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Teaching Course 18

How to diagnose a muscle disorder - Level 1

Electromyography

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I. Introduction

The role of clinical neurophysiology in the management of neuromuscular diseases (NMD) consists of various aspects:

− to localize the lesion to muscle, muscle membrane, neuromuscular junction, peripheral nerve or motor neurone

− to determine etiology, disease severity, disease distribution and treatment response

− to select a site for muscle biopsy

Usually, a combination of neurophysiological techniques has to be applied, the exact selection being decided by the clinician during the examination, based on clinical and laboratory findings. At the end of the studies, only a consideration of all clinical and electrophysiological data will deliver a tentative diagnosis or at least a category of disease.

Typically, nerve conduction studies are performed first to exclude peripheral neuropathies and aid in the differential diagnosis of motor neurone disease (MND) and presynaptic neuromuscular junction (NMJ) disorders. In the appropriate clinical scenario, repetitive nerve stimulation (RNS) and - very rarely - single-fiber EMG are used to confirm NMJ disorders and to establish whether they are presynaptic or postsynaptic. The most valuable electrodiagnostic tool for the evaluation of suspected myopathy is, however, needle electromyography (EMG) using concentric needle electrodes. Special electrodes, such as single-fiber and macro-EMG needles are not used routinely.

Conflict of interest:
The author has no conflict of interest in relation to this manuscript
II. Physiological and technical basis of EMG

II.1 Physiology of the motor units

All muscle fibers innervated by a spinal motor neurone and its axon constitute a motor unit, following the definition of Sherrington [1]. The number of muscle fibers in a particular motor unit is highly variable (5-10 fibers in eye muscles, 2000 fibers in leg muscles). The territory occupied by a motor unit is 5-10mm in diameter and fibers of several motor units are intermingled in this territory [Fig 1]. In this area, fibers belonging to the same motor unit occur isolated or in pairs, very rarely in multiplets. This avoids interference of contractions between neighbouring motor units and has consequences for the shape of the motor unit action potentials (MUAP) in the EMG.

Figure 1: Muscle fibers of an individual motor unit are intermingled

II.2 Technical aspects of EMG recordings

Cutaneous electrodes record the sum of all MUAPs from the motor units under the electrode (compound muscle action potential = CMAP) and are used for nerve conduction studies. In contrast, concentric needle electrodes record single or only few MUAPs in the vicinity of the needle
tip, thus necessitating frequent repositioning of the needle to allow for multiple sampling during an EMG-examination.

Concentric needle electrodes consist of an active recording thread which is surrounded by a metal shaft acting as a reference that is electrically isolated [Fig 2]. In single-fiber electrodes, the recording tip is exposed at the side of the cannula and has enhanced selectivity for individual muscle fibers through a much smaller recording area [Fig 2]. The active recording site of a macro-electrode is the uninsulated tip of the cannula with a distant subcutaneous electrode as reference. A small side port allows a MUAP from an individual muscle fiber to be used as a trigger to time-lock and average the other fibers of the unit [Fig 2]. Macro-EMG is not routinely used any longer.

Commercially available EMG-machines permit low- and high frequency filtering of signals and now also allow for automated analysis of MUAP and recruitment pattern (quantitative EMG). The electronic settings may considerably affect the interpretation of the automated analysis which should therefore be regarded with caution.

**Figure 2:** Recording areas of various EMG electrodes

Concentric needle electrode  single-fiber electrode  macro-electrode
II.3 Motor unit morphology [Fig 3]

Generally, reduced diameters and reduced numbers of muscle fibers, as observed in myopathies, will create low MUAP-amplitudes, which are an EMG-hallmark of myopathies. Since MUAP-amplitudes fall off sharply with increasing distance from the needle tip (90% loss of amplitude at 1mm distance), very few fibers in the immediate vicinity (0.5mm) of the needle tip contribute largely to the amplitude of the MUAP. Thus, isolated hypertrophic muscle fibers as seen in muscular dystrophies, may create high amplitude MUAPs, which classically reflect neurogenic rather than myopathic muscle damage. Repeated sampling and demonstration of small MUAPs in other parts of the muscle will, however, rectify this impression.

