex to the spinal motoneurons, is usually assessed. There are two methods of estimating the peripheral conduction time. The first depends on eliciting F waves; the second on stimulating the motor roots at the vertebral column (see Fig. 6–3A,B). The F-wave method assumes that conduction is
normal in the proximal segments of the motor roots and is obviously only applicable in nerves where F waves are elicitable. The second method is done with electrical or magnetic stimulation over the vertebral column, a procedure that excites motor roots at their exit foramina.\(^1\) This method involves a small proximal root segment between cord and exit foramen and therefore overestimates CMCT somewhat. In patients with greatly reduced peripheral nerve conduction velocity or proximal conduction block (e.g., Guillain-Barré), the small root segment included in CMCT can introduce significant inaccuracy. When using a high-voltage electrical device, supramaximal root stimulation should not be aimed at because this makes the stimulus reach out into the periphery producing artifactual latencies. With the magnetic stimulator, supramaximal root stimulation can usually not be achieved. For lower limb studies, magnetic stimulation of the lumbar-sacral roots is not always satisfactorily possible, necessitating high-voltage electrical stimulation (see Fig. 6-3B). For the mere purpose of estimating a peripheral conduction time, supramaximal stimulation of the motor roots is not needed.\(^1\) If the peripheral conduction time cannot be measured for technical or medical reasons (e.g., vertebral column instability), the total cortical-muscle latency must be related to arm lengths or body stature for upper or lower limb muscles respectively.

The facial nerve is the only cranial nerve that can be reliably stimulated by TMS at a constant site within the skull. Given the relatively proximal stimulation site, this is a useful technique to calculate the central motor conduction time of facial muscle MEPs. The actual site of intracranial facial nerve stimulation can be localized to the inner part of the facial petrosal canal,\(^1\) hence the term canalicular stimulation. For this canalicular stimulation, the optimal coil position and orientation is distinct from that of cortical facial area stimulation: The stimulating coil is placed ipsilateral to the target nerve, preferably posterior to the ear with the inducing current in the relevant coil segment flowing anterolaterally (i.e., with a vector of about 120 degrees when the sagittal backward direction on the scalp is defined as 0 degrees).\(^1\) By electrically stimulating the nerve at the stylomastoid foramen and comparing with the response from transcranial canalicular stimulation, a transosseal conduction time of 1.2 ms (SD 0.18) could be calculated.\(^1\) When using TMS to the (contralateral) facial area to obtain facial MEPs and using (ipsilateral) transcranial magnetic canalicular stimulation, a central conduction time of 5.1 ms (SD 0.60) was assessed for the nasalis muscle. However, the central motor conduction time assessed in such a way still comprises a short peripheral segment of the facial nerve, the portion between exit from brain stem and entrance into the petrosal (fallouian) canal.

**Cortical Silent Period**

In a contracting muscle, the TMS-induced MEP is immediately followed by an electrical silence lasting 40 to 300 ms that interrupts the ongoing EMG pattern. The early part of the cortical silent period (CSP) is thought to reflect spinal inhibition, whereas the later part originates from cortical inhibition which hence determines its duration.\(^1\) The inhibitory phenomenon is independent of the preceding excitatory MEP, because it can occur in isolation in some situations, such as in ALS patients.\(^2\) The duration of the SP depends on the specific muscle tested,\(^2\) the stimulus intensity,\(^2\) the instruction set,\(^3\) and the possible intake of certain central nervous system active substances, particularly dopaminergic, GABAergic drugs and ethanol.\(^2,4\) The CSP duration probably reflects GABA\(_B\) function,\(^4\) which makes it an attractive phenomenon to investigate certain neurological disorders. The duration is not much influenced by the degree of tonic voluntary activation.\(^5\) The CSP duration has shown statistically significant group differences between normal subjects and various neurological disorders, which along with cortical threshold and short-interval paired stimulation testing, have enabled interesting insights into disease mechanisms. Apart from cerebral disorders, the SP also seems to be altered in spinal cord pathology.\(^5,6\)

As diagnostic tool for the individual patient, the CSP duration is hampered by the very large interindividual variability\(^7\) and its
dependence on the examiner, the stimulation intensity, and instruction set. The latter two factors make very strict standardization of the test procedure and the use of high stimulation strength mandatory. Even then, the range of normal limits remains quite broad. Deciding at what time the silent period starts and ends may be a problem.

An evaluation of the CSP for diagnostic purposes in neurological disease is still awaited. However, the CSP duration shows a high degree of re-test reliability within the same subject, making it potentially suitable for longitudinal monitoring of the course of a disease and of treatment effects.

An ipsilateral silent period (ISP) can be recorded, with an onset latency of about 35 ms after the TMS and lasting about 25 ms. It is thought to be conveyed by transcallosal connections, although this may not be the only route. Several studies showed an abnormal ISP in patients with corpus callosum pathology.

**Corticomotor Threshold**

The corticomotor threshold (CMT) is the lowest stimulation intensity able to evoke a MEP of minimal size and is usually assessed in a small hand muscle. The CMT depends on the excitability of spinal motoneurons and motor cortex neurons. In theory, to define CMT, a minimal MEP should be elicited in 50% of the trials. In practice, the stimulus intensity is increased at 5% steps until reaching a level that induces approximately 100-μV responses in about 50% of 10 consecutive trials. There is a CMT at rest (i.e., resting threshold) and one during contraction (i.e., active threshold) that is lower. Distal muscles have a lower CMT than proximal ones.

