Electromyography

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2.1 Introduction

Myopathies are a heterogeneous group of diseases induced by numerous pathogenic mechanisms that include many different phenotypes and show a variable muscle pathology. Diagnostic approach can be simple in some instances, but it can also be ambiguous when symptoms are very light or when the hyposthenia involves distal muscles. In the majority of cases, a careful clinical examination, the personal and family history, and the biochemical data are sufficient to formulate a differential diagnosis with a neurogenic process. When this is not possible, the most useful investigations are the electrodiagnostic studies and more specifically the muscle examination by means of needle EMG. This technique is also very useful for guiding the choice of the muscle to be eventually biopsied, to characterize the distribution of the involved muscles, and to set the severity of the myopathy. Nerve conduction studies and tests for neuromuscular transmission (NMT), which includes the repetitive nerve stimulation (RNS) and single-fiber electromyography (SFEMG), are needed in special cases with the aims to confirm the clinical suspect of a NMT disorder and to establish whether it is presynaptic or postsynaptic.

In this chapter, we will illustrate the neurophysiologic findings most useful for the differential diagnosis of a myopathy with respect to a neurogenic disease, and moreover we will try to correlate EMG findings with muscle pathology with the aim to give useful data for the identification of a specific form of myopathy.

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2.2 Anatomo-physiological Basis

A motor neuron in the anterior horn of the spinal cord, its axon, and all the muscle fibers it innervates constitute a motor unit (MU), according to the definition of Sherrington [1]. The MU is the smallest part of a muscle that can be activated voluntarily. The number of muscle fibers belonging to the same MU (innervation ratio) varies considerably among the muscles. Normally, the muscles which perform fine movements have few fibers for MU (i.e., 5–10 in the external muscles of the eye), while muscles whose task is to generate as much strength as possible can have thousand of fibers in their MU (i.e., almost 2 thousand in the gastrocnemius muscle). Each MU occupies a circular territory in the muscle of about 5–10 mm in diameter, and in this area, fibers of several MU (from 5 to 30) are intermingled. The distribution of muscle fibers in the cross-sectional area of a muscle shows that fibers sharing the same innervation (belonging to the same MU) are generally isolated, less often in pairs and very rarely they are associated in number of three or more. This peculiar distribution avoids the interference between twitches of neighboring MUs and limits the interaction between action potentials of muscle fibers of the same MU. According to their biochemical and physiological characteristics, the MUs of human muscle can be classified into three main groups, namely, the slow-twitch, oxidative type which have the smallest axons, slow firing frequency, high content of oxidative enzymes, low content of glycogen and phosphorylase, and high resistance to fatigue and express low tension. The second type of MUs is called fast-twitch, oxidative, and glycolytic type, and they have high content of both oxidative enzymes and glycogen and phosphorylase; they also have high resistance to fatigue but can express a medium tension. The last type are the fast-twitch, glycolytic type; these MUs have the largest axons, high content of glycogen and phosphorylase, low content of oxidative enzymes, and low resistance to fatigue but can express a high tension during bursts of high-frequency discharge [2]. The electrical activity produced by voluntary contraction of muscles or in response to motor nerve stimulation can be recorded by intramuscular electrodes (needle EMG) or by cutaneous electrodes (motor nerve conduction) and is a very important tool for the investigation of muscle and peripheral nerve diseases. Cutaneous electrodes can record the electrical potential generated by the whole muscle (compound muscle action potential, CMAP), while concentric needle intramuscular electrode can record the electrical potential generated by a single MU (motor unit potential, MUP); both potentials are in volume since they are recorded in the extracellular space; therefore, their peak-to-peak voltage declines steeply with radial distance from muscle fibers that originate the corresponding transmembrane potential. Needle electrode can also capture the single-fiber potential when they originate spontaneously from a denervated muscle fiber and are called fibrillation or denervation potentials. The MUPs recorded with a concentric needle electrode have three parameters that need to be considered for a reliable evaluation of the investigated muscles: duration, amplitude, and morphology. All the parameters largely depend on the number of muscle fibers, belonging to the same MU, included in the recording area of the electrode, on their caliber, and on their degree of synchronization. In other words, the clustering of muscle