Figure 3: Motor unit morphology

In contrast, duration of the MUAPs is a much more stable parameter than the amplitude and largely depends on the number of fibers present in a larger recording area (2-2.5mm) from the needle tip. Loss of muscle fibers in myopathies will therefore reduce MUAP duration.

A further measurement of interest in MUAP morphology is the number of phases above and below the baseline. Polyphasic MUAPs (>4 crossings of the baseline) indicate asynchronous discharges of the muscle fibers.
belonging to one motor unit. This may be due to higher variability of muscle membrane conduction velocity which is proportional to muscle fiber size, compromised neuromuscular transmission in severe axonal loss or alteration of motor unit morphology by non-contractile tissues (fibrosis) in muscular dystrophies. Polyphasia of MUAP is therefore not a specific feature of myopathies, but may also occur in regeneration of neuropathies. Moreover, remodeling of motor units in chronic myopathies (split fibers, regenerating fibers) may also induce increased amplitudes (see above) and durations of the MUAP, thus making interpretation difficult. In such patients, the presence of two populations of MUAPs (short- and long duration) in the same muscle or the demonstration of “myopathic” MUAPs in other muscles may clarify the underlying pathological process.

II.4 Motor unit recruitment

With slowly increasing force, motor units are recruited according to the size principle of Henneman [2], i.e. smaller units are recruited first followed by larger ones until a maximum, where single MUAP cannot be distinguished from each other anymore (interference pattern). In myopathy, an early recruitment pattern may be observed, where the interference pattern at a given submaximal force is fuller than expected [Fig 4]. This occurs, because with reduced strength in myopathies, a higher firing frequency of the motor units is required to maintain a given target force. By contrast, in severe myopathies with only few remaining muscle fibers a reduced recruitment pattern with a small number of rapidly firing motor units may be detected. This reduced pattern is also typical for patients with neurogenic or motor neurone disease and might therefore pose differential diagnostic difficulties. In these cases, other
parameters (fasciculations, analysis of other muscles) are necessary to establish a diagnosis.

**Figure 4:** Recruitment pattern at a given force

A) normal

B) indolent Myopathy

C) muscular dystrophy

(note high-amplitude discharges in muscular dystrophy)
II.5 Quantitative EMG

Quantitative EMG-studies automatically identify and analyse individual MUAPs of the same motor unit, which are selected by a trigger according to their morphology and are then averaged before analysis [3]. For statistical purposes, a sample should consist of at least 20 MUAPs.

MUAP parameters (duration, amplitude, phases, turns, area, area/amplitude ration, rise) are then analysed by an appropriate computer algorithm and compared to age-matched normative data. The most sensitive parameters for the identification of myopathies seem to be MUAP duration and area/amplitude. Both parameters are particularly sensitive to loss of muscle fiber action potentials within a motor unit.

Automated analysis of the interference pattern assesses the “density” of the interference pattern by measuring the number of turns (=phase changes >0.1mV, which do not cross the baseline) per second and the mean amplitude of the potentials between turns. Patients with muscle disease will have an increased turns/amplitude ratio, whilst those with neuropathy will have a reduced ratio [4]. Some studies have shown that quantitative analysis of the interference pattern is more sensitive for the detection of myopathy than analysis of motor unit morphology [5]. On the other hand, everyday experience does not always support this notion, because interference pattern analysis is highly dependent on the force of the contraction [6]. Strictly speaking, standard forces should therefore be employed for interference pattern analysis, which is not practical in everyday routine EMG. It is therefore not clear, whether quantitative studies significantly improve the sensitivity or specificity for the diagnosis of myopathies [4].
II.6 Special EMG-investigations

II.6.1 Single-fiber EMG

The single-fiber EMG electrode records MUAPs within about 0.3mm of the recording tip, and thus a single muscle fiber belonging to a motor unit [Fig 2b]. Two parameters, fiber density (FD) and jitter, are of the greatest value in SF-EMG.

