Clinical Presentations and Phenomenology of Myoclonus

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Summary: The term “myoclonus” has been used to describe heterogeneous phenomena involving sudden movements, but there is no generally accepted, precise definition of myoclonus. Myoclonus can often be classified based on electroencephalographic (EEG) and/or electromyographic (EMG) data. Some myoclonic epilepsy syndromes, including juvenile myoclonic epilepsy, may frequently be misdiagnosed because of failure to obtain a complete patient history and/or failure to appreciate characteristic EEG changes. A good understanding of the features associated with myoclonic disorders (particularly the myoclonic epilepsies) and of features associated with other neurologic disorders that are often confused with myoclonic disorders is an invaluable aid in obtaining an accurate diagnosis and will ultimately help in determining the best course of treatment for patients. Key Words: Myoclonus—Seizures—Epilepsy.

DEFINITION OF MYOCLOMUS

In 1968, Gastaut (1) referred to the term and concept “myoclonus” as a “long-standing source of confusion and debate,” and this confusion remains today. There is no generally accepted, precise definition of myoclonus, despite the many reviews of the subject (1–6). Definitions in textbook articles are variations on a theme: “quick muscle jerks, either irregular or rhythmic” (4), a “sudden, brief involuntary movement” (7), and a “brief, shocklike jolt in a muscle” (8). The scope of definitions ranges from the very general “[any brief muscular contraction]” (1) to the more qualified “a sudden, brief, shock-like muscle contraction arising from the CNS” (9) and “abrupt, jerky, involuntary movements unassociated with loss of consciousness” (6).

Halliday (10) noted the difference between the “lightning-like” movements of “epileptic myoclonus” and the rhythmic movements of “subcortical myoclonus” but retained the latter within the definition of myoclonus. This concept has been followed by Hallett (4). The inclusion of rhythmic movements within the definition of myoclonus leads to the categorization of epilepsy partialis continua (EPC, continual focal motor seizures), segmental myoclonus, and palatal myoclonus as myoclonic disorders. For myoclonus to arise only from the central nervous system would exclude some peripheral disorders often termed myoclonic. A logical and appealing classification was proposed by Adams and Victor (11), who described myoclonus as a “shocklike, irregular jerk,” clonus as “rhythmic, uniphasic jerking,” and tremors as “biphasic jerking.” Following this reasoning, EPC and palatal myoclonus are forms of clonus. Palatal myoclonus might better be termed palatal tremor since it is biphasic.

One problem with all of the definitions given is the question of whether or not movements clearly falling within these definitions, but not often described as myoclonic, should be considered myoclonus or not. Tics, startle responses (epileptic and nonepileptic), fasciculations, myokymia, hemifacial spasm, chorea, and even infantile spasms are examples of such movements. Although, strictly speaking, such movements are myoclonic in nature, and some authors include some of these terms under the umbrella of myoclonus (5), describing them as such or categorizing them as myoclonic disorders confuses, rather than clarifies, diagnostic schemes. Even in 1881, Friedreich’s purpose in originally coining the term “paramyoclonus,” which was later shortened by others to “myoclonus,” was to distinguish myoclonic epilepsy from chorea (12). Noting that hiccoughs, hypnic jerks, and similar physiological phenomena are in fact examples of physiological myoclonus causes less confusion than including pathological terms within the definition of myoclonus.

This report will describe the phenomenology of myoclonic movements, particularly as they are observed in the common varieties of myoclonic epilepsies; examine the differences between these movements and similar sudden, jerky movements that imply different diagnoses; and review the most common clinical settings in which myoclonus is observed.
EPILEPTIC MYOCLONUS

Juvenile myoclonic epilepsy

This common, genetic, primary generalized epilepsy usually brings a teenager or young adult to medical attention after the occurrence of a generalized tonic-clonic seizure. A careful patient history often reveals that early morning myoclonic jerks have been present for months or years before a seizure occurrence. The diagnosis is often missed if this history is not solicited. Common reasons for diagnostic error are failure to ask about myoclonus and failure to appreciate the typical electroencephalogram (EEG) findings associated with juvenile myoclonic epilepsy (JME) (13).

Myoclonic jerks in JME can be asymmetrical or even unilateral, which can lead to a misdiagnosis of focal motor seizures due to localization-related epilepsy. The presence of the characteristic generalized polyphasic spike-wave EEG discharge, often with an initial frequency of 3.5–4 Hz, usually clarifies this issue. Simple partial seizures with motor manifestations will have unilateral frontal discharges, or sometimes no EEG correlate, with the movement. The latter phenomenon does not occur with JME, and an EEG correlate of the myoclonic jerk will always be present. However, the reverse is not true in JME: that is, EEG discharges up to several seconds long are sometimes seen without a discernible jerk.

