SPECIALISED ELECTROMYOGRAPHY AND NERVE CONDUCTION STUDIES

K R Mills

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This article covers a variety of techniques that might be thought of as out of the usual run of the mill neurophysiological testing. Investigation of the neuromuscular junction with repetitive nerve stimulation and single fibre electromyography (EMG), a number of quantitative EMG techniques, motor unit number estimation, cervical root stimulation, and some aspects of transcranial magnetic stimulation will be covered.

INVESTIGATION OF THE NEUROMUSCULAR JUNCTION

Neurophysiology offers the most sensitive diagnostic tests for disorders of neuromuscular transmission. The tests are, however, not absolutely specific. Repetitive nerve stimulation shows a decrementing response in myasthenia gravis (MG), the decrement being more pronounced in proximal muscles. Single fibre EMG (SFEMG), however, is much more sensitive; SFEMG of facial muscles detects an abnormality in virtually all cases of MG. In Lambert-Eaton myasthenic syndrome (LEMS), the compound muscle action potential (CMAP) evoked in hand muscles is small and increases dramatically after exercise. Decrement is seen on repetitive nerve stimulation (RNS) and stimulated SFEMG, if required, shows a frequency dependent increase in jitter (table 1).

The neuromuscular junction is most simply investigated by recording from a muscle with surface electrodes and repetitively stimulating the peripheral nerve at supramaximal intensity. The size of the evoked CMAP reflects the number of muscle fibres accessible from the nerve and will be reduced by atrophy (from whatever cause), by conduction block in the peripheral nerve or at the neuromuscular junction. RNS stresses the neuromuscular junction. In healthy subjects, the safety factor for transmission is sufficiently high for all impulses to be transmitted across the junction and so the evoked CMAPs are all of identical size. If neuromuscular transmission is compromised, either from a presynaptic abnormality (for example, LEMS) or from a post-synaptic abnormality (for example, MG), then RNS may result in some junctions failing and the resulting CMAPs will fall in amplitude—a so-called decrementing response to RNS. This decrementing response to RNS is therefore only seen when the disorder of neuromuscular transmission is sufficiently severe so as to cause neuromuscular block. Decrementing responses can also occasionally be seen in amyotrophic lateral sclerosis (ALS) and polymyositis.

In practice, a train of 10 supramaximal stimuli are delivered and CMAP amplitude reduction, relative to the first CMAP, is measured (fig 1). A reduction of 10% or more is abnormal. However, the CMAPs should fall gradually, reaching a nadir at the fourth or fifth; sudden reductions are usually artefactual. Hand stabilisation and firm attachment of both recording and stimulating electrodes are essential. RNS is usually performed at frequencies of 1 Hz and 3 Hz; there is little to be gained by using higher frequencies. The patient is then asked to perform a 15 second maximal contraction of the muscle and RNS is repeated immediately after exercise and again at two minutes. In practice, skin temperature control is usually not critical but decrement is greater at higher temperatures.

SFEMG is more sensitive than RNS because it can detect an impairment of neuromuscular transmission short of complete block. Thus SFEMG may be abnormal even though there is no clinical weakness or fatigue. A single fibre needle is used to record the potentials from pairs of fibres belonging to the same motor unit which is being voluntarily activated. The variability in the timing of discharge of the two fibres or jitter is a measure of the security of neuromuscular transmission. Jitter is increased in disorders of transmission. Voluntary SFEMG is time consuming, requires the isolation of pairs of single fibre potentials, and demands the cooperation of the patient to make a weak constant muscle contraction. Alternatively, the needle can be positioned close to just one fibre and then the intramuscular axons stimulated electrically. Again the variability of evoked fibre discharge is measured. Stimulated SFEMG has the advantages that it does not require the cooperation of the patient, just one fibre needs to be found, and the effect of axonal stimulation at a variety of frequencies can easily be investigated. In practice, several distinct single fibres can be found at each needle position, the jitter of each one of which can be

