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Role of EMG evaluation in muscle hyperactivity syndromes

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Abstract Muscle hyperactivity can be a clinical feature on its own or, more commonly, an observation on electromyography (EMG) examinations. Whatever manifestation it takes, muscle hyperactivity always means enhanced excitability of muscle, axons or neurons. Clinical findings may be variable, ranging from fasciculations to muscle cramps. Even though clinical examination may lead in most instances to suggest the diagnosis of the underlying disease, EMG studies are necessary to identify the type of abnormal discharges and suggest the site of their suspected origin. Although in clinical studies, the action potential showing abnormal muscle hyperactivity is practically always recorded from muscle fibers, the site in which the impulse has arisen will determine its shape and firing patterns. In this review, we describe the EMG characteristics observed in syndromes featuring muscle hyperactivity and the pathophysiology underlying the abnormal firing of muscle fibers.

Key words muscle hyperactivity · EMG · fasciculation · high frequency discharges · myokymia · neuromyotonia · stiff person syndrome

Introduction

Muscle hyperactivity can manifest as involuntary twitches of muscle fibers or muscle groups or, more rarely, as a long lasting spasm. Clinically evident muscle hyperactivity must be considered abnormal only when it is consistent. Occasional involuntary twitches such as those experienced in the eyelids or in other muscles are probably only reflecting transient states of general stress or nervousness. Complaints of nonspecific muscle tension or tightness are usually accompanied by almost unapparent signs on clinical inspection or superficial examination. In these instances, however, EMG studies may reveal a fair amount of sometimes unsuspected activity that may present as isolated potentials, bursts, or more complex discharges, and are usually accompanied by peculiar sounds, which call for full attention from the examiner and colleagues around. EMG recordings carry useful information regarding the characteristics of the abnormal muscle hyperactivity, its site of origin, and the underlying pathophysiological mechanisms. When muscle hyperactivity does not have clinical expression, it may become evident only if an EMG examination is carried out because of symptoms or signs that may or may not be related to the same disorder as muscle hyperactivity. In these instances, the physician performing electromyography should be aware of the significance of the finding that, even apparently unrelated to the clinical problem that brings the patient to the examination, may reveal an underlying process of diagnostic relevance.

There is a very wide spectrum of conditions that lead to muscle hyperactivity. One possible classification of these disorders is the one taking into account the site of origin of the hyperactivity. Although in clinical practice the action potential showing abnormal muscle hyperactivity is always recorded from muscle fibers, the site in

which the abnormal impulses arise will determine the shape and firing patterns of the action potentials. In the following paragraphs, we will consider three possibilities:

- the muscle fiber or motor end-plates
- the terminal branches of the axons, or any point along the axonal membrane
- the motoneuronal axon hillock

Muscle hyperactivity originating in muscle fibers or motor end-plates

Table 1 summarizes the syndromes in which muscle hyperactivity can be attributed to muscle membrane hyperexcitability. The simplest form of it is the fibrillation potential, which is due to the depolarization of a denervated muscle fiber, induced by the mechanical stimulus of needle movements or any chemical stimulus, such as small amounts of circulating acetylcholine. Denervated muscle fibers are sensitive to any of these stimuli, as well as to relatively low intensity electrical stimuli. This possibility is worth knowing not only for its physiological content, but also because of some clinical utility: In denervated muscles, hyperexcitable muscle fibers may be responsible for muscle action potentials recorded over the same muscle when trying to stimulate the unexcitable motor nerve. A variant of fibrillation potentials are the positive sharp waves, which arise from muscle fibers damaged by the needle. In this situation, the needle detects only the propagating action potential approaching the site of injury, not being able to pass through to generate the negative spike.

A reverse situation occurs with the end-plate spikes and bursts of insertional activity.

This type of activity is generated in the muscle end plate by irritation of the motor axon terminal twig or the muscle membrane. The action potentials, called end-plate spikes, always begin with a negative rising phase, not preceded by any approaching activity. They are single muscle fiber action potentials that may discharge in a short lasting burst of very high internal frequency, decreasing rapidly in both frequency and amplitude (Fig. 1). These high frequency discharges may be seen in muscles of otherwise healthy subjects, but may also be an early manifestation of diseases presenting with muscle fiber hyperexcitability, such as motor neuron disease, radiculopathies, polyneuropathies or myopathies.

Myotonic discharges are pathognomonic of myotonia (either myotonic dystrophy, myotonia congenita, or paramyotonia). Clinically apparent myotonia may be seen in glycogenosis, centronuclear myopathy, the Schwartz-Jampel syndrome, and other channelopathies. EMG recordings may be of help to distinguish true myotonic discharges from other types of muscle hyperactivity that can resemble myotonia in clinical inspection,

Table 1 Muscle hyperactivity generated in the muscle fiber

Type of activity	EMG correlate
end-plate spikes/insertional activity	Short bursts of single fiber action potentials
denervation	Fibrillation potentials/Positive sharp waves
myotonia	Repetitive firing of single fiber action potentials
complex repetitive discharges*	Repeated bursts of a group of muscle fibers
contracture	No electrical activity

* other terms such as 'bizarre high frequency discharges' and 'pseudomyotonia' are discouraged