fibers of the same MU close to the leading-off surface of the electrode will increase the peak-to-peak amplitude of the MUP; vice versa, a reduced number of muscle fibers will reduce the amplitude. However, if the caliber of few surviving fibers is clearly increased (i.e., hypertrophic fibers), it is still possible to record a high-amplitude MUP. The MUP duration is a more stable and repetitive parameter than the amplitude and largely depends on the number of the MU fibers present in a large recording area (almost 2.5 mm). Therefore, the pathological processes which induce primary loss of muscle fibers habitually also determine a reduced MUP duration, while the diseases which imply axon sprouting or regeneration with clustering of muscle fibers belonging to the same MU increase MUP duration. The MUP morphology can vary from the classical biphasic or triphasic shape to a polyphasic shape (more than four phases crossing the baseline) when muscle fibers do not discharge synchronously. This can happen when the neuromuscular transmission is compromised or when noncontractile tissues (lipids or connective) have modified the MU spatial distribution. All the MUP parameters vary according to the patient age and the examined muscle; therefore, every evaluation must be performed with respect to the normative data that should be produced by the laboratory which has performed the neurophysiological exam. The CMAP amplitude is the most important parameter for evaluating the integrity of MU number in an examined muscle. However, some variability due to technical and anatomical aspects is always present, and a variation from normal values of at least 40 % should be considered. In addition, it is true that the loss of motor units is the most frequent cause of reduction of CMAP amplitude; however, if there is a severe loss of muscle fibers in a long-standing dystrophic process, the same finding can also be recorded. The order of MU recruitment is task related and can also vary according to the preexisting experience. However, the size principle of Henneman is the rule when a gentle movement is required; therefore, the small MU will be recruited first [3]. Thereafter, if a greater tension is needed, the large MU will intervene. The electromyography system can analyze the single MUPs of small MU, but cannot see individual MUP of large MU, which can be analyzed only by automatic system. It is possible to record the MU recruitment, and this is normally progressively increasing until a maximum where the single MUP cannot be recognized from each other (interference pattern). This technique needs the cooperation of the patient and is anyway difficult in some muscles (e.g., gastrocnemius). With this limitations, it is however possible to observe a reduced recruitment pattern (single oscillations or mixed pattern) with high amplitude in neurogenic diseases, while a fast interference pattern with low amplitude is frequent in myopathic diseases, at least if this is not very long lasting. Overall, a normal MUP requires that in the recording area of the needle electrode, muscle fibers of a single MU are present with normal density and have a homogenous caliber and an efficient neuromuscular transmission. When a disease modifies the anatomical setting with a new pattern that occupies a large part of the muscle, the MUP parameters will change accordingly. In these cases, the analytical evaluation of at least 20 MUPs will show an increase or a decrease of duration and of amplitude and a high or normal percentage of polyphasic shape. All myopathic processes change the anatomical picture of the muscle, and many induce a prevalent

pattern. However, some muscular diseases are characterized by a variegated anatomical picture in the muscle, and the EMG findings will change and will depend on the characteristic of the area where the needle has been collocated. Therefore, one of the most striking EMG findings in muscle diseases is the high variability of MUP parameters in the same muscle.

The neuromuscular junction (NMJ) consists of the motor axon terminal, the synaptic cleft, and the highly organized postjunctional folds on the muscle membrane. The chemical transmitter at the NM junction is acetylcholine (ACh). The nerve terminal is the site of synthesis and storage of ACh, which is released in the discrete quanta. The quanta are located in three separate stores: primary (immediately available), secondary (mobilization store), and tertiary (reserve store). The number of ACh molecules in each quantum was estimated to be fewer than 10,000.

When a nerve action potential depolarizes the presynaptic terminal, voltage-dependent calcium channels are activated, allowing an influx of calcium that results in a release of ACh from the presynaptic terminal through the proteins of SNARE complex. A nerve impulse results in a release of 50–100 quanta.

The ACh diffuses across the synaptic cleft and binds to ACh receptors (AChR) on the postsynaptic membrane, resulting in an end-plate potential (EPP).

In the healthy condition, the EPP always reaches the threshold for the opening of voltage-gated sodium channel on muscle membrane, and hence EPP triggers a muscle fiber action potential (MAP) that, propagating along sarcolemma down T tubules, results in muscle contraction. The amplitude of the EPP above the threshold value needed to generate a MAP is called the safety factor (SF).

The SF is reduced in patients with a disorder of NMT. The failure of the EPP to reach MAP threshold represents the basis of the electrodiagnostic abnormalities in patients with disorders of NMT [4]. The resulting impulse blocking accounts for the decremental responses seen on repetitive nerve stimulation (RNS) studies and the impulse blocking seen with single-fiber electromyography (SFEMG). In addition, the time variability of when the EPP reaches MAP threshold accounts for the neuromuscular jitter seen in the latter technique [5, 6].

SFEMG is an electromyography (EMG) technique that allows to record action potentials from individual muscle fibers (i.e., single MAPs). The selectivity of this technique relies on the small recording surface of needle electrodes. This can be obtained by using either dedicated SFEMG needle electrodes that have a small recording area (0.0005 mm^2) or conventional EMG needle electrodes after proper filter setting since these have larger recording area (0.07 mm^2).

SFEMG recordings can be performed during electrical stimulation of the nerve (S-SFEMG) or during voluntary activation (V-SFEMG) of the tested muscle [7–10].

