ABSTRACT: The presence of myotonia and paramyotonia on clinical examination and of myotonic discharges during electrodiagnostic (EDX) studies are important for the diagnosis of certain neuromuscular conditions. The increased muscle activity of myotonia produces muscle stiffness that improves with repeated activity. Paramyotonia produces a similar symptom, but the stiffness paradoxically increases with activity. Myotonic discharges are easily recognized on EDX testing because of the waxing and waning discharges. Myotonic dystrophy and myotonia congenita share both clinical and electrodiagnostic myotonia. Paramyotonia congenita and hyperkalemic periodic paralysis are associated with clinical paramyotonia and electrical myotonia. Acid maltase deficiency often produces myotonic potentials without clinical evidence of myotonia or paramyotonia. The differential diagnosis of these myotonic disorders is discussed.
amplitude and frequency, producing a characteristic audio profile often compared to a dive-bomber.\textsuperscript{1,2,15} These potentials are repetitive discharges with a rate of 20–80 Hz and are of two types: (1) biphasic spike potentials less than 5 ms in duration that resemble fibrillation potentials, and (2) positive waves, 5–20 ms in duration, that resemble positive sharp waves. A single myotonic potential may look and sound exactly like a fibrillation potential or positive sharp wave, but it is the multiple runs with the characteristic waxing and waning that distinguish the discharges as myotonic potentials. Needle insertion and movement, muscle contraction, or tapping the muscle will often provoke the myotonia. Although single myotonic potentials can resemble fibrillations or positive sharp waves, myotonic potentials are rarely confused with other discharges.

Waning discharges are easily distinguished from myotonic discharges because they lack the characteristic waxing that is part of the classic definition. However, these potentials may represent a subset of myotonia. Logigian et al.\textsuperscript{21} found that 4 of 17 patients with genetically confirmed proximal myotonic myopathy (DM2) had only waning discharges without evidence of classic myotonic discharges. As expected, all of the 16 patients with myotonic dystrophy (DM1) in their study had classic myotonic discharges.

Myokymic potentials are spontaneous potentials that have rhythmic firing of grouped motor unit action potentials. Typically the discharges are in groups of 2–10 at a frequency of 2–60 Hz, with a sound like marching soldiers. Neuromyotonic discharges are secondary to continuous muscle activity firing at 100–300 Hz. The potentials do not wax and wane, but may abruptly decrease in amplitude, producing a “ping” sound. Neuromyotonic discharges are not affected by voluntary activity, sleep, or anesthesia, but may be interrupted by a local blockade of peripheral nerve, the presumed generator of the discharges. Tapping on the nerve provokes neuromyotonia. Complex repetitive discharges (CRDs) are repetitive complex potentials with a sudden onset and cessation, resembling the sound of a motorboat or motorcycle. These potentials do not wax and wane like myotonia, although the waveform shape, amplitude, and frequency may change during discharge. Cramps are rarely captured on EMG, but may be distinguished by their sudden painful contraction accompanied by high-frequency discharges, which can be up to 150 Hz. The discharge frequency and the number of motor unit discharges increase gradually during the development of the cramp, and subside gradually as the cramp fades.

![Figure 1](image-url)
Electrodiagnostic Studies That May Aid Differential Diagnosis. Myotonia is the most useful finding on standard EMG and nerve conduction examinations. However, several specialized tests may also aid in making or confirming the diagnosis of a disorder associated with myotonia: repetitive stimulation, the “short” and “long” exercise tests, and the provocative cold test.

Repetitive Stimulation. It has long been recognized that in myotonic syndromes repetitive stimulation at 5–10 Hz leads to a decrement in the compound muscle action potential (CMAP).\textsuperscript{3,7,12,42} This decrement has been attributed to transient inexcitability of the muscle membrane. Although consistent with a myotonic disorder, this finding is not specific.