Correspondence to:
Professor Kerry R Mills,
Department of Clinical
Neurophysiology, King's
College Hospital, Denmark
Hill, London SE5 9RS, UK;
kerry.mills1@kingsch.nhs.uk

Table 1 Neurophysiological measurements in myasthenia gravis and Lambert-Eaton myasthenic syndrome

	MG	LEMS
CMAP amplitude (resting)	Normal	Reduced
CMAP amplitude (immediately post exercise)	Normal	Increased
RNS at 3 Hz (resting)	Decrement	Decrement
RNS at 3 Hz (immediately post-exercise)	Normal	Normal
RNS at 3 Hz (2 min after exercise)	Enhanced decrement	Decrement
SFEMG or stimulated SFEMG	Jitter	Jitter
Stimulated SFEMG at 3 Hz	Jitter	Increased jitter
Stimulated SFEMG at 10 Hz	Increased jitter	Reduced jitter

CMAP, compound muscle action potential; LEMS, Lambert-Eaton myasthenic syndrome; MG, myasthenia gravis; RNS, repetitive nerve stimulation; SFEMG, single fibre electromyography.

measured. With each technique, it is recommended that 20 separate jitter measurements are made in each muscle. In practice, if the clinical suspicion is high and the first 10 fibres isolated all show abnormal jitter, then little is to be gained by sampling more fibres. Conversely, if the patient has clinical ptosis and the first 10 fibres isolated in orbicularis oculi show normal jitter, then a defect in neuromuscular transmission is very unlikely and alternative diagnoses should be entertained. Single fibre EMG can be performed in a number of muscles, but muscles around the eye, orbicularis oculi and frontalis, are the most likely to show an abnormality. Although very sensitive, SFEMG is not specific for a neuromuscular transmission defect; jitter abnormalities have been described in chronic progressive external ophthalmoplegia, oculopharyngeal muscular dystrophy, and in neurogenic conditions such as peripheral neuropathy and ALS. SFEMG is also abnormal after injection of botulinum toxin and may remain abnormal for many months even at sites remote from the injection.

All patients with suspected myasthenia gravis should be investigated with RNS and SFEMG. A useful scheme is for RNS to be performed on a hand muscle and on a more proximal muscle, such as trapezius, and then for SFEMG to be performed on a limb muscle, usually extensor digitorum brevis, and on a facial muscle, usually orbicularis oculi. Even though the rate of abnormal RNS is lower in hand muscles than proximal muscles, it is technically more robust and will detect the small resting CMAP should the case turn out to have LEMS. The form of the CMAP may also be important; a double discharge suggests either pyridostigmine toxicity or the slow channel syndrome. In generalised MG, RNS of the ulnar nerve shows a decrement in only about 40% of patients, whereas RNS of the spinal accessory nerve will produce a decrementing response in trapezius in about 60% of patients. Immediately after exercise, there is usually no decrement, but two minutes later the decrement is more pronounced. In occasional patients, decrement is only seen two minutes after exercise.

If the clinical suspicion is high and RNS gives unequivocal decrementing responses, then SFEMG is not necessary. If RNS is normal, then SFEMG of orbicularis oculi is the most sensitive investigation, being positive in some 98% of patients with either generalised or ocular MG. If there are unilateral symptoms, then the clinically affected muscle is chosen. A branch of the facial nerve is stimulated with surface

Figure 1 Repetitive nerve stimulation in a patient with mild generalised myasthenia gravis. (A) Recording from abductor digiti minimi during 3 Hz supramaximal stimulation of the ulnar nerve. (B) Recording from trapezius during 3 Hz supramaximal stimulation of the spinal accessory nerve. The latter shows a significant decrementing response.

electrodes placed some 2 cm lateral to the outer canthus; a fine concentric recording needle electrode in orbicularis oculi can be used because facial motor units contain few muscle fibres and there is little difficulty isolating single fibres. Isolation of 10 single fibres can then be achieved in 10–20 minutes. Mean normal jitter in this muscle is less than 23 µsec and individual potentials should have jitter less than 45 µsec. SFEMG of the facial muscle is particularly useful in those 25% of patients who are negative for acetylcholine receptor antibodies.