When MAPs are elicited by nerve stimulation, the latency from stimulus to response (i.e., MAP) varies. This variation is due to physiologic fluctuation in the time for EPP to trigger MAP, and it represents the neuromuscular jitter.

When SFEMG is performed during voluntary activation, the needle electrode, inserted into the tested muscle, records from two or more MAPs that belong to the same motor unit (MU) and that hence depolarize synchronously. In this case, the

neuromuscular jitter is the variations in the time intervals between pairs of MAPs. This variation is related to physiologic fluctuation in the time that EPP takes to trigger each MAP in the examined pair of potentials.

Jitter is the most sensitive electrophysiological measure for the safety factor of NMT. In disorders of NMJ, the reduction of EPP may cause a delay in triggering MAPs, or if the EPP falls below the threshold, MAP is not generated. In the former, jitter will be increased; in the latter, SFEMG recording will demonstrate neuromuscular blocking. For *V-SFEMG* the subject is asked to maintain a steady contraction, and recordings of two or more MAPs belonging to the same MU can be performed by dedicated SFEMG or conventional EMG needle electrode. Around 20 different potential pairs are collected from the tested muscle. Theoretically, all muscles can be investigated with SFEMG. However, OO and EDC muscles are commonly investigated in clinical practice even though in some patients (e.g., MuSK positive), the examination of the most severely involved muscles to demonstrate abnormal jitter may be necessary. The following parameters should be recorded: the mean jitter (MCD) of all ($n=20$) potential pairs or stimulated MAPs, the percentage of potential pairs or stimulated MAPs in which jitter is abnormal, and the percentage of NM blocking.

The SFEMG examination is considered abnormal if at least one of the following criteria is satisfied:

1. The mean jitter (MCD) of all potential pairs or stimulated MAPs recorded exceeds the upper limit of mean jitter for that muscle.
2. Ten percent or more of potential pairs or stimulated MAPs have jitter that exceeds the upper limit of normality in that muscle or if more than 10 % of potential pairs/stimulated MAPs exhibits NM blocking.
   (a) Generally, NM blocking is observed when also jitter value is markedly increased.

Repetitive nerve stimulation (RNS) is a variant of the nerve conduction study since electrical stimulation is delivered to a motor nerve repeatedly several times per second [6].

The function of NMT is assessed by measuring after a train of stimuli the change in amplitude/area of the compound muscle action potential (CMAP) that represents the sum of the individual MAPs generated in a muscle. The train of stimuli may be carried out at low- (3 Hz) or high-frequency stimulation (20–50 Hz).

Low-frequency stimulation (e.g., train of 10 stimuli at 3 Hz) causes a depletion of ACh level in synaptic space since after the releasing of primary (immediately available) storage, it will be needing a time of 1–2 s for the mobilization of quanta from secondary storage. In this meantime, the amplitude of the EPP reduces (this phenomenon is known as synaptic fatigue). However, in normal subjects for the safety factor, EPP never falls below the threshold needed to generate a MAP. Vice versa for patients with NMJ disorders, the EPP of some muscle fibers may fall below the threshold level, and MAPs will not be generated. This reduction of MAPs is responsible for decremental response of CMAP when performing RNS studies.

The size of CMAP may be assessed by measuring either the amplitude or the area of the negative peak of the CMAP. In disorders of NMT, there is a progressive decrement of the second through the fourth or fifth response, with some return toward the initial size during the subsequent responses, a so-called U-shaped pattern. Decrement is defined as the percent change comparing the negative peak amplitude or area between the fifth (or fourth or lowest potential) and the first CMAP. The decrement is generally considered abnormal when greater than 10 %.

High-frequency stimulation (20–50 Hz for 5–10 s) may be used to investigate presynaptic level of NMJ. The high-frequency stimulation induces (rate faster than time needed [100–200 ms] for exit of calcium from terminal nerve) the accumulation of calcium ions in the preterminal space producing a transient increase in the amount of ACh released from the motor nerve. This greater ACh release increases the EPP and may improve synaptic transmission briefly (this phenomenon is known as facilitation). In healthy subjects, the EPP is already (safety factor) above the threshold for eliciting MAP, and high-frequency stimulation does not induce any change in CMAP size. A phenomenon of "pseudofacilitation" (increase of amplitude associated with reduction of duration of CMAP; area remains unmodified) can be observed, and it is attributed to increased synchronization of MAPs or to hyperpolarization of the muscle fiber membrane from increased sodium-potassium pumping. In normal muscle, pseudofacilitation may increase the CMAP amplitude to 50 % during stimulation at rates up to 50 Hz.

In a patient with a disorder that affects NMJ at presynaptic level (e.g., Lambert-Eaton myasthenic syndrome), after single electrical stimulus, few quanta of ACh are released, and the EPP frequently fall under the threshold. Therefore, the CMAP size may be reduced after single electrical stimulus, while during (or immediately after) high-frequency stimulation, the calcium accumulation in terminal nerve causes a massive releasing of ACh, and the EPP raises above MAP threshold resulting in an incremental response of CMAP. An increment greater of 60–100 % is considered of significance.