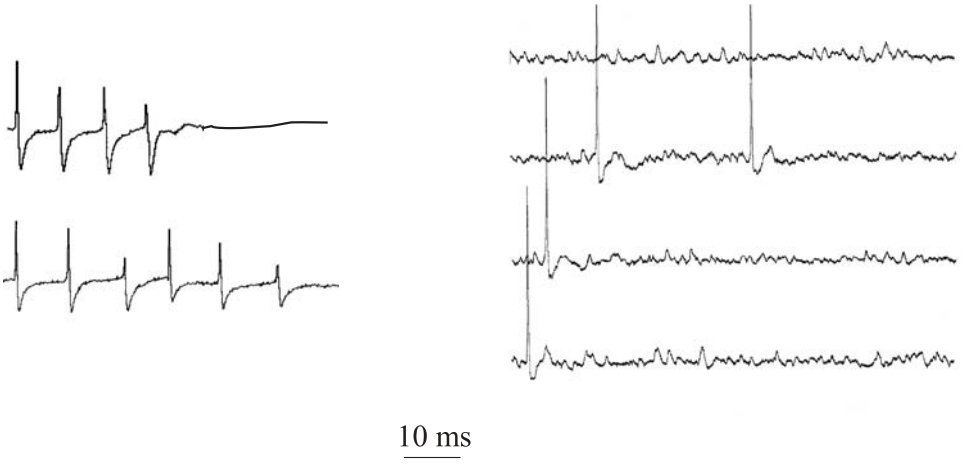

Fig. 1 Left: High frequency discharges of muscle fiber action potentials due to irritation of the muscle fiber with the needle electrode. The recording was done in a healthy subject. Note the initially negative rising phase, which is consistent with an action potential generated in the vicinity of the needle. This is the case with spike potentials, shown in B, recorded occasionally when the needle is approaching the motor end plate

such as is the case with neuromyotonia, myokymia or continuous muscle fiber activity (Isaacs syndrome). Myotonic discharges are actually bursts of single muscle fiber action potentials activated by motor commands or mechanical stimuli. In normal conditions, the action potential becomes extinguished after propagation along the whole muscle fiber. However, during the supernormal period in the negative phase of the muscle fiber action potential, there is a lower threshold for generation of a new depolarization wave. If, for any reason, normal (or hyperexcitable) muscle fibers become re-depolarized at that moment, the slow return of potassium conductance to the baseline serves as a further factor of security to prevent continuous firing, as it may be the case with the high frequency discharges of insertional activity described above. This is not the case in myotonia, in which the action potential begins again. Most electromyographers have already experienced the typical myotonic burst of action potentials, with their characteristic waxing and waning behavior, which sounds as the engine of a motorcycle or a chainsaw and is due to re-excitation of the muscle fiber. The exact reason for this re-excitation is not completely clear, although it may be due to multiple factors. In animals with myotonia, the defect lies in chloride conductance, which is usually helping to stabilize the membrane after the action potential (chloride shunting). In humans with myotonic dystrophy, myotonic discharges are believed to be due to a defect in skeletal muscle Na+ channel gating because of reduced levels of myotonic dystrophy protein kinase [38]. Other channelopathies may explain hyperactivity in myotonia congenita, paramyotonia, periodic paralysis or even malignant hyperthermia [20]. In the Schwartz-Jampel syndrome or chondrodystrophia myotonica [37], myotonia may be due to Na+ channel defects in the context of more widespread sarcolemic membrane deficiencies [23]. This syndrome affects children and is characterized by a genetically mediated abnormal cartilage development, which leads to several possible malformations [16].

Complex repetitive discharges (CRDs), also known by the now discouraged terms of bizarre high frequency discharges and pseudomyotonia, are groups of muscle fibers activated ephaptically after an action potential has been generated in one of them (the pacemaker). The firing may repeat if the pacemaker is receptive again when the activity has reached that site. Conditions in which CRDs are likely to occur are many, including common neuropathies and myopathies. CRDs may be more frequent in certain conditions such as when groups of fibers that have regenerated after a neuropathic insult become denervated again, or when hypertrophied muscle fibers have undergone longitudinal splitting in myopathic or neuropathic disorders [11, 35]. The characteristic of CRDs is the absence of jitter between the action potentials forming the discharge (Fig. 2). The EMG finding of CRDs is not specific for neuropathic or myopathic disorders. However, absence of CRDs in a patient with