The CMT augments with increasing age and is enhanced by sodium or calcium channel blocking anticonvulsants but not by drugs acting on GABA or glutamate transmission. The CMT is based on mechanisms different from those of the CSP, which it ideally complements when investigating disease mechanisms. The CMT has, for example, been increased in advanced cases of ALS, MS, spinal injury above the lesion, and it is reduced in early cases of ALS, idiopathic generalized epilepsy, and progressive myoclonic epilepsy. Normal values for resting and active threshold for various hand muscles have been compiled in specialized monographs (see page 180 of reference 10). Based on a large cohort of 89 normal subjects (age range, 12 to 49 years) using a circular coil and abductor digiti minimi (ADM) recordings, Reutens and coworkers found a mean CMT of 55.8 ± 12.9 (SD). Because of the large normal range, CMT is more useful for statistically comparing groups of patients and normal subjects rather than for determining abnormalities in individual cases.

**Normal Values of Central Motor Conduction**

To judge whether a CMCT is within or beyond normal limit, published normal values of the specific target muscle assessed with the same method may be used. Although the exact stimulator and coil type is not so critical, it is important to use the same method of assessing peripheral conduction time (i.e., root stimulation or F-wave technique) and consider presence or absence of facilitation by voluntary contraction, because MEPs from relaxed target muscles have longer CMCTs. Magnetic and high-voltage electrical root stimulation provide similar latencies at cervical level as long as not very high electrical currents are used in an attempt to stimulate supramaximally. Supramaximal stimulation is however essential when amplitude measurements are used (e.g., in a search of conduction block). At the lumbar sacral level, magnetic stimulation often does not suffice and an electrical high-voltage device is preferred. If for some reason the peripheral conduction time cannot be assessed and a CMCT cannot be calculated, normal values for the total corticomuscular latency must be taken. Normal values of the total corticomuscular latency are preferably related to the arm length (upper limbs) or height (lower limbs). The CMCT to lower limbs is slightly height dependent, and when recording from the TA, for example, the upper limit of a normal CMCT value has been described by CMCT−0.076 × height (cm) + 3.4 ms. There is also a weak correlation with age, which usually can be neglected in routine diagnostic work. Some normal values of the most
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
<td>Range</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>ADM</td>
<td>19–59</td>
<td>6.2 ± 0.9</td>
<td>4.2–7.4</td>
<td>6.3 ± 0.8†</td>
</tr>
<tr>
<td>ADM</td>
<td>17–35</td>
<td>19.3 ± 1.2</td>
<td></td>
<td>7.0 ± 1.0†</td>
</tr>
<tr>
<td>APB</td>
<td>20–83</td>
<td>20.4 ± 1.5</td>
<td>16.8–23.8</td>
<td>6.7 ± 1.2†</td>
</tr>
<tr>
<td>FDI</td>
<td>17–74</td>
<td>6.5 ± 0.9</td>
<td>4.3–7.6</td>
<td></td>
</tr>
<tr>
<td>Biceps br.</td>
<td>20–83</td>
<td>11.8 ± 1.2</td>
<td>9.1–14.7</td>
<td>6.1 ± 1.3†</td>
</tr>
<tr>
<td>Trapezius</td>
<td>23–72</td>
<td>9.6</td>
<td>7.4–12.0</td>
<td>7.5 ± 1.1†</td>
</tr>
<tr>
<td>Nasalis (fac)</td>
<td>24–42</td>
<td>10.0 ± 0.96</td>
<td></td>
<td>5.1 ± 0.60†</td>
</tr>
<tr>
<td>Tongue, right</td>
<td>20–53</td>
<td>8.8 ± 0.9</td>
<td>7.4–10.8</td>
<td>6.2 ± 0.9</td>
</tr>
<tr>
<td>Tongue, left</td>
<td>&quot;</td>
<td>8.6 ± 0.9</td>
<td>7.3–10.2</td>
<td>6.4 ± 1.0</td>
</tr>
<tr>
<td>Tongue, right</td>
<td>20–53</td>
<td>8.9 ± 0.9</td>
<td>7.6–11.2</td>
<td></td>
</tr>
<tr>
<td>Tongue, left</td>
<td>&quot;</td>
<td>9.1 ± 1.1</td>
<td>7.5–11.6</td>
<td></td>
</tr>
<tr>
<td>Masseter</td>
<td>19–25</td>
<td>6.9 ± 0.71</td>
<td>6.2–7.3</td>
<td></td>
</tr>
<tr>
<td>Masticatory†</td>
<td>23–50</td>
<td>5.5 ± 0.7</td>
<td></td>
<td>12.5 ± 1.7†</td>
</tr>
<tr>
<td>TA</td>
<td>19–59</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA</td>
<td>20–76</td>
<td>27.7 ± 2.4</td>
<td>20.2–32.5</td>
<td>13.1 ± 3.8</td>
</tr>
<tr>
<td>AH</td>
<td>19–74</td>
<td>39.3 ± 2.4</td>
<td></td>
<td>17.3 ± 1.8†</td>
</tr>
</tbody>
</table>

*Peripheral CT assessed by the F wave technique according to the formula PCT = (F+M−1)/2.
†Peripheral CT assessed by motor root stimulation using a magnetic or high-voltage electrical device.
‡Stimulation of the accessory nerve at the neck.
§Magnetic "canicular" stimulation of the facial nerve.
¶M. pterygoideus (enoral).
ADM, abductor digiti minimi; AH, abductor hallucis; APB, abductor pollicis brevis; FDI, first dorsal interosseus; TA, tibialis anterior.
important target muscles are summarized in Table 6–1.