High-frequency stimulation is painful and requires patient tolerance, and thus in clinical practice, maximal voluntary muscular contraction (protracted for 10–60 s) is used to obtain the same effect of high-frequency nerve stimulation.

After the phase of facilitation, NMJ develops a phase of postactivation exhaustion, in which less ACh is released by each nerve impulse. The exhaustion lasts 2–5 min (maximum at 3 min) after the end of activation. In this period, low-frequency stimulation worsens the decrement of CMAP or may unmask a decrement not evident at the basal stimulation performed before the activation. Generally, after 5 min the change of CMAP size observed during low-frequency stimulation comes back to basal condition. RNS is more likely to be abnormal in proximal and facial muscles, rather than in limb distal muscles. To have the maximum diagnostic sensitivity, examination of several muscles, including those that are involved clinically, may be necessary. Hand muscles are easy to test but scarcely sensitive. Recording can be made from thenar or hypothenar muscles by stimulating median or ulnar nerves at wrist. Such stimulation is suitable if prolonged high-frequency stimulation is required. Proximal muscles have greater sensitivity than distal muscles. The

trapezius is the easiest shoulder muscle to test. The spinal accessory nerve is stimulated at the neck where it is superficial so that it can be maximally stimulated with low-intensity pulses, minimizing discomfort and stimulation of other muscles. Recordings can be also made from biceps brachii or deltoid muscles by stimulating musculocutaneous nerve in the axilla or axillary nerve at the Erb point. However, such stimulations are often disturbed by movement artifacts and stimulation/activation of near muscles. Facial muscles have the greatest sensitivity. Recordings are made from orbicularis oculi or nasalis muscles by stimulating facial nerve at tragus or stylomastoid foramen. This study may be performed with the patient either sitting or lying. Temperature influences the CMAP size and decremental response is less evident when the muscle is cool. Low temperatures reduce enzymatic activity of acetylcholinesterase in synaptic cleft, increasing the availability of ACh and increasing the EPP. Hand or foot muscles should be warmed to a surface temperature of at least 34 °C to avoid false negative results in patients with a disorder of NMT. In a patient with suspected disorder of NMT, the standard procedure consists of:

1. Low-frequency stimulation (10 stimuli at 3 Hz) to detect the decrement of CMAP amplitude/area.
2. If the test is positive (decrement of CMAP >10 %), the patient should undergo:
   (a) High-frequency stimulation (20 Hz for 5 s) or preferentially maximal voluntary muscular contraction (protracted for 30 s) to evaluate facilitation
   (b) Low-frequency stimulation every minute up to 5 min to evaluate postactivation exhaustion
3. If the test is negative (decrement of CMAP ≤10 %), the patient should undergo:
   (a) High-frequency stimulation (20–50 Hz for 5–10 s) or preferentially maximal voluntary muscular contraction (protracted for 60 s)
   (b) Low-frequency stimulation every minute up to 5 min in order to unmask a decremental response of CMAP during the phase of postactivation exhaustion

The high-frequency stimulation or maximal voluntary muscular contraction is essential in detecting presynaptic neuromuscular diseases by showing a significant increment of CMAP size (>60 %). If a small CMAP amplitude is observed at basal examination after single electrical stimulus, a presynaptic disorder should be strongly suspected. In this case, also a brief maximal voluntary muscular contraction (10 s) may be sufficient to disclose an incremental response of CMAP size.

In the next paragraphs, we will describe how to plan the EDX examination and the interpretation of most frequent findings according to the anatomical picture [11, 12].

2.3 Plan of the Electrodiagnostic Examination

Nerve conduction studies (NCS) in patients with suspected myopathy should include at least one motor and one sensory recording, in at least one upper and lower limb. Both sensory and motor nerve conduction studies are generally

normal in myopathies. However, in some distal phenotypes, it is possible that the loss of muscle fibers is enough to decrease the CMAP amplitude, but in this case, the distal latency and motor conduction velocity should be normal. Needle EMG is required to differentiate a motor neuron disease. A reduced CMAP amplitude is also present in case of presynaptic disorder (e.g., Lambert-Eaton disease), and a differential diagnosis is required by means of RNS. Sensory nerve conduction could be distally reduced in some myopathic disorders as the myotonic dystrophy type 1 or the critical illness myopathy, in which sensory endings can be involved in the context of a coexistent neuropathy. Proximal and distal muscles should be investigated, and upper and lower limb of one side must be considered. The most easy muscle to explore are deltoid, biceps, abductor digiti minimi, quadriceps (rectus), and tibialis anterior; however, the choice should be guided by clinical observation or by the diagnostic hypothesis. If an inclusion body myositis (IBM) is supposed, the flexor digitorum muscle should be considered; when a glycogen storage disease (e.g., Pompe disease) is a possibility, then paraspinal muscles must be investigated. In this case, cervical and lumbosacral levels should be avoided for the frequent coexistent radiculopathy, and a thoracic level is the best choice. EMG analyses can help for choosing the muscle to be biopsied; it should be a weak but not severely affected muscle. The EMG examination is more sensitive than clinical observation and can reveal an involved muscle that has escaped clinical evaluation. However, the biopsy cannot be performed in a muscle recently investigated by needle EMG. Needle EMG should give data about the presence of muscle irritability on insertion of the needle, the state of the muscle at rest, and the analyses of MUPs during slight effort. Finally, it is important to record the recruitment behavior at moderate and maximum effort [13].