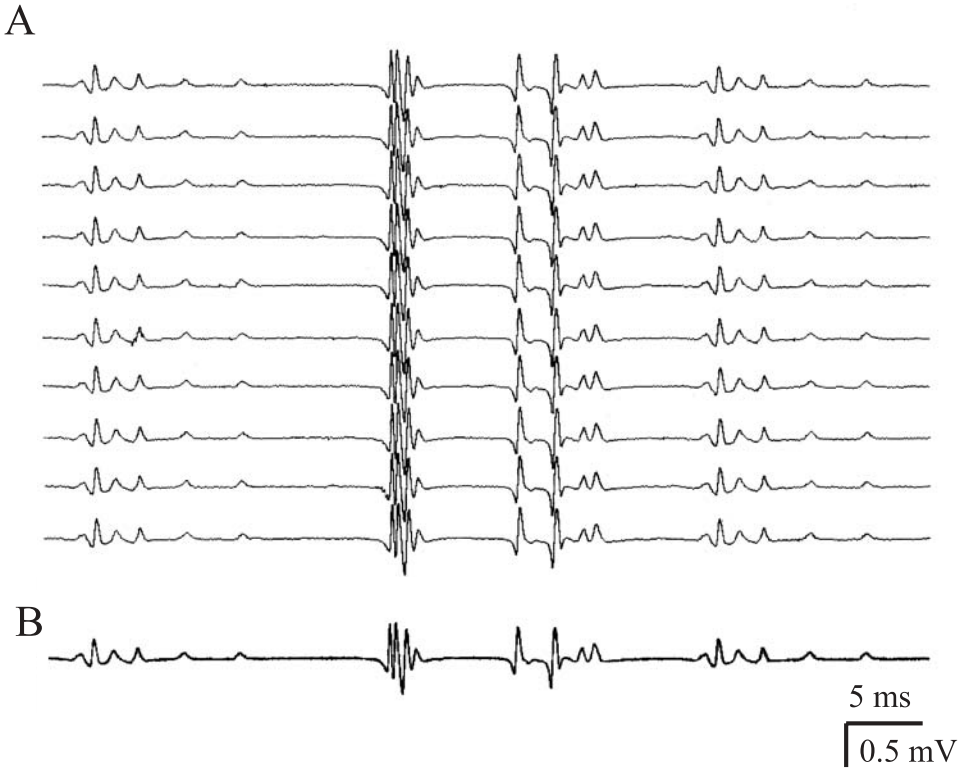

Fig. 2 Complex repetitive discharges recorded in a patient with chronic axonal polyneuropathy of toxic origin. Note the absence of jitter between the various action potentials of the discharge, which is compatible with muscle membrane transmission rather than transynaptic activation. **A** Single recordings of successive action potentials. **B** Superimposition of all the above traces to see the absence of jitter

muscle atrophy may indicate less probability of motor neuron disease or myopathy [11].

In McArdle disease and other glycogenoses, patients may present with contracture, a non-electrical activation of the muscle, that may be initiated by muscle contraction itself. In these instances, the needle electrode does not record electrical activity because the contracture originates at a site beyond the excitation-contraction coupling, and does not involve electrical activity or the generation of any action potential. The contracture is caused by the difficulty in disrupting the actin-myosin bridges, created by preceding action potentials, because of the lack of available ATP. This mechanism is the same as that causing 'rigor mortis' in cadavers. Contracture should be distinguished from the benign muscle cramps that all of us have probably experienced on some occasions, for instance in the calf muscles. The term 'cramps' is highly unspecific and may be misleading, containing a large variety of meanings that will be considered again in the following sections.

Muscle hyperactivity originating in the axon

Table 2 summarizes the syndromes in which muscle hyperactivity can be attributed to axonal hyperexcitability. The term fasciculation was proposed by Denny-Brown and Pennybacker to describe the twitches of muscle bundles, in opposition to fibrillation. Fasciculations indicate hyperexcitability of motoneurons (and their axonal membrane), and may occur in healthy persons (up to 70 % of the general population) as well as in patients with a variety of neuromuscular disorders, even though they are the most conspicuous diagnostic clue in patients with motoneuron diseases [24]. The electromyographic counterpart, the fasciculation potential, is the spontaneous synchronous discharge of all (or a significant group of) muscle fibers belonging to the same motor unit. Fasciculation potentials usually arise from any point along the motor axon, predominantly in distal terminal branches [36], probably due to alterations in various ion channels [5]. Fasciculations more likely originate in growing terminal axons in diseases with compensatory sprouting of distal axonal rami related to motoneuronal death, such as in amyotrophic lateral sclerosis [6, 10, 19]. If fasciculations arise from the proximal axonal segments, or from the cell body, the action potentials would have the same shape, amplitude and duration of a motor unit action potential activated voluntarily. In these instances, care should be taken not to confound the fasciculation with the unnoticed firing of a giant motor unit action potential (fasciculation contraction syndrome). Although the observation of large motor unit action potentials would also indicate a long-standing neurogenic disorder, the identification of true fasciculation potentials may significantly change the diagnosis. A characteristic of fasciculation potentials is that their shape changes in successive discharges because of changing the site of origin, the amount of muscle fibers participating in the discharge, or both. Fasciculations can be seen primarily in calf muscles in the so-called benign muscular pain-fasciculation syndrome [9]. Persistent calf fasciculations, together with other abnormal electromyographic activity, may lead to focal hypertrophy [15]. They may also derive onto a classical motoneuron disease [13].