- fiber density is the average number of muscle fiber potentials in the uptake area of the single-fiber electrode on 20 separate insertions. It is normally about 1.5 - 2. FD is reduced when muscle fibers atrophy and is increased as a result of nerve fiber sprouting and collateral innervation of denervated muscle fibers. FD is increased in most myopathies due to fiber splitting, even in muscles which are clinically not affected yet [7].

- jitter is the small difference in the interpotential time interval between successive discharges [Fig 5]. In myopathy, jitter may be raised because of increased variability of signal velocity along abnormal muscle fibers. But jitter may also be very low due to muscle fiber splitting, where both fragments are innervated by the same endplate and fire simultaneously. Traditionally, SF-EMG is used for the diagnosis of neuromuscular junction disorders, but may also be pathological in motor neurone disease.

Figure 5: Single-fiber EMG
II.6.2 Macro-EMG

This is not used routinely.

II.6.3 Short- and long-exercise test

Exercise produces characteristic changes of CMAP amplitudes in myotonic disorders. Short exercise (10sec) induces an immediate drop of the CMAP-amplitude followed by recovery within 2min - this is typical, but not diagnostic of, sodium channelopathies. Long-exercise is useful in patients with hypokalemic periodic paralyses and induces a prolonged drop of CMAP-amplitudes by more than 40% [8]. Due to the widespread availability of molecular genetic testing, exercise testing is now rarely performed.

III. General findings during an EMG

For primary muscle disorders, EMG is the most sensitive electrodiagnostic procedure. Symptomatic (weak) muscles should be specifically examined, but depending on the disease some muscles may be particularly informative, for example the infraspinati and glutaei in inflammatory myopathies [9].

EMG examines neuromuscular status in four steps:

- insertional activity (needle movement with muscle at rest)
- spontaneous activity (needle stationary with muscle at rest)
- MUAP analysis with mild voluntary contraction
- recruitment pattern with maximum force

III.1 Insertional activity

Needle insertion into the muscle provokes a short (<250msec) burst of electrical activity caused by mechanically induced spontaneous depolarization of muscle fibers. Reduced or absent insertional activity is
seen in muscles which have been replaced by connective tissue or fat (end-stage myopathies) or in inexcitable muscle cells during attacks of periodic paralyses. Prolonged insertional activity occurs when muscles are abnormally excited as in acute myonecrosis (myositis, dystrophies) or denervation. The prolonged and high-frequency activity seen when the needle is placed in the end-plate zone (=end-plate noise) must not be confused with increased insertional activity; the former disappears when the needle is repositioned.

### III.2 Spontaneous activity

Spontaneous activity comprises fibrillations and positive sharp waves, complex repetitive discharges (CRD), fasciculations and myokymia.

*Fibrillations and positive sharp waves* originate from single fibers and represent spontaneous oscillations of the membrane potential. They are short (<5msec) and have bi- or triphasic wave-forms and usually fire in a regular pattern at rates of 1-20Hz [Fig 6a]. Although fibrillations are commonly seen in neurogenic disorders, they also appear in myopathies with prominent fiber necrosis (dystrophies) or in inflammatory or necrotizing myopathies. In these cases, fibrillations probably result from denervation of intramuscular nerve fibers secondary to muscular necrosis. Also, myonecrosis may cause changes to the muscle membrane channels and thus induce spontaneous depolarisations. Inherited disorders of muscle membrane function (channelopathies) are also frequently associated with fibrillations and positive sharp waves. Less consistently, fibrillations are found in myopathies where apoptosis rather than necrosis is predominant (FSHD, OPMD, LGMD).
The quantity of fibrillations is graded on a four-point scale:

+1 rare potentials, recordable in one or two sites only
+2 occasional potentials, recordable in more than two sites
+3 frequent potentials, recordable regardless of needle position
+4 abundant potentials, filling the screen

Complex repetitive discharges (CRD) typically have an abrupt onset, maintain a constant firing rate and cease abruptly. They represent a cluster of muscle fibers firing as a group which is driven by a pacemaker fiber that ephaptically spreads its activity to adjacent fibers and thus synchronizes the discharges within the group [11]. Other - now discarded - terms for CRD are “pseudomyotonia” and “bizarre high-frequency discharges”.