2.4 General Findings

2.4.1 Resting Activity

In a normal resting muscle, the only electrical activity that is possible to record derives by the miniature end-plate potentials when the needle electrode is very close to the end plates. However, the needle introduction in the muscle can induce discharges of MFs that are called insertional activity and is generally very short (less than 250 ms). This activity is produced by the mechanical irritation of the needle electrode on the nearby end plate. The insertional activity can be abnormally prolonged when the muscle is denervated or in case of myotonias, polymyositis, or some muscular dystrophies suggesting an aspecific hyperexcitability of MFs. However, the normal insertional activity can also be decreased, e.g., in long-lasting or end-stage myopathies, when most of the muscle fibers are replaced by fat or connective tissue. In this case, it is also possible to feel an increased resistance to needle insertion due to the advanced fibrotic substitution of the muscle. Other types of abnormal electrical activity can

originate in the muscle itself [14] as fibrillations, complex repetitive discharges (CRD), and myotonia.

Fibrillation potentials are muscle fiber action potentials recorded outside the end-plate zone; are spontaneous, biphasic, or triphasic in shape; and are of very short duration (1–5 ms) [15]. They are generally seen in neurogenic diseases but can be present in several primary muscle disorders, as Duchenne muscular dystrophy, dermatomyositis and polymyositis, Pompe disease, sporadic inclusion body myositis (sIBM), and centronuclear myopathy (CNM). The origin of fibrillation potentials in these diseases can be produced by the denervation of muscle fibers secondary to focal fiber necrosis, as in Duchenne dystrophy, or to the inability of a regenerated but isolated fiber to be innervated for the excessive distance from the innervation zone. An additional explanation could be a modification of muscle membrane properties with an increased excitability. In polymyositis, it is also possible that there is an inflammatory direct damage of intramuscular axon branches [16]. Less consistently fibrillation can be observed in facioscapulohumeral (FSHD), limb girdle (LGMD), and oculopharyngeal dystrophies. Overall fibrillation potentials are the most frequently pathological spontaneous activity that can be observed in muscle diseases [17].

CRD are complex potentials showing multiple spike components, with a total duration ranging from 50 to 100 ms. They discharge repetitively at a low (5 Hz) or high (100) frequency, generally with a stable waveform that is typically polyphasic, from one discharge to another, and they have an abrupt onset and cessation. However, the waveform can change suddenly at the higher firing frequency due to the intermittent block of some spike components. The origin of CRD is the spontaneous firing of a pacemaker muscle fiber which ephaptically drives few or several adjoining muscle fibers [18]. The CRD have been described both in muscle and peripheral nerve diseases. Since CRD are very frequent in adult onset form of Pompe disease and especially in paraspinal muscles, they have been included as a diagnostic feature in the diagnostic guidelines of the American Association of Neuromuscular and Electrodiagnostic Medicine [19]. CRD are rarely observed in LGMD and FSHD, while they seem to be more frequent in Duchenne than in Becker muscular dystrophies [20]. CRD are also present in almost half of patients affected by sIBM, with a higher frequency in paravertebral muscles. According to a recent analysis, CRD seem to occur more frequently in myopathies with protein accumulations, vacuoles, and nuclear protein defects, e.g., Pompe disease, sIBM, and centronuclear myopathy, rather than in myopathies with a sarcolemmal protein defect, e.g., Becker and LGMD [17].