Table 2 Muscle hyperactivity generated in the axon (mainly terminal branches)

Type of activity	EMG correlate
fasciculation*	Large action potentials of slightly varying shapes
tetany	Doublets, triplets, multiplets
myokymia	Myokymic discharges
neuromyotonia	Neuromyotonic discharges

* fasciculations may be generated in the cell body or in the axonal terminal branches

Spontaneous activation of the axonal membrane is favored by certain conditions such as hyperventilation-induced hypocalcemia. Hyperventilation induces respiratory alkalosis, which should be compensated by metabolic acidosis, responsible for the change in Ca++ concentration. Fasciculation potentials may fire repetitively in doublets, triplets or multiplets (Fig. 3). These are the typical discharges seen in tetany, in which patients with CA++ metabolism disregulation may suffer from cramps in hands and feet. The two action potentials of the doublet are of the same shape, although the second may be of smaller amplitude if generated during the partial refractory period, which lasts up to 9 ms [32]. Because of the same shape, it may be hypothesized that the two action potentials of the doublet originate in the same site, although multiple sites of action potential generation may also be envisaged. The pathophysiology of the hyperactivity observed in tetany is not completely understood. Baker and Bostock [3] demonstrated a pH-related increase in axonal excitability, which may explain the generation of ectopic discharges with hyperventilation. The role of Ca++ metabolism is not completely clear. According to Piccolino and Pignatelli [33], activation of voltage-dependent Ca++ channels may actually change with Ca++ concentration in the plasmatic membrane, owing to a change in the surface potential.

Repetitive firing of action potentials occurs also in syndromes presenting with myokymia. Its electromyographic equivalent, the 'myokymic discharge', is composed of grouped muscle fiber action potentials that fire repetitively. Like fasciculation potentials, they are generated at any location along the axon, either at proximal or at distal segments. Myokymic discharges can be

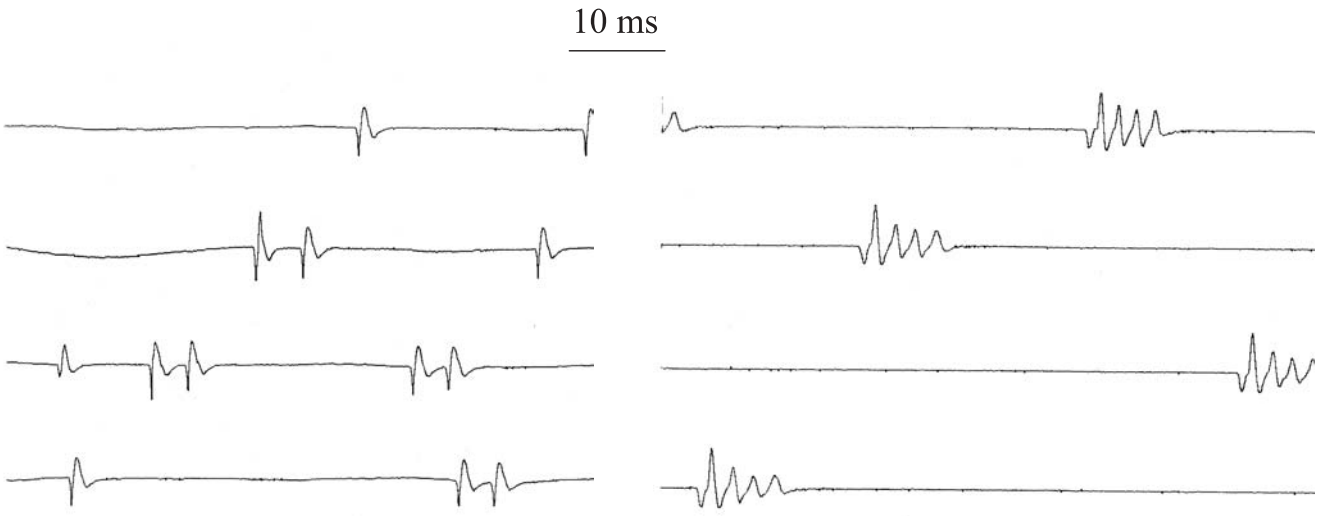

Fig. 3 Two sets of recordings of action potentials firing in doublets, triplets or multiplets, obtained from the 1st dorsal interosseous muscle of a 58 year old hypoparathyroidectomized patient after 10 minutes of forearm ischemia, followed by 1 minute of hyperventilation

recorded in many diseases such as Guillain-Barré syndrome, radiation plexopathies, traumatic nerve injuries, polyneuropathies, etc. While a single myokymic burst could be generated by the ectopic firing of an axon or by the passage of a motor command, repeated generation of the same burst should occur if there are multiple sites for ephaptic transmission. The whole burst may repeat itself with a rather fixed rhythm if the ectopic site is activated again. Circular activation of the same axons, and collision of impulses in some terminal branches, may explain why the myokymic discharge is always formed by the same muscle fiber action potentials without necessarily spreading to the whole motor unit. The same line of reasoning brings an explanation for why myokymic discharges may continue firing repeatedly regardless of any manoeuver. Muscle fiber activation when performing voluntary movements or following electrical nerve stimulation may not reach the locus of the myokymia because of conduction block in some damaged fibers in such a way that the locus may be clustered and closed to external influences (Fig. 4).