CRD occur in a variety of chronic denervating conditions, but are also encountered in some chronic myopathies (Pompe, Duchenne, inclusion body myositis). CRD are found more frequently in myopathies with protein accumulations, vacuoles and nuclear protein defects, such as Pompe, IBM and centronuclear myopathy, compared to myopathies with sarcolemmal protein defects.

Fasciculations and myokymia are spontaneous discharges of groups of muscle fibers which belong to the same motor unit. They are always of neurogenic origin and may develop anywhere along the peripheral nerve or in the motor neuron, most often in distal sections of the nerve or near the motor terminals.

Myokymia is characterized by more complex bursts [Fig 6c] and is seen in chronic neurogenic (radiation plexopathies, Guillain-Barre-syndrome) and
even central disease (Multiple sclerosis, brain stem glioma), but not usually in myopathies.

*Myotonic discharges* are usually triggered by needle insertion, but outlast the insertion activity interval. They are characterized by bursts of potentials of short duration which progressively increase and decrease their amplitude and firing frequency ("wax and wane") [Fig 6d]. The basic abnormality is failure of membrane repolarization beyond the threshold level, thus allowing further spontaneous depolarizations. The underlying disorders include congenital myotonias, dystrophic myotonias, Pompe disease and some rare myopathies (cytoplasmic body myopathy). Indeed, EMG may uncover myotonic discharges even in the absence of clinical myotonia.

**Figure 6:** Spontaneous activity

A) Fibrillations

B) Complex-repetitive discharges
C) Myokymia

III.3 MUAP analysis

MUAP analysis is performed during light voluntary contraction. Important parameters of MUAP morphology are amplitude, area, duration and phases (also see II.3).

In myopathies, MUAP-amplitude and MUAP-duration are decreased due to loss of muscle fibers within the motor unit. Fewer than 5-10 fibers lying in proximity to the needle tip, contribute most to MUAP-amplitude, thus making MUAP-duration more consistent for the diagnosis of a myopathy than MUAP-amplitude. Therefore, an increased variability of MUAP-amplitudes is suggestive of primary muscle disease.

Polyphasia is caused by desynchronization of muscle fiber excitation and is a feature of myopathies, neuropathies and motor neuron disorders. In the context of a myopathy, it is indicative of myonecrosis with fiber splitting and increased variability of fiber diameters.
In addition to polyphasia, the \textit{MUAP-waveform} may change with recurrent discharges, i.e. be unstable, which is a further indicator of myonecrosis and is often seen in conjunction with spontaneous activity.

\textbf{III.4 Recruitment pattern}

This was discussed in II.4

\textbf{IV. EMG-findings in specific myopathies}

Normally, EMG does not permit a differential diagnosis between individual muscle diseases. Some particular aspects may, however, point towards a specific myopathy and greatly aid the further diagnostic pathway, in particular the choice of molecular genetic analysis.

\textbf{IV.1 Muscular dystrophies}

The presence of considerable spontaneous activity (fibrillations, positive sharp waves, CRD), increased insertion activity and short, polyphasic MUAP with early recruitment indicates myonecrotic pathology, as commonly seen in dystrophinopathies. Other dystrophies, such as FSHD or LGMD, have much less or no spontaneous activity, although MUAPs may also look “myopathic”. EMG findings can also give information about disease stage: in late stages insertional activity is reduced (replacement of myocytes by fibrous tissue), MUAPs may be of long duration and the interference pattern may be incomplete (loss of muscle fibers in motor units).