Myotonic rhythmic discharges can be induced by a voluntary movement or by an electrical or mechanical stimulation of a muscle and can be seen in congenital myotonias (induced by both Na and Cl channel alterations), dystrophic myotonia (DM1 and DM2), congenital paramyotonia, Pompe disease, and sodium channel myotonias. Myotonic discharges may be present with or without clinical myotonia. They are characterized by a burst of potentials, with positive or negative spikes, of short duration (less than 5 ms), which progressively increase and then decrease their amplitude and frequency of firing. The pathophysiology of myotonic discharges is

not completely known in human diseases, but it probably relates on Na and Cl channel abnormalities. In fact, a reduced conductance for chloride can reduce the leak of this ion in the transverse tubular extracellular space after the depolarization with a consequent relative increase of extracellular potassium concentration (K ions are released with chloride ions). This K concentration could raise until a level which determines depolarization of transverse tubular membrane with repetitive responses to a single presynaptic impulse. The reduced chloride conductance theory can be applied to congenital myotonia, but it has not been shown in myotonic dystrophies or congenital paramyotonia. In these diseases, mutations of Na channels can cause cellular membrane instability and sensibility to temperature. In fact, myotonic discharges are increased with cooling in DM1 and paramyotonia and with warming in DM2. Several observations describe a longer myotonic discharge in myotonic dystrophies than in congenital myotonias. The electrophysiologic differential diagnosis among myotonias can be approached using the short-exercise protocol. With this technique, the variation of amplitude of the CMAPs, habitually recorded in the abductor digiti minimi muscle, at baseline and after 10 s of maximum effort every 2 s for one minute can show three different patterns. These patterns have a good sensitivity and specificity in distinguishing among the chloride and sodium myotonias [21].

2.4.2 MUP Analysis

In myopathic disorders, the number of functional muscle fibers per MU is reduced. This has the consequence of a contraction of the area of the MUs, since some of the most distant fibers are lost. The MUP duration is largely dependent on the number of muscle fibers active in the relatively large (2.5 mm) recording area of the needle electrode; therefore, if the fiber loss is consistent, the MUP duration can be shortened. Sometimes the duration and the shape of the MUP suggest that it is composed by one fiber only. In this case, it is likely that the surviving fibers belonging to the same MU are too thin to evoke a recordable potential or too isolated by the recording electrode for the presence of no contractile tissue. This finding can be more evident in weak muscles and in patients with chronic myopathy [22, 23]. However, in some instances, the short and often polyphasic main component of MU potentials is linked to late or less often preceding small potentials that discharge several ms (at least 5 ms) far from the main component of the MUP. These satellite components, if included in the measure of the MUP duration, make it very long, sometimes more than 30 ms. This finding is recordable in dystrophic diseases when there is some fiber regeneration from satellite muscle fibers or from splitted fibers. Overall, MUP duration in myopathies is shorter than normal when MUPs with satellite components are not considered. The presence of MUPs with late component is frequent also in neurogenic diseases, but in this case short MUPs are not or exceptionally recorded. The amplitude of the main component of the MUPs depends on the number and diameter of muscle fibers very close (within 1 mm) to the recording area of the

needle electrode. This makes the amplitude parameter variable also in normal subjects when single MUPs are analyzed. In muscle diseases, the fiber loss and their reduced diameter induce habitually a reduction of MUP amplitude, but the occasional presence of hypertrophic fibers close to the electrode can determine an increased amplitude of a MUP spike, otherwise short in duration. Therefore, a highly increased variability of MUP amplitude can be a finding suggestive of a primary muscle disease.

The biphasic or triphasic shape of the majority of normal MUPs is due to the homogeneity of fiber diameter and to the regular distribution of end-plate zone within the MU area, with consequent synchronous contraction of the recordable component of the MU. When there is an increased variability of muscle fiber diameter, the reinnervation of splitted or regenerated fibers and the presence of fat or connective tissue, the synchrony of MU components can be lost, and MUPs can appear polyphasic and sometimes with late components. This finding is very frequent in many muscle disorders.

2.4.3 MU Recruitment

In normal subjects, the number and the discharge frequency of MUs recruited are proportional to the tension required by the voluntary movement. If the MUs have a reduced number of functional muscle fibers or there is uncoupling between electrical and mechanical events, it is necessary to increase the number and the rate of discharge of recruited MUs. This is what happens in myopathic patients when they are requested to develop a certain muscle tension. In other words, in muscle disorders, it is possible to see in weak muscles a recruitment pattern very similar to that of normal muscles (interference pattern) with regard to the richness of MUs, but with a reduced amplitude. The increased number of recruited MUs, their high rate of discharge, and the complex shape of MUPs all determine the interference patterns seen in myopathic patients even in weak contraction, while the reduced number of functional muscle fibers in each MU is the explanation of the reduced amplitude of the potentials. This finding can be no more present when the myopathic process is long lasting and has induced a severe reduction of muscle fibers with the possibility that the electrical activity of some MUs is no more recordable.

2.5 Specific Findings

Electromyographic findings obtained with needle electrode do not permit a differential diagnosis among the several muscle diseases. However, some peculiar aspects can orientate toward a specific myopathy and can likely anticipate the histological aspects. In the following paragraphs, these findings will be shortly described for some muscular dystrophies; inflammatory, endocrine, metabolic, and congenital myopathies; and myotonias.