Exercise Testing. In the “short” exercise test the patient is asked to exercise briefly (10–30 s). A CMAP is recorded and compared with the CMAP recorded prior to exercise. In patients with DM1, this brief period of exercise causes a decrease in the CMAP, whereas in DM2 there is no change.\textsuperscript{39}

In the “long” exercise test both the period of exercise and the subsequent time of recording are “long.” As first described by McManis et al.,\textsuperscript{24} the CMAP is tested over a 30–45-min period following 5 min of sustained exercise. In all forms of periodic paralysis, both genetic and metabolic (e.g., thyrotoxic periodic paralysis), there is a decrease in CMAP over time. The CMAP decrement in patients with hypokalemic periodic paralysis (HypoKPP) and hyperkalemic periodic paralysis (HyperKPP) differs qualitatively from the decrement in those with paramyotonia congenita. In paramyotonia congenita, there is a rapid decline in CMAP amplitude followed by a slow increase back to baseline over the next 60 min. In HypoKPP and HyperKPP, the amplitude increases immediately after exercise and then declines slowly over the course of 15–30 min. Patients with myotonia congenita also may show a decrement on the exercise test, but this is not consistent.

Cooling Test. Cold provokes the symptom of weakness in patients with paramyotonia congenita. This cold effect may be reproduced in the EDX laboratory by recording the CMAP for an individual muscle before and after cooling the limb for 15–30 min at 15°C.\textsuperscript{28,35} The CMAP decrement in paramyotonia congenita patients is typically greater than 75%. Cooling may initially provoke myotonia in pa-
tients with paramyotonia congenita, but after prolonged cooling there will be a decrease in electrical activity.

DISORDERS WITH BOTH CLINICAL AND ELECTRICAL MYOTONIA

Myotonic Dystrophy. Myotonia congenita, DM1, and DM2 all share prominent clinical classic myotonia and electrical myotonia.

The best-known myotonic disorder is DM1. The characteristics of this CTG-repeat disorder include cranial muscle wasting/weakness and distal-predominant limb weakness. The small temporalis muscles, ptosis, and a long, lean face produce a characteristic facial appearance. Cranial muscle abnormalities may also include dysphagia, dysarthria, and sometimes eye-movement abnormalities. The limb muscle weakness affects distal muscles to a greater degree than proximal muscles. Along with inclusion-body myositis, this muscle disease has the distinction of prominent finger-flexor weakness. Reflexes are depressed in proportion to weakness. The rate of disease progression is slow; longevity is not affected in many patients, but overall life expectancy is reduced secondary to respiratory diseases, cardiovascular diseases, neoplasms, and sudden deaths presumably from cardiac arrhythmias. The manifestations outside of the nervous system are also characteristic and include frontal balding, cataracts, and cardiac abnormalities. The major distinction of DM2 is the later onset and predominant proximal weakness. Myotonia also prominent in this disorder both clinically and on EMG. Congenital DM2 does not occur.

Myotonia Congenita. Myotonia is the prominent clinical symptom of myotonia congenita. The severe classic myotonia causes stiffness especially when first starting an activity. Once these patients have warmed up, they may perform activities at a normal or advanced level, including competitive sports. The disorder presents in early childhood and may be described by the parents as weakness and clumsiness in addition to or instead of stiffness. Despite the reported difficulties, affected children appear "athletic," with increased muscle bulk, presumably because of the sustained muscle activity. The myotonic symptoms often improve with age but do not completely disappear.

Myotonia congenita is secondary to a mutation in the CICN1 chloride channel, and may be transmitted either dominantly or recessively. Curiously, a particular mutation may be recessive in some families and dominant in others. The reasons for this are not clear. Recessively inherited myotonia congenita is referred to as Becker’s myotonia congenita and dominantly inherited disease as Thomsen’s myotonia congenita. The chloride channel defect leads to an elevation of the resting membrane potential and thus a tendency toward repeated muscle contractions. Genetic testing for myotonia congenita may be performed in some specialized centers, many of which are best located at www.genetests.org.
Schwartz–Jampel Syndrome. Schwartz–Jampel syndrome, also known as chondrodystrophic myotonia, is associated with severe myotonia as well as short stature, muscular hypertrophy, diffuse bone disease, ocular and facial abnormalities, and joint contractures. Muscle stiffness is one of the first symptoms that presents in childhood. There is no warm-up phenomenon for the myotonia. The EMG findings of this rare disorder more closely resemble neuromyotonia or CRDs. Unlike typical myotonia, the repetitive, high-frequency discharges in this disorder do not wax and wane. Schwartz–Jampel syndrome is caused by loss-of-function mutation in the HSPG2 gene, which encodes perlecan, a heparan sulfate proteoglycan secreted into basement membranes.