As long as the degree of voluntary background pre-innervation is not monitored, an MEP amplitude reduction can be taken as abnormal only when it is very pronounced and when recording from a distal muscle. As a rule of thumb, an MEP amplitude equal to 20% of the distally evoked CMAP must be considered normal, and an amplitude of \( \leq 15\% \) is always abnormal (valid also for TA recordings). For the trapezius muscle, the limit of normal is more than 44%.\(^{40}\) Absent responses are abnormal also in recordings from proximal muscles. The relatively high corticomotor threshold of lower limb muscles in elderly subjects must be taken into account, necessitating maximum stimulator output and thorough search for the optimal coil placement on the scalp before an absent response can be taken as abnormal.

**Interpretation of Motor Evoked Potential Abnormalities**

The MEP abnormalities usually encountered include delay in onset latency, amplitude reduction, or absence of response to brain stimulation. Dispersion of the response (i.e., a prolonged MEP potential\(^{41}\)) and an increased variability of the responses have also been considered and found in central nervous system disorders by some investigators.\(^{42-44}\) Various combinations of these can also occur. When interpreting MEP results, it should be recalled that prolonged CMCT and reduced MEP amplitude are nonspecific findings and can be caused by a variety of mechanisms, including hypoxic excitability of spinal or cortical motoneurons. In particular, CMCT prolongations do not necessarily imply a demyelinating pathology, because marked delays are also encountered in disorders of pure axonal degenerations. Prolongation of CMCT can also occur in motoneuron disorders or hereditary disorders of neuronal degeneration. However, there is a limited specificity in that absent responses is a rare finding in MS and spondyloctic myelopathy but readily found in disorders of axonal degeneration such as ALS, hereditary spastic paraplegia (in lower limbs), and cerebrovascular disorder. Conversely, great CMCT prolongations are a rare finding in cerebrovascular disorders.\(^{13}\)

Although slowed conduction along demyelinated fibers is an obvious mechanism of CMCT prolongation, the mechanism of prolongation in axonal loss or conduction block is not precisely known, and various possibilities exist. First, it must be remembered that MEP onset latency reflects conduction of the largest myelinated pyramidal fibers, which constitute a minority of all corticospinal tract fibers. In case of conduction failure of these large fibers, transmission may occur by small, slowly conducting fibers or by some alternative, oligosynaptic pathway, such as the corticorubrospinal tracts. This mechanism may account for the great delays sometimes encountered in axonal and demyelinating (conduction block) disorders.

Another mechanism probably accounts for small prolongations of up to 5 ms. The rapidly conducting corticospinal neurons use high frequency activity (about 600 to 800 Hz) to excite bulbar and spinal neurons, and they are known to send short descending volleys in response to a transcranial cortical stimulus. The spinal motoneurons, particularly the larger ones, require much excitatory input to reach firing threshold. Drop-out of corticospinal fibers reduces the spatial summation of excitatory input on spinal motoneurons, necessitating more temporal summation to get the spinal motoneurons to discharge. It is likely that fewer functioning corticospinal neurons take longer to get the spinal motoneurons to fire (if at all) in response to the impinging excitatory burst. A burst of four to five impulses, each about 1.3 ms apart, makes a difference of about 3 to 5 ms when the motoneuron fires in response to the last rather than first or second impulse. A similar delay can theoretically also result from pathological hypoxic excitability of spinal motoneurons.

A mechanism of apparent CMCT prolongation without true slowing operates when the cortical stimulus is unable to activate the large, fast-conducting spinal motoneurons, but these fibers are still excitable by cervical root stimulation. Whether this mechanism comes into play very frequently (which may be the case) and whether it also operates
when using the F-wave technique to assess peripheral conduction is unknown.

The MEP amplitudes are much degraded from the beginning because of the great temporal dispersion of the descending activity over a long pathway with intercalated synapses. In a much dispersed biphasic response, cancellation phenomena of the negative and positive deflections further abate the amplitude. This makes appreciation of MEP amplitudes difficult. Normal values for conventional MEP amplitudes are only valid for distal target muscles as long as the voluntary pre-activation is not monitored. Because pure slowing of conduction due to demyelination increases temporal dispersion, further attenuation of amplitude may result without drop-out of active fibers. However, in MS, this mechanism does not seem reduce MEP amplitude additionally to a relevant extent. An absent MEP response strongly indicates conduction failure due to axonal degeneration, because it is a rare finding in demyelinating disorders.