2.5.1 Muscular Dystrophies

The most frequent muscular dystrophies are the dystrophinopathies, Duchenne muscular dystrophy (DMD), and Becker muscular dystrophy (BMD). The diagnostic procedure, after the clinical evaluation, can be addressed with genetic testing, particularly when there is a positive family history or in some cases on muscle biopsy. Therefore, the EMG examination may be helpful in sporadic cases when clinical and biochemical data are equivocal. In these cases, needle EMG can reveal increased insertional activity, some sparse fibrillation potentials, and short, small, polyphasic MUPs with early recruitment. In late stages, EMG findings can be somewhat different according to the supervening morphological changes (muscle tissue necrosis, muscle fiber splitting, reinnervation, and muscle replacement by connective and fatty tissue). In these stages, the insertional activity is reduced and alongside with short MUP; long duration MUPs with satellite components can be appreciated [23]. At the MU recruitment, the interference pattern may be incomplete.

In other dystrophies, as LGMD, FSHD, and oculopharyngeal needle EMG can be necessary when disease onset is in adult age, CK levels are mildly elevated and clinical data are not clearly expressed. In these forms of dystrophies, fibrillation potentials and CRD are rare, while MUPs can be short, small, and polyphasic [17]. The EMG can be also useful to evaluate the distribution of weak muscles.

2.5.2 Inflammatory Myopathies

In classical poly-dermatomyositis (PM and DM), the majority of patients show classical myopathic EMG abnormalities with short, small, and polyphasic MUPs, but the presence of spontaneous activity in the form of fibrillation potentials is a constant finding. In addition, the fiber irritability is revealed also by the occasional presence of CRD or myotonic discharges (only electrical). Fibrillation and CRD can decrease with the improvement of the disease [24]. On the other end, in long-lasting forms, it is possible that long duration and complex MUPs will appear, making the differential diagnosis with a neurogenic lesion more difficult. For this the MU recruitment and the distribution of involved muscles should be useful. In polymyositis, the EMG sampling of several muscles is also very useful for the choice of the muscle to be biopsied, since sometimes the biopsy can miss the morphological abnormalities.

The sporadic inclusion body myositis (sIBM) is likely a degenerative disorder rather than an inflammatory muscle disease; however, it is traditionally included in the inflammatory myopathy chapter. The electrodiagnostic findings are similar to those in DM and PM, but the incidence of the irritative aspects and the presence of a double population of MUPs, with myopathic and neurogenic aspects, is higher in IBM than in PM and DM [25, 26]. The differential diagnosis with a neurogenic disease can be further complicated by nerve conduction studies that can reveal a mild sensory axonal polyneuropathy in up to 30 % of patients with IBM [27]. A confirmatory muscle biopsy is mandatory.

2.5.3 Endocrine Myopathies

The presence of a thyrotoxicosis can be complicated by a concomitant autoimmune myasthenia gravis. This possibility must be excluded by adequate neurophysiological techniques. Otherwise, EMG analysis does not show fibrillation; rarely, it is possible to record some fasciculations, and MUPs are generally normal but short, small MUP can be present. A steroid myopathy is more commonly induced by a prolonged prescription for the treatment of inflammatory disorders. This can happen during the treatment of a PM and can induce some diagnostic error. The EMG findings are habitually normal since there is the selective atrophy of type 2 muscle fibers and a biopsy is necessary.

2.5.4 Metabolic Myopathies

Glycogen and lipid are both important source of energy for muscle fibers. Therefore, disorders of their metabolism may have significant muscle involvement. There are several glycogen storage diseases and two well-known diseases (carnitine deficiency and carnitine palmitoyltransferase deficiency) of lipid metabolism that induce weakness, hypotonia, and sometimes respiratory insufficiency in patients of different age. Unfortunately, EMG examination can be normal or not specific for most of these diseases, with the exception of two glycogen storage forms (acid maltase deficiency-glycogenosis II or Pompe disease and myophosphorylase deficiency-glycogenosis V or McArdle disease). In all Pompe disease forms, needle EMG shows a prominent spontaneous activity with fibrillation potentials, CRD, and myotonia discharges without clinical myotonia. Myotonia discharges origin very often from a single muscle fiber [28]. Spontaneous activity is widespread in infantile and childhood onset, while in adult form it must be investigated in proximal and paraspinal muscles [19]. McArdle disease is characterized by painful muscle contracture after a vigorous exercise that shows electrical silence at needle examination. This finding is different from all other diseases with painful cramp, where an intense electrical activity can be recorded. The contracture can also be induced by a high-frequency (50 Hz) repetitive stimulation of a motor nerve, but this painful procedure is not recommended.

2.5.5 Congenital Myopathies

Congenital myopathies are a group of clinically and genetically heterogeneous muscle disorders, which cannot be distinguished from each other by means of the neurophysiological examination. Some recent observations have shown that among the centronuclear myopathy in the adult onset form mutations were identified in DNM2 gene [29], and some of patients showed CRD at needle examination (personal observation).