The neurophysiological hallmark of LEMS is a small CMAP from hand muscles which increases by at least 50% in amplitude immediately after exercise (fig 2). This incrementing response is the electrophysiological correlate of clinical post-tetanic tendon reflex potentiation. It is usually unnecessary to use high frequency (10–30 Hz) stimulation to demonstrate this increment. It is far kinder to patients to utilise the high frequency motor unit discharge provided by a short voluntary contraction. Usually it is sufficient to demonstrate the increment, which is often dramatic, in two

Figure 2 Recording from the abductor pollicis brevis muscle in a patient with the Lambert-Eaton myasthenic syndrome. A supramaximal median nerve stimulus with the patient at rest evokes a compound muscle action potential (CMAP) of 3.5 mV. The patient then performs a 15 second maximal voluntary contraction during which the amplitude of EMG activity is seen to increase. A second stimulus immediately after the exercise evokes a CMAP of 9.7 mV.

hand muscles. Increments after exercise are most easily detected in hand muscles, despite the fact that weakness and fatigue are more evident proximally. The CMAP gradually falls exponentially to its resting level over about one minute. RNS demonstrates a decrement similar to that seen with MG.

The diagnosis of LEMS should always be considered in cases with proximal fatigability where the conventional EMG shows a myopathic pattern; because many junctions are blocked with the muscle at rest, the recruitment pattern during voluntary contraction may contain small and spiky motor unit potentials. In such cases it is mandatory to measure hand muscle CMAPs before and after exercise. In occasional patients, there is an increment after exercise but this fails to convince. In this situation stimulated SFEMG is required. It may be difficult to isolate single fibres because they rapidly become blocked, but jitter is usually obvious. It may be possible to show that jitter is high with low frequencies of axonal stimulation, but becomes less abnormal as stimulation frequency is increased (fig 3). About 50% of LEMS patients are associated with small cell carcinoma of the lung, the remainder being autoimmune with antibodies against voltage gated calcium channels. The two groups cannot be differentiated neurophysiologically.

QUANTITATIVE EMG ANALYSIS

In general, quantitative EMG analyses, in their current state of development, are unlikely to help the experienced electromyographer in an individual case. Usually, when there

is doubt after qualitative EMG, quantitative EMG does not provide an unequivocal answer. Quantitative EMG, however, does have a role in a number of situations: inexperienced electromyographers will find it useful when they are unsure, and, in a research situation where groups of patients are being compared, there is a need to quantify the EMG for comparisons to be made.

There are two basic approaches: either the features of individual motor unit potentials can be measured, or the recruitment pattern can be analysed.

Individual motor unit potential analysis

All modern EMG machines have programs to facilitate motor unit potential (MUP) analysis. The patient is required to make a small constant voluntary contraction of the muscle and a trigger is set to isolate a single MUP, the amplitude, duration, and number of phases of which are then measured automatically. Duration is the most difficult measurement because it depends on assessing where a slowly changing MUP waveform returns to baseline. The program sets criteria of amplitude at which it sets the offset cursor. Small satellite potentials which form part of a complex MUP may be missed and the cursors will need to be reset manually. A sample of 20 MUPs is collected and the mean duration, amplitude, and number of phases calculated. Normal values for these parameters are available. In myopathy, MUPs are small, of short duration, and have an increased number of phases. In chronic neurogenic disease, MUPs are large, have long

Figure 3 Stimulated single fibre EMG in a patient with Lambert-Eaton myasthenic syndrome (LEMS). The axon to the single fibre has been stimulated at 1, 3, 5, and 10 Hz. Jitter increases up to 5 Hz but then is less with 10 Hz stimulation.