Demyelinating lesions can cause conduction block, which also results in drop-out of active fibers. However, demyelinating diseases probably always comprise a certain degree of axonal loss as well. This becomes obvious when using the triple-stimulation MEP to quantify amplitude, which eliminates the temporal dispersion of the descending volleys and still demonstrates considerable degree of "genuine" amplitude reduction also in MS. The high frequency descending activity of the thickly myelinated corticospinal neurons is particularly vulnerable to slight myelin damage because a little increased refractoriness may suffice to block the descending volley leading again to a drop-out of active fibers.

Using the triple-stimulation technique, it was also shown that, irrespective of the precise mechanism (i.e., conduction block or axonal damage), conduction failure is the clinically relevant abnormality in the motor system leading to weakness, whereas pure latency prolongation does not translate to much in the way of clinical symptoms or signs, if at all. For this reason, latency prolongation is more likely to represent a subclinical abnormality than amplitude reduction. Because slowed conduction is, however, unlikely to exist in isolation very often, a positive correlation between clinical signs and prolonged CMCT can nevertheless be expected, although it may not be a very close one. The MEP findings in various neurological disorders are summarized in a qualitative way in Table 6-2.

**Multiple Sclerosis**

MS was the first and probably still is the best-studied neurological condition using magnetic brain stimulation. Clear-cut CMC abnormalities of hand muscles were readily disclosed in MS patients, demonstrating the usefulness of the method in early days of TMS and confirmed earlier studies with electrical stimulation of the motor cortex. A larger follow-up study in 83 MS patients established the typical MEP findings of MS, which have since been reproduced. Moderate to marked prolongation of CMCT with additionally reduced amplitude in about one half of the cases was shown in 79% patients with definitive MS and in 55% with probable MS categorized according to the Poser criteria and was demonstrated in 50% patients with possible MS by the McAlpine criteria. The prolonged CMCT and abnormally small MEP correlated with increased finger flexor reflexes, and marked CMCT prolongation correlated with impaired dexterity. Because weakness of the target muscle was infrequent, no clear correlation between paresis and CMC findings emerged. However, if there was weakness of the target muscle, CMC was mostly abnormal. In particular, the rare finding of a completely absent MEP was associated with a weak target muscle along with impaired fine finger movements.

Ingram and coworkers for the first time measured CMC to a lower limb muscle (i.e., TA muscle) in MS, which proved even more sensitive, and CMC abnormality correlated more closely with clinical signs of upper motoneuron disturbance such as hyperreflexia, spasticity, and the Babinski sign. Weak muscles were almost invariably associated with abnormal central conduction, but increased CMCT was also found for one half of the muscles with normal strength. Increased CMCT for lower limb muscles was directly
<table>
<thead>
<tr>
<th>Disease</th>
<th>% Abnormal CMC Findings</th>
<th>Prolonged Latencies</th>
<th>Reduced Amplitudes</th>
<th>Duration Cortical Silent Period</th>
<th>Cortico-motor Threshold</th>
<th>Subclinical CMC Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spondylopathic Cervical Myelopathy</td>
<td>80-100%</td>
<td>+++</td>
<td>++</td>
<td>shortened</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Multiple Sclerosis (MS)</td>
<td>80-90%</td>
<td>++</td>
<td>++</td>
<td>prolonged</td>
<td>enhanced</td>
<td>+</td>
</tr>
<tr>
<td>Amyotrophic Lateral Sclerosis (ALS)</td>
<td>50-85%*</td>
<td>+</td>
<td>+++</td>
<td>shortened</td>
<td>enhanced*</td>
<td>++</td>
</tr>
<tr>
<td>Friedreich's Ataxia</td>
<td>~90%</td>
<td>++</td>
<td>+++</td>
<td></td>
<td>enhanced</td>
<td></td>
</tr>
<tr>
<td>Early Onset A. with retained reflexes</td>
<td>60-70%</td>
<td>++</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late Onset Cerebellar Ataxia (e.g., OPC)</td>
<td>20-80%*</td>
<td>(+)</td>
<td>+(+)</td>
<td>SCA1: enhanced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hereditary Spastic Paraplegia (HSP)</td>
<td>80-100%**</td>
<td>(+)</td>
<td>++++</td>
<td></td>
<td></td>
<td>(+)</td>
</tr>
<tr>
<td>Spinal Muscular Atrophy (SMA)</td>
<td>none</td>
<td>-</td>
<td>-</td>
<td>shortened</td>
<td>±</td>
<td></td>
</tr>
<tr>
<td>Parkinson's Disease</td>
<td>none</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple System Atrophy (MSA)</td>
<td>10-45%o</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive Supranuclear Palsy</td>
<td>40% (ei Stim)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilson's Disease</td>
<td>30-65%</td>
<td>+</td>
<td>++++</td>
<td>prolonged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huntington</td>
<td>0-10%</td>
<td>(+)</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dystonia</td>
<td>none</td>
<td>-</td>
<td>-</td>
<td></td>
<td>normal</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>70%</td>
<td>+</td>
<td>+++</td>
<td></td>
<td></td>
<td>(enhanced)</td>
</tr>
<tr>
<td>Mitochondrial Myopathy</td>
<td>~25%</td>
<td>+</td>
<td>?</td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Functional Weakness</td>
<td>none*</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Only to lower limbs abnormal; *Westphal variant: shortened; †Often absent responses;
*More frequent or more pronounced abnormality to lower limb muscles; **CMC to upper limbs usually normal;
*Only in plegic limb reliable evidence; †Often conduction times/latencies and amplitudes considered/approximate values;
*Lowered threshold at very early stages of the disease.
related to functional motor disability, which has been amply confirmed since. Using recordings from three muscles in the upper limbs and two in the lower limbs in 68 patients, Ravnborg and colleagues, found 83% abnormal CMC in the 40 patients who were ultimately definitely diagnosed as having MS. In a larger study of 101 MS patients, combining CMC to two upper limb (i.e., ADM and biceps brachii) and one lower limb muscle (i.e., TA), the additional use of TA significantly increased the proportion of abnormal CMC findings in the probable and possible MS cases (as defined earlier) to 64% and in definite MS to 82%.