2.5.6 Myopathies with Myotonic Discharges

Myotonic discharges with or without clinical myotonia can be observed in dystrophic (DM1 and DM2) and in congenital myotonias which include some channelopathies. Myotonia on needle EMG is the electrophysiologic hallmark of myotonic dystrophies. The discharges are more easily obtainable in distal and proximal muscles in DM1 than DM2 and tend to be classically waxing and waning in DM1 and waning only in DM2. Moreover, myotonic discharges are longer in DM than in congenital myotonias. However, both in dominant (Thomsen disease) and recessive (Becker disease) congenital forms, the discharges are very frequent and at times it is impossible in the analysis of single MUPs. In congenital paramyotonia, cold temperature and exercise exacerbate myotonia. This paradoxic myotonia is more easily seen during hand grip or eye closure [30, 31]. Sodium channel myotonias could be distinguished from other congenital myotonias using the short-exercise protocol [21].

2.5.7 Myasthenia Gravis

MG is an autoimmune disease caused by the presence of antibodies against components of the muscle membrane localized at the NMJ. In most cases, the autoantibodies are against the acetylcholine receptor (AChR). Recently, other targets have been described such as the MuSK protein (muscle-specific kinase) or the LRP4 (lipoprotein-related protein 4) [32–34].

RNS demonstrates an abnormal decrement in a facial or shoulder muscle in 70–80 % of patients with generalized MG and in only 50–60 % of patients with ocular MG. However, in patients with MuSK-positive MG, RNS studies are frequently normal in commonly examined muscles, and testing the most severely involved muscles to detect a decremental response may be useful. SFEMG demonstrates abnormal jitter in at least one muscle in 99 % of patients with generalized MG and in 97 % of those with ocular MG. Increased jitter and blocking frequently are found in muscles in which no decrement is detected on RNS. Unlike RNS, SFEMG cannot differentiate presynaptic from postsynaptic disorders. However, in MG characterized by a postsynaptic defect, the rapid firing rate of MU increases the jitter, while in presynaptic disorders (LEMS, botulism), jitter increases at slow firing rates and decreases at fast rates.

2.5.8 Congenital Myasthenic Syndromes (CMS)

CMS are a heterogeneous group of genetically determined structural disorders of the presynaptic, synaptic, and postsynaptic element of the NMJ. Decremental response is absent in asymptomatic CM with episodic apnea and is absent at rest but elicited by 10 Hz stimulation (protracted for 5 min) in congenital choline acetyltransferase (ChAT) deficiency. Decreased amplitude of CMAP after 10 Hz RNS for 5 min may persist up to 30 min.

Lastly, in slow-channel syndrome, there is a peculiar repetitive CMAP response to single stimulus. This response is typically observed in the small muscles of the hand and foot and is abolished by RNS at 10 Hz [6, 35].

2.5.9 Lambert-Eaton Myasthenic Syndrome

Electrodiagnostic studies in LEMS are exemplificative of presynaptic disorder of NMT. LEMS is a rare autoimmune disorder due to antibodies against presynaptic voltage-gated calcium channels; most of patients with LEMS have an underlying malignancy. The most striking electrophysiological features are a reduction in the basal CMAP amplitude after single stimulus and a marked postactivation facilitation following a brief period (generally are sufficient 10 s) of maximal voluntary contraction or high-frequency stimulation (20–50 Hz for 5–10 s). Generally, CMAP amplitude increases greatly (over 150–200 %).

Decremental response to slow stimulation rates before and after the phase of facilitation can be observed as well [5, 36].

2.5.10 Botulism

Botulism is a rare and potentially fatal disease caused by toxin produced by the bacteria *Clostridium botulinum*. Botulin toxin cleaves some of the SNARE proteins inhibiting or reducing the release of ACh into the synaptic cleft. The electrodiagnostic abnormalities are quite similar to those observed in LEMS. However, the degree of facilitation is usually less marked than that observed in LEMS (>60 %). Moreover, facilitation may be initially absent in adult in whom facilitation may require more prolonged high-frequency stimulation (up to 20 s). Postactivation exhaustion is not seen in botulism [6].

Highlights

Motor unit potentials in myopathies are generally shortened and of polyphasic shape. However, the most frequent finding of needle EMG in myopathies is the increased variability of MUPs.

Some fibrillation potentials can be found in most myopathies, but they are more frequent in sIBM, acute necrotizing myopathy, and polymyositis.

CRD are present when some hyperexcitable muscle fibers act as pacemaker with ephaptic transmission to near fibers. This happens more frequently in Pompe disease and sIBM.

Cramps are associated to a florid electrical activity, while muscle contractures (McArdle disease) are electrically silent.

A reduced CMAP amplitude in a patient with fatigability must induce the suspicion of a presynaptic disorder.

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