Abbreviations

- ▶ **ALS:** amyotrophic lateral sclerosis
- ▶ **CMAP:** compound muscle action potential
- ▶ **CMCT:** central motor conduction time
- ▶ **EMG:** electromyography
- ▶ **LEMS:** Lambert-Eaton myasthenic syndrome
- ▶ **MG:** myasthenia gravis
- ▶ **MMN:** multifocal motor neuropathy
- ▶ **MS:** multiple sclerosis
- ▶ **MUP:** motor unit potential
- ▶ **RNS:** repetitive nerve stimulation
- ▶ **SFEMG:** single fibre electromyography
- ▶ **TMS:** transcranial magnetic stimulation

durations, and have a normal number of phases. More sophisticated computer programs are available to dissect single MUPs from a more complex recruitment pattern. They use a technique known as template matching in which the waveform of a single MUP can be extracted. This has the advantage that patients unable to cooperate in producing a small constant contraction can still be studied. One feature of MUP analysis that should be born in mind is that the MUPs it collects are all from early recruited motor units and so the sample is biased.

Macro-EMG

MUP analysis as outlined above is only examining a small fraction of the total number of muscle fibres belonging to a single motor unit. This is because the fibres of a motor unit are distributed widely throughout the muscles and all but a few are outside the pick-up region of the needle. Macro-EMG aims to circumvent this sampling problem by collecting signals from the whole of the motor unit. This is achieved by using a specialised needle in which signals can be collected both from a small side port and from the shaft of the needle. A single fibre discharge is isolated from the side port signal and then the shaft signal is averaged with respect to the single fibre discharge. Thus contributions from all the fibres of the motor unit are collected and averaged using the discharge of one of its fibres as the time locking point. Usually, 20 different macro-potentials are collected and a mean motor unit potential amplitude calculated.

Fibre density

A single fibre or macro needle can also be used to estimate fibre density—that is, the number of fibres of a single MU within the pick-up region of the needle. A single fibre potential is isolated and the recording optimised by small adjustments of the needle position. The number of time locked components associated with the single fibre discharge is then counted. This process is repeated for 20 single fibres. In neurogenic disease the average fibre density is increased; this corresponds to the fibre grouping seen on muscle biopsy in chronic neurogenic disease.

Recruitment pattern analysis

A number of analysis techniques are available: power spectral analysis, turns/amplitude analysis, and so on. Although it is intuitive to think that power spectral analysis would be effective because that is what the experienced electromyographer's ear is doing, in practice the differences between myopathic and neurogenic disease are disappointingly small. Turns-amplitude analysis is available on all modern EMG

machines and is a useful technique in a number of circumstances. Essentially, the computer collects a short epoch of EMG signal, say one second, and then counts the number of times it changes direction (a turn) and calculates the mean amplitude of each turn. In healthy subjects and in patients, the number of turns/second and the amplitude/turn depend on the degree of activation of the muscle, both increasing with increasing force. The solution to this problem is to sample the EMG during a variety of different forces and at a number of sites within the muscle and then to plot turns/second against amplitude/turn. Each epoch of EMG analysed produces a single point on the graph, eventually producing a scatter plot or cloud, the limits of which are known. By moving the EMG needle a small distance and then asking the patient to produce small, medium, and large contractions, the full range of contraction strength is investigated. Normal values are available for tibialis anterior, biceps, first dorsal interosseus (FDI), and vastus medialis muscles. In myopathy, there is an increased number of turns/second and the mean amplitude per turn is reduced. In contrast in chronic neurogenic disease, the number of turns/second is reduced but the mean amplitude of turns is increased. Trainees in neurophysiology find the technique useful in confirming their suspicions that an EMG pattern is indeed myopathic or neurogenic.