In view of the broad range of normal values of MEP amplitudes (normal >15% of peripherally evoked CMAP), the frequency of abnormal amplitudes is remarkable, and we have good reason to assume that this is caused by axonal loss and conduction block of demyelinated pyramidal fibers, some of it probably as frequency-dependent conduction block. Using the novel triple-stimulation method to better quantify MEP amplitude reduction, conduction failure without much CMCT prolongation could be disclosed in early relapsing-remitting MS patients because of the methodical shortcoming of the conventional MEP technique in appropriately assessing MEP size, most clinical neurophysiologists feel more comfortable relying on the unequivocal latency measurements. In theory, CMCT prolongation is more likely to disclose subclinical involvement than amplitude reduction, of which only the latter should translate into weakness. In practice, prominent CMCT prolongation should nevertheless frequently occur along with impaired muscle performance, because severe central involvement is likely to be associated with some conduction block or axonal degeneration, or both. It must, however, be remembered that conventional CMC assesses only the relatively small proportion of rapidly conducting, thickly myelinated pyramidal fibers. Because tonic muscle contraction probably uses slower conducting corticospinal pathways than phasic contractions, the weak correlation between CMC and tonic force is not surprising. Van der Kamp and coworkers did find a strong inverse correlation between prolonged CMCT to the adductor pollicis muscle and voluntary phasic force of that muscle.

Although earlier studies included a mixture of MS types, Kidd and coworkers specifically looked at progressive MS by measuring MEPs to several upper limb muscles and TA and found a weak correlation of CMCT to TA with disability, whereas CMCT to upper limb muscles did not correlate with any clinical measurement. The CMCT to upper limb muscles correlated with the lesion load in the cervical cord as assessed by MRI, but this was not the case for CMCT to the TA. The modest CMCT changes during a 1-year follow-up period correlated with new MRI cervical lesions rather than clinical deterioration. There also was no difference in MEP parameters between primary and secondary MS. These investigators concluded that progressive clinical impairment in such patients might be caused by fiber tract degeneration in the spinal cord that is not reflected by CMCT prolongation or MRI plaques.

When comparing secondary progressive with relapsing-remitting MS patients, Facchetti and coworkers found a significantly longer spinal motor conduction time in progressive MS. This finding may at first glimpse contradict the important role of axonal degeneration recently attributed to the progressive MS. However, it was confirmed by a large study comparing 90 relapsing-remitting MS patients with 51 progressive MS patients, showing significantly longer CMCT to upper and lower limb muscles in progressive MS, and this difference was also true when patients with similar clinical motor deficit or similar disease duration were compared. Although CMCT did not correlate with clinical signs and deficits in either group, the quantified MEP size as assessed by triple simulation was significantly related to clinical signs in the relapsing-remitting and the progressive MS groups. In this study, many relapsing-remitting MS patients showed a considerable degree of conduction failure (i.e., quantified amplitude reduction) in the presence of only slight or moderate CMCT prolongation, and this was explained as caused by conduction block. However, in the progressive MS patients, the prominent conduction failure often found was assumed to be mainly
caused by loss of axons. Axonal degeneration is thought to be the cause of ongoing progression of disability without remittance in progressive MS. The conspicuously long CMCT primarily found in progressive MS cases is presumably caused by persistently demyelinated fibers when the capacity for remyelination has exhausted. However, unmasking of alternative, slowly conducting motor pathways (e.g., corticoreticulospinal tract) also may contribute to greatly prolonged CMCT in progressive MS patients. 58

When comparing with afferent evoked potentials studies in MS, conventional MEPs clearly show the highest yield of abnormality and are surpassed only by MRI, with which MEPs correlate rather closely. 57,62 Despite the high sensitivity, conventional MEPs do not play a major role in ascertaining the diagnosis of MS. MEPs tend to reflect pyramidal disability in MS and therefore do not very often reveal silent lesions. Depending on the precise method used, subclinical involvement was detected in 4% to 13.5% of patients, 46,63,64 which is clearly inferior to visual evoked potentials (VEPs). In a study of 189 consecutive patients referred for suspected MS, 62 conventional MEPs ranked after VEPs in their capacity to enhance the diagnostic certainty in MS, while MRI and cerebrospinal fluid oligoclonal bands were the most powerful ones with this respect. In selected cases, however, when MRI and oligoclonal bands are not diagnostic, MEP may nevertheless be very helpful. 62 The high sensitivity makes MEPs a suitable tool to follow the course of MS with or without treatment. 62

By measuring additional MEP parameters, the sensitivity can be somewhat enhanced, as shown for measuring the MEP latency variability 42 and the MEP potential duration, 41 but no further elaboration on these refinements was done. Other techniques to increase MEP sensitivity in MS include standardized muscle preactivation to improve MEP amplitude assessment, long-interval paired stimulation when recording from relaxed target muscle to improve CMCT sensitivity; TMS-induced silent period, which was shown to be prolonged in MS; 68 and the use of transcallosal (ipsilateral) inhibition in tonically activated muscle. 69 However, the diagnostic power of these procedures has not been evaluated in a larger patient cohort.