The same process causing myokymic discharges may also cause complex repetitive discharges. If this is the case, it might be difficult to tell the two types of discharge apart. One possibility is nerve stimulation (Fig. 5). Abnormal bursts induced by nerve stimulation may arise in ephaptic transmission between muscle fibers, following the main action potential, as in the complex repetitive discharges, or in activation of an ectopic focus of hyperactivity in the axonal membrane, as in the myokymic discharge. If the latter is located at a proximal site with respect to the stimulation point, stimuli applied over the same nerve at a point further proximal will cause a shortening of the burst latency. This change in latency will not occur with complex repetitive discharges generated always distally to the distal-most nerve stimulation point.

Another type of repetitive firing of action potentials with origin in the axon occurs in neuromyotonia. This term is reserved for the clinical observation of long-lasting contractions with impaired relaxation that occurs in syndromes known to present with continuous muscle fiber activity [17, 29]. Neuromyotonic discharges are long duration high frequency discharges of action potentials that end abruptly after decreasing in amplitude and frequency. The only difference between myokymic discharges and neuromyotonic discharges is the duration of the discharge. Neuromyotonic discharges are myokymic discharges repeating themselves several times. The last component of the myokymic discharge closes the ephaptic circuit and activates the pacemaker again. In this form, the same myokymic circuit is activated again repeats at its maximal possible frequency. Neuromyotonic discharges end after a period of burst instability, with increased jitter and block of the different components of the burst. While it might be worth maintaining the differences between myokymia and neuromyotonia from the clinical point of view, neither electromyographic recordings nor the pathophysiology underlying these two abnormal forms of muscle hyperactivity seem to be different. In both conditions there is evidence for an abnormal function of voltage-gated potassium channels. In patients with episodic ataxia/myokymia syndrome, a mutation has been identified in the potassium channel gene [7], and antibodies against voltage-gated potassium channel have been identified in 50 % of patients with acquired neuromyotonia [29] or Morvan's chorea [22].

Muscle cramps have been experienced by many of us, since their nocturnal presentation occurs in up to 16 %

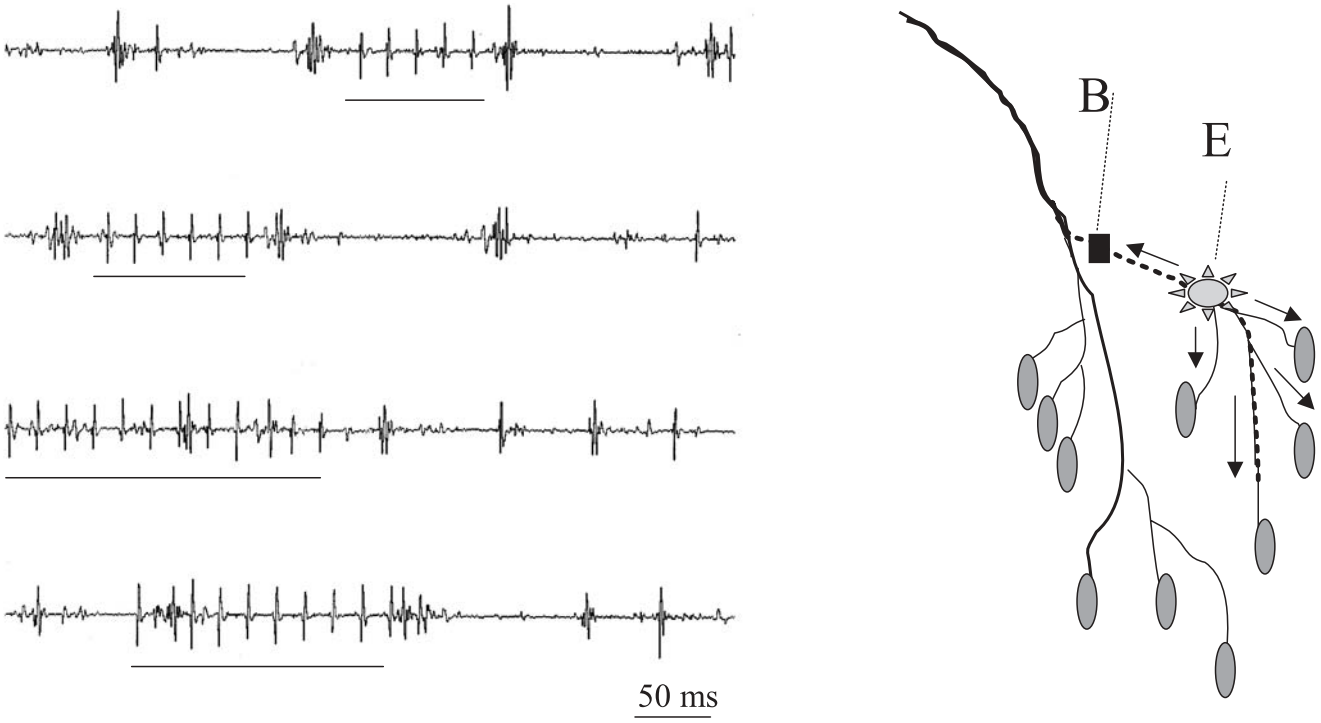

Fig. 4 **Left** Repetitive firing of a myokymic discharge as a burst of various single action potentials (underlined) amid regenerating action potentials recruited during a voluntary contraction in a patient with a 4 months old peroneal nerve lesion. **Right** Schematic illustration of the mechanism hypothesized to explain the observations. *E* Focus of ectopic discharges; *B* Conduction block due to poor myelination in a regenerating axon