\textbf{IV.2 Inflammatory myopathies}

In polymyositis and dermatomyositis, the presence of spontaneous activity (fibrillations, positive sharp waves, CRD) is a constant feature, alongside
with short, small and polyphasic MUAPs. The degree of spontaneous activity may serve as a marker for treatment response, because it tends to decrease when the inflammation subsides. EMG is also very useful for choosing the most suitable muscle for biopsy.

In inclusion body myositis, a typical finding is the co-occurrence of myopathic and neurogenic changes, which might complicate the differentiation from a motor neurone disorder. Spontaneous activity resembles that seen in polymyositis and dermatomyositis.

**IV.3 Endocrine myopathies**

These myopathies show no consistent picture, in the majority of patients EMG is normal. In a myositis patient on steroid treatment, EMG is a valuable tool to distinguish a steroid myopathy (no spontaneous activity) from a myositis relapse (abundant spontaneous activity) and to further guide therapy.

**IV.4 Metabolic myopathies**

In most metabolic myopathies EMG is normal or non-specific, with the exception of two glycogenoses:

- Pompes disease frequently shows prominent spontaneous activity (fibrillations, CRD, myotonia), particularly in proximal and paraspinal muscles.

- McArdles disease displays a peculiar EMG finding: following intense exercise, a painful muscle contracture may develop which is electrically silent. This contrasts to other diseases with painful muscle cramps, where abundant electrical activity is recorded.
IV.5. Myotonias

Myotonic discharges are a major diagnostic clue in myopathies and narrow the differential diagnosis considerably: the myotonic dystrophies (DM1 and DM2) may be distinguished by the distribution of myotonia (more proximal in DM2, more distal in DM1). Congenital non-dystrophic myotonias are reported to have shorter discharges than the dystrophic myotonias, but this does not always hold true. Aggravation of the myotonia by cold and exercise points towards a sodium channel paramyotonia.

IV.6 Lambert-Eaton myasthenic syndrome

A striking feature in LEMS and other presynaptic defects is a massive reduction of basal CMAP-amplitude. Brief maximal voluntary contraction (10-20sec) will greatly increase the CMAP-amplitude (>100%). As in other myasthenic syndromes a decremental response will be observed after low-frequency (3/sec) repetitive nerve stimulation. The EMG in LEMS is normal.
**Table 1a:** Myopathies with spontaneous activity (fibrillations, positive sharp waves)

<table>
<thead>
<tr>
<th>Myositis (DM, PM, IBM)</th>
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<tbody>
<tr>
<td><strong>Myofibrillar myopathies</strong></td>
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<tr>
<td>Centronuclear myopathies</td>
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<tr>
<td><strong>Dystrophinopathies</strong></td>
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<tr>
<td>Some congenital myopathies (nemaline M.)</td>
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<tr>
<td><strong>Myotonias (dystrophic and non-dystrophic)</strong></td>
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<tr>
<td>Glycogen storage disease (Pompe, McArdle, Forbes)</td>
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<tr>
<td><strong>Toxic myopathies</strong></td>
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**Table 1b:** Myopathies with spontaneous activity (complex-repetitive discharges)

<table>
<thead>
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<th>Myositis (DM, PM, IBM)</th>
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<tr>
<td><strong>Dystrophinopathies</strong></td>
</tr>
<tr>
<td><strong>Myofibrillar myopathies</strong></td>
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<tr>
<td>Some distal myopathies</td>
</tr>
<tr>
<td>Glycogen storage diseases (Pompe, McArdle, Forbes)</td>
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**Table 1c:** Myopathies with spontaneous activity (myotonic discharges)

**With clinical myotonia**

| Myotonic dystrophies (Type 1 and Type 2) |
| Sodium channel myotonia (Paramytonia, periodic paralysis) |
| Chloride channel myotonia |
| **Myofibrillar myopathies** |

**Without clinical myotonia**

| Centronuclear myopathy |
| Glycogen storage disease (Pompe, McArdle, Forbes) |
| **Myositis (DM, PM, IBM)** |
| Hypothyroid myopathy |
| **Toxic myopathies (chloroquine, cyclosporine, statins)** |
References