A different picture emerges when the more sophisticated TMS technique of triple-stimulation MEPs is added. It has been shown to be 2.75 times more sensitive than conventional MEPs in disclosing corticospinal conduction failure, 13 but it complicates the MEP procedure somewhat.

The strength of conventional MEPs as a simple procedure is not that of establishing or rejecting the definite diagnosis of MS, but rather that of confirming doubtful and “soft” neurological signs such as equivocal plantar responses or brisk reflexes without increased tone in an early stage of suspected disease.

## Motoneuron Diseases

The diagnosis of amyotrophic laterals sclerosis (ALS) usually poses no problem when the course of the disease is followed and the typical clinical picture eventually emerges. With the advent of medical therapy and when more effective treatment becomes available, early diagnosis of ALS will become more important. MEPs should have the capacity to detect conduction failure in the fast cortico-motoneuronal system, enabling the differentiation of ALS from motor syndromes that can clinically mimic ALS, such as multifocal motor neuropathy, monomelic amyotrophy, postpolio muscular atrophy, inclusion body myositis, and spinal muscular atrophy (e.g., bulbospinal Kennedy disease). The first report using TMS in ALS measured CMC to the ADM muscle and found a CMC abnormality in 64% of patients with ALS. 70 Eisen and coworkers who measured CMC to three upper limb muscles in 40 definite ALS patients found the rate of CMC abnormality approaching 100%. 33 As might be expected from consideration of the pathology with axonal degeneration, abnormally small and absent responses to brain stimulation occurred at higher incidence than found in MS or compressive myelopathy. However, CMCT prolongation is also found in about one half the ALS patients, sometimes to a considerable degree. It is clear from these studies that CMC findings are nonspecific and of little
discriminant value in the individual case. A markedly prolonged CMCT has been found in the slowly progressive familial ALS with the autosomal recessively inherited D90A CuZn-superoxide dismutase mutation.

The reported yield of abnormal MEP findings in ALS has been conspicuously variable, and this is primarily caused by the different patient samples (early versus late stages), the number and type of assessed target muscles, and the considered MEP parameters. Sensitivity tends to be greater with recordings from lower limb muscles. Miscio and colleagues, who looked at various stages of ALS found CMC to be abnormal in 95.4% of definite ALS patients, in 72.2% of suspected ALS cases with probable upper motoneuron signs (most of them later developed ALS), in 50% of pure lower motoneuron syndromes, and in 20% of progressive bulbar palsy. These investigators recorded from the ADM and flexor hallucis muscles and only considered CMC prolongation and absent MEP as abnormal (no reduced amplitudes considered). Di Lazzaro and coworkers measured CMC to the biceps brachii, ADM, rectus femoris, TA, and abductor hallucis and found a sensitivity of 74% and a rate of subclinical involvement of 26% in ALS, which was the highest yield in their large cohort of 1,023 patients of various neurological disorders. Pohl and coworkers looked at 49 ALS patients of various stages according to the 1994 El Escorial Criteria and recorded from the ADM and TA. They found an abnormal measurement (i.e., absent response or prolonged CMCT) in definite ALS in 50% (ADM) and 35% (TA), in probable ALS in 43% (ADM) and 64% (TA), and in possible and suspected ALS taken together in 25% (ADM) and 25.5% (TA).

Several investigators found assessing CMC to cranial muscles particularly rewarding. Trompetto and coworkers found delayed or absent MEP to the masseter muscle in 63% of their patients also when there were no clinical bulbar signs. Urban and coworkers assessed CMC to the tongue and orofacial muscles in addition to ADM and TA muscles in 51 ALS patients and ended up with 82% of patients having CMC abnormality. Truffert and colleagues used the technically simple recording from trapezius muscle in 10 ALS patients and found a CMC abnormality to this muscle in all of them.

Because the pathology of ALS is axonal loss and conventional MEPs are not very sensitive in assessing reduction in MEP size, the amplitude quantification by triple-stimulation MEP was expected to be more sensitive. In a triple-stimulation study of 48 ALS patients of various diagnostic categories (19 with definitive ALS), conduction failure to the ADM was found in 24 patients (38 sides), 12 (20 sides) of which were normal in conventional MEPs. The increased sensitivity of the triple-stimulation MEPs in ALS was confirmed in 19 ALS patients by Komissarov and coworkers, who found more MEP abnormality by triple-stimulation MEPs than with conventional MEPs, particularly in suspected and possible ALS cases, in which a triple-stimulation MEP abnormality was found in all patients.