of normal subjects [31]. A typical site for cramps is the gastrocnemii muscles, although the reason for such preference is unknown. Cramps may be preceded and followed by fasciculation potentials [21], indicating their possible origin in a massive change in excitation of the same structures generating the fasciculation potential. In the hypothesis suggested by Bertolasi et al. [4], cramps would be produced when a phasic contraction is made on top of a tonic contraction because of a sudden increase in excitability of muscle fibers and terminal axons that have become close enough together for widespread re-excitation. In these cases, EMG recordings show a very high frequency discharge of action potentials generating in single or grouped muscle fibers (Fig. 6). A very well known characteristic of muscle cramps is pain. This is probably derived from activation of muscle nociceptors due to mechanical factors and contraction-induced local ischemia. Cramps are relieved with muscle rubbing or lengthening. Lengthening of muscle fibers will physically separate the foci of ectopic discharge generation and eventually stop the re-excitation. Cramps can be induced by repetitive magnetic stimulation over the muscle [8], which will probably contribute in the near future to a better knowledge of the pathophysiological bases of muscle cramps.

Muscle hyperactivity originating in motoneuron activation

Table 3 summarizes the syndromes in which muscle hyperactivity can be attributed to excessive motoneuron activation. The axonal hillock is the site of origin of propagated action potentials arising in the cell body when the motoneuronal stationary potential reaches its firing threshold. The stationary potential is the summation of all inhibitory and excitatory inputs arriving at the motoneuron. The characteristic of all syndromes in which there is uncontrolled firing of alpha motoneurons is that all action potentials are normal motor unit action potentials, with no difference from those activated during voluntary contraction and, in many instances, abnormal activity is made up of bursts of normal interference pattern. Abnormally enhanced muscle activity with origin in the motoneuron is common to all central nervous system diseases in which there is an abnormal control of movement, such as in those involving pyramidal and extrapyramidal tracts. The differences between these diseases are not in the form or characteristics of the motor unit action potential, but in the timing, reciprocity, or periodicity of bursts (Table 4). Because of that, EMG recordings in patients with disorders of motor control are usually done with surface electrodes, as a

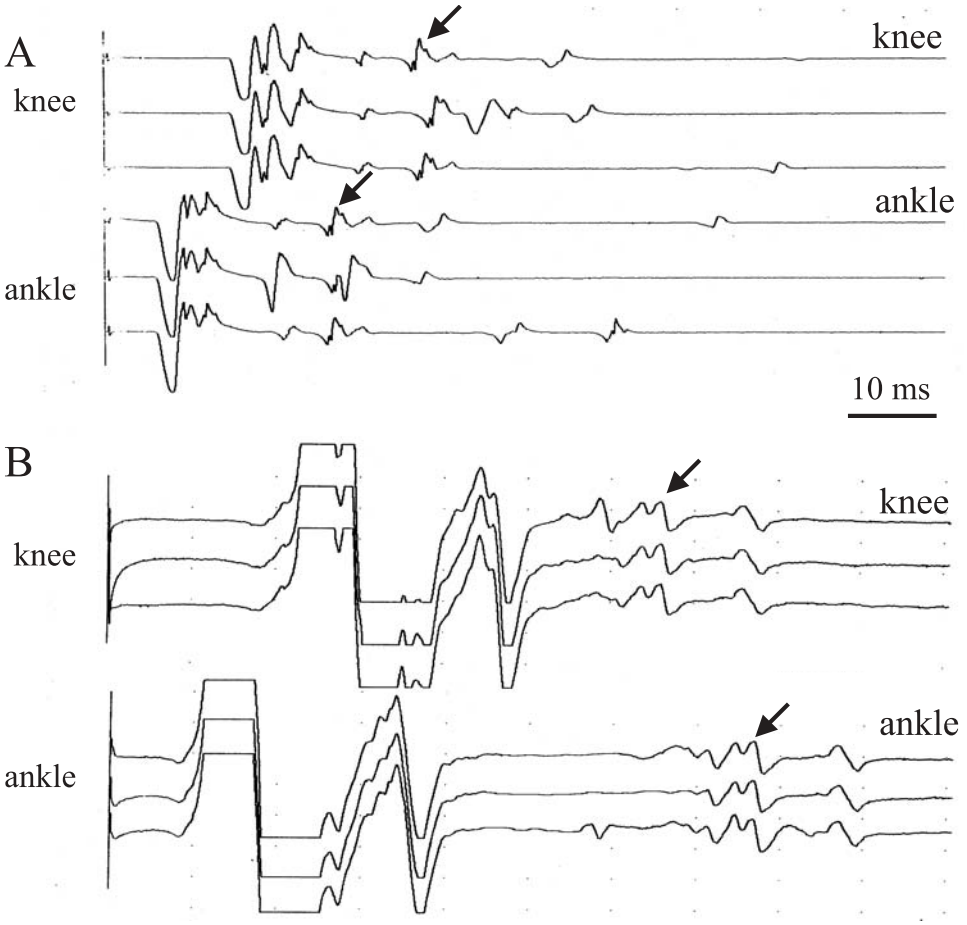

Fig. 5 Abnormal activity induced by electrical stimulation of the motor nerve in two patients after stimulation of the peroneal nerve in the knee and the ankle. Three traces are shown for each stimulation site and patient. In **A**, obtained from a patient with suspected lead poisoning-related distal axonal polyneuropathy; the abnormal activity follows the main action potential at a similar latency in both stimuli (ankle and knee), indicating that the abnormal activity is generated in a site distal to the ankle stimulation point. In **B**, obtained from a patient with S1 radiculopathy, the latency of the burst of abnormal activity shortens with stimulation at a proximal site, indicating that the abnormal activity is generated in a site proximal to the knee stimulation point