Motor unit number estimation

An estimate of the number of motor units within a muscle can be obtained using surface recording electrodes. All methods depend on estimating the average size of a single MUP and then dividing this value into the size of the maximal CMAP. Various methods for measuring the size of single MUPs are available and the best is yet to be identified. Several are implemented as software on current EMG machines. In the original method, weak stimuli applied to the nerve will evoke a single MUP identifiable by its all-or-none response. Slight increases in stimulus intensity will

Figure 4 Recordings of CMAPs from the adductor digiti minimi muscle in a patient with multifocal motor neuropathy. The ulnar nerve has been stimulated at six sites from the wrist to the C8 root. Focal conduction block is present between Erb's point and the axilla.

produce a stepwise increase in CMAP amplitude, each step being the contribution of an additional motor unit recruited by the stimulus. By subtraction, the amplitude of each additional MUP can be obtained and an average calculated. Because the threshold for motor axons is very similar, it is difficult to extend this process beyond about the first five motor units recruited.

A second method relies on the variations in CMAP amplitude when subthreshold stimuli are applied to a nerve. If Poisson statistics are assumed for this variability (that is, the standard deviation is equal to the mean), then an estimate of average motor unit amplitude can again be made. A third method depends on finding single motor units with a needle electrode and then averaging the associated surface EMG to extract the contribution of that particular motor unit; this process is repeated and an average single motor unit amplitude calculated. There are clearly technical issues and assumptions with all these techniques, but they show promise—for example, in documenting the fallout of motor units in ALS and may be of use in clinical trials.

Cervical root stimulation

This is useful in the differentiation of multifocal motor neuropathy (MMN) with conduction block from ALS. The two can look very similar clinically. In MMN, focal motor conduction block should be demonstrated in at least two peripheral nerves. The block is at non-usual entrapment sites. A proportion of patients have block in the motor roots, and cervical stimulation with a high voltage electrical stimulator is then useful in delineating this (fig 4). The method relies on being able to provide a supramaximal stimulus to the roots; TMS has been used for this purpose but it is difficult to ensure maximal activation of the nerve reliably. The method can be used to investigate the C8 root fibres innervating the abductor digiti minimi but is less reliable for median innervated hand muscles.

Transcranial magnetic stimulation

The technique of transcranial magnetic stimulation (TMS) will not be described here, but the clinical scenarios in which TMS has proved useful will be highlighted.

Firstly, TMS to measure central motor conduction time (CMCT) is useful in multiple sclerosis (MS) where patients are unable or unwilling to undergo magnetic resonance imaging (MRI) scanning. The pick-up rate of slowing of central motor conduction, especially where there are pyramidal signs, is similar to that of the visually evoked potential (VEP) when there are visual symptoms. CMCT can be measured to a wide range of muscles and normal

values are available for muscles in which the peripheral component of conduction is difficult to estimate. MS gives rise to pronounced slowing of conduction; the CMCT is on average prolonged by two times when there are pyramidal signs in the limb investigated. CMCT can also be prolonged in clinically unaffected muscles.

Second, in early ALS where there are no upper motor neurone signs, slowing of central motor conduction can provide valuable evidence of an additional pyramidal lesion. Only some 20% of idiopathic ALS patients show prolonged CMCT and the prolongation is very modest, amounting to only 3–4 ms in intrinsic hand muscles. However, by studying up to eight muscles in upper and lower limbs the pick up rate can be improved. The modest slowing of conduction is useful when cervical myelopathy forms part of the differential (see below) since in that condition, slowing is often pronounced. Central motor conduction to the tongue can also be measured and this can give useful diagnostic information in patients with bulbar onset ALS.

Third, in cervical myelopathy, where there is doubt from imaging studies of the level of compression, TMS with recording from a sequence of upper limb muscles can provide evidence of the level of functional impairment. For example, normal central motor conduction to say, biceps, with prolonged central motor conduction to extensor digitorum communis (EDC), FDI, and muscles further caudally would localise the impairment of cord function to the C6 segment. Slowing of central conduction is often pronounced since the primary pathology resulting from cord compression is demyelination.

In some cases of non-organic weakness, TMS has proved useful in management. The demonstration to the patient that there is continuity between brain and the paralysed limb can result in rapid resolution of the weakness. Conversely, occasional patients thought to have non-organic weakness can be shown by TMS to have a pyramidal tract abnormality.

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