Apart from central motor conduction time and amplitude, assessment of increased cortical motor threshold, of shortened silent period, and of altered peristimulus time histograms have been demonstrated in ALS, sometimes also detecting subclinical abnormality in patients with doubtful or missing upper motoneuron signs. In some patients with enhanced threshold and absent MEP, the cortical silent period could nevertheless be evoked.

From a pathophysiological point of view, it is interesting that the corticomotor threshold has a tendency to be abnormally low in the early stages when there are only few clinical signs and rises to abnormally high levels later during the advanced stages. This dynamic feature makes assessment of corticomotor threshold useless for clinical diagnosis in the early stage. When comparing with groups of MS and treated Parkinson's disease, the discriminative value of the CMT was found to be low, because these disorders also tend to have an elevated CMT. Because of the relatively large scatter and large range and standard deviations in normal subjects, CMT is not very helpful as a diagnostic indicator in the individual patient.

The CSP has been found to be reduced in ALS to various degrees, which often
makes group comparisons with normal subjects significantly different. Differences become more distinct with greater stimulus intensity, because this reduces the variability of CSP duration. In ALS, the CSP duration depends less on the stimulus strength (i.e., it does not prolong to the same degree as in normal subjects when stimuli are enhanced). In normal subjects, the CSP duration is positively related to the stimulus intensity.

Mills, who followed 76 ALS patients (49 until death) with serial measurements of corticomotor threshold, central motor conduction time, silent period duration, and the amplitude of compound muscle action potentials from both first dorsal interosseous muscles, concluded that none of the measures of central motor function in ALS is likely to be useful for monitoring patients in a clinical trial setting.

Studies of only few patients with primary lateral sclerosis have been published, and CMC to upper and lower limb muscles was abnormal in virtually all of them. Responses were frequently absent, and very marked prolongations of CMCT were found. In hereditary spastic paraplegia (HSP), CMC is usually abnormal to the lower limbs only, with the typical pattern being an abnormally small and moderately prolonged CMCT with absent responses in one third of the patients. With a sensitivity of approaching 100%, the MEPs were closely related to the physical signs but without revealing subclinical clear-cut CMC abnormality, which obviously limits their use in diagnostic workup. Schnider and coworkers nevertheless found an abnormally small MEP amplitude in the unaffected juvenile member of a family with HSP, for whom using MEP amplitude quantification might have revealed subclinical involvement.

In the spinal muscular atrophies, the MEPs have invariably been found to be normal.

### Myelopathy

Compressive myelopathy due to spondylosis or disc herniation is the one condition for which MEPs are most sensitive. When recording from the TA muscle, the sensitivity approaches 100% in some studies, with often considerable CMCT prolongations, making it a suitable test for monitoring and helping to decide for surgery. Additional amplitude reduction is frequently found in about 50% of MEPs to small hand muscles. After surgical decompression, MEPs do not normalize, except for the very mild cases without much clinical disability. Subclinical lesions are found in 10% to 15% of patients. When combined with somatosensory evoked potentials (SEPs), neurophysiological abnormalities were reported in up to 50% of patients with “silent” compression. CMC prolongations in spondylotic cervical myelopathy are often considerable, whereas absent MEP responses are rarely encountered.

It was hoped that recording from multiple muscles supplied by motor roots of varied segments would allow precise localization of the crucial compression level. Because the cervical column is the most frequently affected segment, recording from the trapezius, biceps brachii, intrinsic hand muscle, and TA should allow narrowing down the lesion to, for example, the mid-cervical level and determine whether a radiological narrowing is functionally relevant. This is a practically important question, because many elderly subjects have benign spondylotic alterations and imaging by MRI tends to overestimate these narrowings. Several investigators did show that the pattern of prolonged CMCT below and normal CMC above the segment in question was frequently encountered providing valuable confirmatory information. The encountered patterns are, however, not completely reliable. Mathis and coworkers compared 72 patients with compressive myelopathy and 101 patients with MS and found a “mid-cervical compressive pattern” (i.e., CMCT to biceps normal, to ADM abnormal) in 10% of the MS patients and 19% of patients who had their proved compression above C4 level. Truffert and colleagues compared cervical myelopathy with ALS, found an abnormal CMC to the trapezius in one of nine patients with myelopathy. For suspected thoracic myelopathy, multiple-level paraspinous recordings were suggested. Taniguchi and coworkers found false-negative results in paraspinous recordings when the lesion was below T10.
MEPs are less sensitive in intramedullary lesions such as syringomyelia or spinal cord tumors. They seem to be sensitive and perhaps of prognostic value in patients with human immunodeficiency virus (HIV), because subclinical involvement was evidenced in HIV-positive patients who tended to progress to acquired immunodeficiency syndrome (AIDS) more rapidly. In spinal injuries, MEP measurements have given mixed results, but they appear to be of some prognostic value.

**Degenerative Ataxic Disorders**

Classification of the hereditary ataxias is usually based on clinical features with the age of onset as the crucial factor, but genetic determination is becoming an essential supplement. The most important of the early-onset hereditary ataxias (i.e., those with symptoms before the age of 20 years) is Friedreich's ataxia, an autosomal recessive, triplet-repeat disorder. Clinically, it is characterized by progressive gait difficulty, loss of tendon reflexes, a Babinski sign, and cardiomyopathy. MEPs in Friedreich's ataxia usually have been abnormal in lower and upper limbs, with moderate to marked CMCT prolongations and often with diminished amplitudes. The CMAP duration of the MEPs were significantly longer in Friedreich's ataxia than in the other disorders.