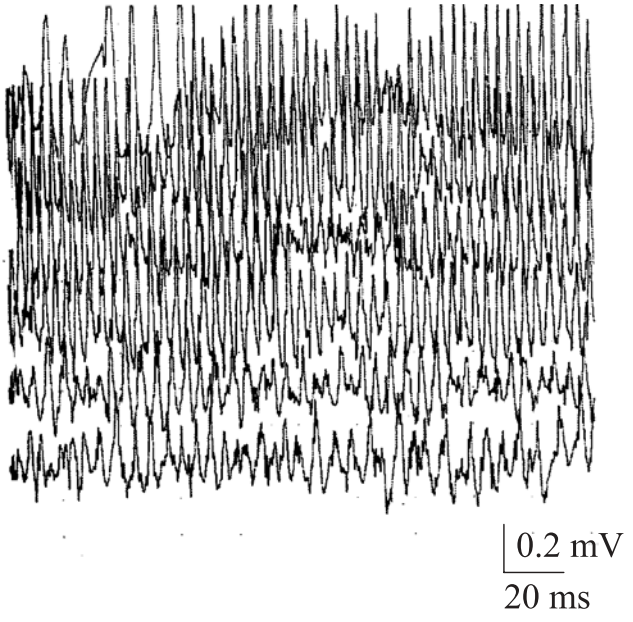

Fig. 6 Common spasm of the gastrocnemius medialis muscle in an otherwise neurologically normal subject. The spasm, shown in 5 consecutive epochs of 200 ms, was induced by sudden shortening of the muscle in the middle of a sustained tonic contraction, and relieved by muscle stretching

Table 3 Muscle hyperactivity generated in the motoneuron

Type of activity	EMG correlate
fasciculation*	Motor unit action potentials
cramp	Normal interference pattern
pseudomyotonia	Motor unit action potentials
stiffness	MUAPs or normal interference pattern
pyramidal tract lesions	MUAPs or normal interference pattern
extrapyramidal disorders	Different forms of interference patterns

* fasciculations may be generated in the cell body or in the axonal terminal branches

difference from the other types of abnormality, which require needle recording.

Reduction of inhibitory inputs induces uncontrolled firing of motoneurons in many diseases. Probably the paradigm of syndromes due to reduced inhibition of motoneurons is the stiff-person syndrome [26, 27]. This syndrome features generalized spasms and rigidity. Its electrophysiological counterpart is the observation of continuous activity of otherwise normal motor units (Fig. 7), together with motor reflex response enhance-

Table 4 Types of electromyographic abnormalities in patients with movement disorders

Tremor	Rhythmic bursts of some 100 ms duration
Chorea/Dystonia	Arhythmic and irregular bursts of various durations
Myoclonus	Bursts or silent periods of short duration (less than 100 ms)
Akathisia/Restless legs/Tics	Full interference pattern corresponding to the movement
Painful legs and moving toes	Low frequency rhythmic activation of motor units
Hyperekplexia	Reflex generalized bursts of variable duration