DISORDERS WITH CLINICAL PARAMYOTONIA AND ELECTRICAL MYOTONIA

Both HyperKPP and paramyotonia congenita are characterized by attacks of weakness and paramyotonia. Both of these dominantly inherited diseases present in infancy or childhood and are associated with sodium channel mutations. In HyperKPP the attacks of weakness dominate the clinical picture. These attacks are often provoked by resting after exercise, skipping meals, or eating foods containing a high potassium content. The attacks occur relatively frequently (one per day to one per week), are short-lived (minutes to hours), and usually are not completely disabling. Some patients complain of stiffness with exercise and demonstrate paramyotonia on examination. EMG studies show myotonia in ~75% of HyperKPP patients. During the attack, the serum potassium level is often elevated. Muscle biopsy shows a vacuolar myopathy. Patients with paramyotonia congenita mainly complain of stiffness, but also have attacks similar to those of HyperKPP. One of the major factors provoking stiffness in these patients is cold temperature. EMG demonstrates myotonia in all paramyotonia congenita patients. In both HyperKPP and paramyotonia congenita the paramyotonia and attacks of weakness decrease in middle age. In cases where periodic paralysis or paramyotonia congenita are being questioned, the exercise test and cooling test may be particularly helpful. Nearly all cases of periodic paralysis are associated with mild to moderate weakness in later adult life.

Both HyperKPP and paramyotonia congenita are secondary to mutations in the sodium-channel SCN4A gene. T704M and M1592V are the most common mutations in HyperKPP. In paramyotonia congenita, R1448C and T1313M are the most common residues affected. These mutations cause a chronically depolarized muscle membrane. Genetic testing is available for these disorders in specialized centers. Potassium-aggravated myotonia is also linked to a sodium-channel mutation. In this disorder, potassium administration “aggravates” or brings on myotonia. These patients also experience episodic myotonia. They do not have attacks of weakness. The myotonia is not sensitive to cold and is most prominent ~20 minutes after exercise.

When considering HyperKPP or paramyotonia congenita, the main differential consideration is HypoKPP, which does not show any paramyotonia clinically or myotonia on EMG. Attacks of weakness are more prolonged in HypoKPP (lasting hours to days) and are more severe, often leaving the patient unable to walk. Inherited forms of HypoKPP are secondary to calcium-channel mutations. Metabolic causes are most often secondary to hyperthyroidism, although chronic potassium wasting (e.g., renal tubular acidosis) may also cause episodic muscle weakness. Andersen–Tawil syndrome, which is associated with mutations in KCNJ2, consists of the triad of cardiac arrhythmias, dysmorphic features, and periodic paralysis; there is no myotonia.

MYOTONIA ONLY ON EMG, NOT PHYSICAL EXAMINATION

Myotonia on clinical examination is always associated with myotonic discharges on EMG. The converse is also nearly always true, with one notable exception. Acid maltase disease consistently shows myotonic potentials on EMG with absent clinical myotonia. Adult-onset acid maltase deficiency (glycogenosis type II) is a glycogen storage disease that presents with truncal and proximal limb weakness that is slowly progressive over the years. Death is usually caused by weakness of respiratory muscles. Occasionally, the presenting weakness is diaphragmatic. Unlike certain other glycogen storage diseases, the heart and liver are not enlarged. Serum creatine kinase levels are increased. EMG shows evidence of multiple spontaneous discharges including myotonic discharges, fibrillation potentials, positive sharp waves, CRDs, and small motor unit action potentials. Diagnosis is confirmed by muscle biopsy with periodic acid–Schiff positive vacuoles. A more malignant form of the disease may present in infancy with heart muscle and neuronal involvement.

OTHER DISORDERS

There are other disorders in which myotonia is occasionally recognized, although usually not as a pre-
dominant or essential part of the presentation. Muscle diseases such as polymyositis and inclusion-body myositis, or severe active denervation are rarely associated with myotonic potentials. In some of these cases, CRDs may be mistaken for myotonic potentials. Fibrillation potentials, positive sharp waves, and myotonic discharges have been reported previously in hypothyroid patients, but the myotonic discharges are not common. Electrical myotonia may also be seen with some drugs: 20,25-diazacholesterol, clofibrate, 2,4-dichlorophenoxyacetic acid, chloroquine, colchicine, and hydroxymethylbutyryl coenzyme A reductase inhibitors.

CONCLUSIONS

Recognizing the associated clinical and EMG characteristics of myotonia and paramyotonia greatly aids neuromuscular diagnosis. During routine EDX testing a few additional historical details and a brief physical examination are likely to provide the correct diagnosis or suggest further investigations.

REFERENCES