Friedreich's ataxia is distinguished from early-onset cerebellar ataxia with retained tendon reflexes with better prognosis, in which tendon reflexes may be normal or increased and in which there is no cardiomyopathy. MEPs were found to be abnormal in about 60% (upper limbs) to 70% (lower limbs), and abnormalities were a bit less pronounced than in Friedreich's ataxia.

The late-onset cerebellar degenerations are a complex and heterogenous group of autosomal dominant disorders, many of them genetic with the triplet-repeat expansion mechanism. Pyramidal tract involvement is variable, as are such diverse features as ophthalmoplegia, dementia, and myoclonus. In genetically unclassified patients, a MEP abnormality was found in about one half of the cases, and CMCT was only moderately prolonged, with amplitudes often normal. In genetically classified spinocerebellar ataxia type 1 patients (SCA1), MEPs to lower limbs were mostly abnormal, whereas in SCA2 and SCA3, this was only the case in 18% and 28%.

**Cerebrovascular Disease**

CMC abnormalities are often found in the acute stage of stroke, but the sensitivity of MEPs in cerebrovascular disease is generally low. For instance, MEPs were found normal in one third of middle cerebral artery strokes, and no subclinical CMC abnormality has been reported. MEPs are usually absent only in total middle cerebral artery strokes with profound hemiplegia. The correlation between MEP findings and site of pathology does not seem to disclose more than what can be expected from the clinical sign. Using electrical brain stimulation, Librizzese and coworkers found an abnormal CMC in 18 of 32 patients with focal deficits due to minor cerebral ischemia of the lacunar type.

Most investigators found that early MEP testing is of prognostic value in strokes in that absent MEPs predicted a persistent motor deficit rather more precisely than the clinical examination at the time of MEP testing. Evocable MEPs in a locked in syndrome probably is a good prognostic sign. CMC prolongations are found in about 20% of strokes, but a great prolongation is the exception. Intracerebral hemorrhage tends to prolong CMC more than ischemic stroke. Ipsilateral MEPs from stimulating the unaffected hemisphere are occasionally evoked with remarkably ease in stroke patients, a phenomenon that seems to bear an unfavorable prognosis.

Measuring the CSP in strokes has produced conflicting results, which may be because of the divers locations of the infarct in the brain. Several investigators found an abnormally and persistently prolonged CSP on the affected side, and Uozumi found a shortened CSP in patients with spastic hyperreflexia due to cerebral infarction. It appears that the CSP is only shortened when the ischemic zone lies
within the motor cortex. Catano and colleagues have shown that in stroke patients other than in normal subjects, the duration of the CSP depends on the exerted tonic background force, making it abnormally short with great tonic contraction, and this might explain some of the discrepancies in literature. In normal subjects, the CSP duration does not depend much on the degree of tonic contraction. Measuring CSP is impeded by a great interindividual variability and requires a highly standardized procedure.

### Extrapyramidal Disorders

CMC as conventionally assessed has been found normal in Parkinson's disease, dystonias, and largely in Huntington's disease. In the latter disorder, a modest CMCT prolongation and MEP amplitude reduction was found in some patients, and an increased latency variability was found in many patients.

In multiple system atrophy and sporadic olivopontocerebellar atrophy, CMC to the lower limbs often was abnormal. Abbruzese and associates found abnormal CMC in 40% of progressive supranuclear palsy (i.e., Steele-Richardson-Olszewski syndrome) when using electrical brain stimulation. MEPs in Wilson's disease were found abnormal in about one half of the patients showing prolonged CMCT, reduced amplitude, or absent responses. CMCT was more often abnormal to the hand (first dorsal interosseus) than leg (TA) muscle.

### Psychogenic Weakness

In assessing psychogenic weakness, MEPs can be helpful in three ways. First and most importantly, an abnormal CMC in a clinically frank psychogenic paresis may give the crucial hint about an underlying organic disorder that would otherwise be easily missed. Second, an normal CMC in a completely plegic limb confirms the psychogenic nature of the weakness. Strictly speaking, it only confirms the weakness being largely functional and cannot rule out a minor concomitant organic component. The normal MEP in a mildly parietic muscles does not rule out an organic cause. Third, the overt jerking of the paralyzed limb during the MEP procedure in a psychogenic plegia can be used therapeutically if the examiner acts skillfully. It is important in such a situation to avoid any trace of triumphant outwitting, but rather to show relief and optimism in the face of the still functioning pathways and muscles. The latter must be learned to be properly controlled again. Cooperation of the patient with psychogenic weakness is sometimes a problem, because we need some pre-innervation of the target muscle. This is usually achieved when manipulating the limb while having the EMG loudspeakers switched off.

### REFERENCES


34. Ravnborg M, Blinkenberg M, Dahl KAD. Standardization of facilitation of compound muscle action potentials evoked by magnetic stimulation of the cortex. Results in healthy volunteers and in patients with multiple
62. Beer S, Rössler KM. Hess CW. Diagnostic value of paraclinical tests in multiple sclerosis Relative sensitivities and specificities for reclassification according to Poser committee