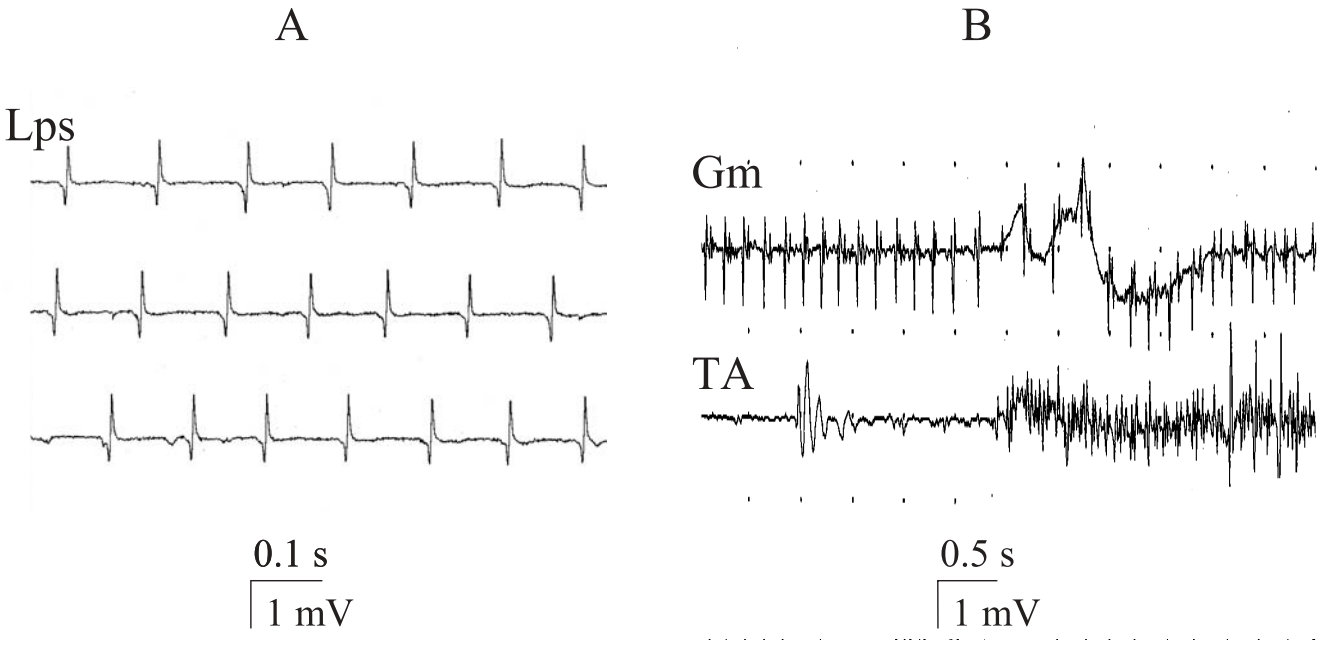

Fig. 7 **A** Continuous firing of otherwise normal motor units in lumbar paraspinal muscles (Lps) of a patient with stiff-person syndrome. **B** The same type of activity recorded in the gastrocnemius medialis (Gm) despite activation of the tibialis anterior (TA)

ment to various stimuli. The observation of continuous electromyographic activity is not specific for the stiff-person syndrome. A similar type of abnormality may be observed with tetanus infection [12, 34], in which neurotransmitter-mediated inhibition of motoneurons is impaired. In this case, however, the abnormality is usually focused in some segments, and typically affects the jaws (trismus). A conspicuous difference between the stiff-person and the tetanus-induced spasms can be found in the silent period induced by peripheral nerve stimulation. This is abnormally reduced in tetanus, owing to the impairment of Renshaw cell (glycinergic) mediated inhibition of motoneurons. In contrast, it is normal in the stiff-person syndrome, which is more likely to feature abnormalities in GABAergic mediated inhibition at a presynaptic level [14]. An abnormally sustained firing of motoneurons should be distinguished from the inability to relax properly, which is a common phenomenon in many conditions. It can be related to reflex or automatic protection against focal pain or other source of discomfort. It is not rarely observed in some diabetic patients with no clinical or laboratory signs of the stiff-person syndrome.

Persistent activity of motor units can be seen after muscular contraction in some disease entities such as amyotrophic lateral sclerosis or syringomyelia. This post-contraction activation may be experienced by the patient as a spasm or a cramp. It might be interesting to speculate on its physiology: In these cases, an ectopic focus may fire repetitively upstream of the motoneuron which, being hyperexcitable, would respond easily to such inputs. Some have used the name 'pseudomyotonia' to describe this persistent motor unit activity. Although the old use of this term as synonymous with neuromyotonia is discouraged [1], we think that it may well be applied to this type of abnormal activity because of its clinical resemblance to the characteristic myotonic dimple elicited by a tap to the muscle in myotonic dystrophy.

The term cramps is again used to describe muscle hyperactivity generated in the motoneurons. One typical example is the concept of 'writer's cramp' to define the task-specific dystonic-like abnormality of patients with

tension or tiredness of forearm muscles when writing. Electromyographic recordings of these forms of cramps show typical interference patterns. A different condition is that of a spasm. A muscle spasm can occur as a result of reflex response to various types of sensory inputs in spastic patients. It is probably the result of an exaggerated stretch reflex. The spasms observed in patients with spasticity as a consequence of damage to the pyramidal tract also correspond to a full interference pattern in electromyographic recordings. The spasms occurring in hemifacial spasm might be accompanied by electromyographic activity consisting of a very high frequency repetitive firing of single spikes, probably MUAPs. This type of activity is likely to be generated in repetitive firing of hyperactive axons [18, 30]. However, a contribution of exaggerated facial motoneuronal firing has also been considered [25, 28]. The question is still open on whether an increased flow of excitatory inputs to the motoneuron may be the actual source of the spasm in patients in whom the EMG activity shows an interference pattern rather than the repetitive firing of action potentials [2].

Conclusion

Electromyographic recording of muscle hyperactivity helps in ascertaining the origin of the abnormalities. All who perform electromyographic recordings have at some point been startled by the observation of strange bursts and the hearing of peculiar sounds. This is actually one area in which electromyography can furnish information not available by any other means, and it is worthwhile for the neurologist to become familiar with the meaning of such electromyographic observations. As in many other parts of the electrodiagnostic testing, practice is the most important part of learning. Graphic representation of examples such as those used to illustrate this review are not the most useful way for the reader to be acquainted with the abnormalities of EMG activity. The reader interested in gaining a more profound knowledge in the field of muscle hyperactivity should look for the many video, compact disks, or other types of sound recordings commercially available.

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