Myoclonic jerks in JME typically involve the upper body, including the arms, hands, and sometimes the head and trunk. They may affect flexors or extensors. Probably the most common movement is elevation at the shoulder with flexion at the elbow. The amplitude varies considerably, from rather violent upper body flexion resembling an infantile spasm to very minimal hand or finger twitching, which can resemble chorea or fasciculation. This small-amplitude twitching has been called “minipolymyoclonus” (14).

Although myoclonus is almost always defined as a quick movement, some patients exhibit relatively slow arm movement (up to 1 s in duration) with an even slower relaxation phase. Such myoclonus can resemble voluntary movement or a normal response to an environmental stimulus. The EEG can confirm the epileptic nature of such atypical myoclonic movements.

The phenomenology of the myoclonic jerks seen in JME is similar to that of other primary generalized epilepsies that are relatively benign. These syndromes include benign myoclonus of infancy, which is seen before age 3 years; childhood absence epilepsy (mainly with photic stimulation); and adult-onset benign myoclonic epilepsy.

The myoclonus of progressive myoclonic epilepsies

The diverse etiologies of progressive myoclonic epilepsies (PMEs) are discussed in the article by Leppik in this supplement (15) and in a previous article (16). However, the phenomenology of myoclonus in the PMEs is relatively similar across different pathophysiological causes and differs in some respects from the myoclonus of JME (16). For example, there is no early-morning predominance of myoclonus in PMEs. The myoclonus in PMEs tends to be multifocal, of variable amplitude with many small jerks, relatively constant, and increased by voluntary movement. In these characteristics it may resemble chorea.

Somatosensory or auditory reflex precipitation of seizures is more common in PME and light precipitation of seizures is more common in JME (17). Exceptions to this rule include PME caused by Unverricht-Lundborg disease, in which photosensitivity is marked; the sensitivity to single flashes seen in PME due to some forms of neuronal ceroid lipofuscinosis; and benign myoclonic epilepsy of adulthood (possibly a late-onset variant of JME), in which somatosensory precipitation occurs.

Several EEG features are useful in distinguishing PME from more benign epilepsies (18) (Table 1). Unlike JME, most of the myoclonic movements in PME syndromes—especially the almost continual, small-amplitude jerks—are not time-locked to EEG discharges. Whether they represent subcortical phenomena or restricted-field cortical discharges is unclear. Large-amplitude jerks may have EEG correlates, often very high-amplitude generalized spike-wave bursts, which are slower and less rhythmic than those associated with JME.

The distinction between PME and more benign myoclonic epilepsies like JME does not ordinarily depend on recognition of differences in the myoclonic movements themselves. The associated neurological deterioration affecting cognitive function, EEG background activity, other motor systems, and (in some PME syndromes) retina, skin, and other organs, eventually leaves no doubt as to the category to which a particular patient belongs.

NEGATIVE MYOCLONUS

This paradoxical term refers to sudden relaxations in tonic muscle contraction. It might better be referred to as an atonic phenomenon. Tassinari et al. (19) first described it as “the related epileptic silent period,” but the term “negative myoclonus” appears to have been coined by Shahani and Young in 1976 (20) in reference to posthypoxic intention myoclonus. They noted that the events “appeared

TABLE 1. Characteristics of the EEG in patients with progressive myoclonic epilepsies (17)

| Generalized multiple spike waves |
| Slow background, disorganized sleep |
| Photosensitivity (to single flash: neuronal ceroid lipofuscinosis) |
| Imperfect relation of spikes to myoclonus |
| Giant somatosensory evoked potentials |
| Focal, especially occipital, epileptiform discharges |
| Vertex positive spikes in sialidosis |
clinically to be myoclonus” but were associated with a pause in electromyographic (EMG) activity. Later, these authors noted that asterixis is an essentially identical phenomenon (21). Fahn et al. (3) reported that asterixis is associated with a 25- to 200-ms pause in the EMG, similar to other forms of negative myoclonus.

Negative myoclonus can be seen in various myoclonic epilepsies (3,19,22). It has been described not only in some PMEs and other secondary or cryptogenic generalized epilepsies, but also in a syndrome that is not often considered to be a myoclonic epilepsy, benign epilepsy with centrotemporal spikes (benign Sylvian-Rolandic epilepsy). In this case, the negative myoclonic movement occurs simultaneously with the centrotemporal spike-wave complex (22).

Although classifying atonic seizures as negative myoclonus may be logical, doing so would create diagnostic confusion by replacing a term in common use with an alternate one that generally refers to a phenomenon seen in completely different syndromes. The term negative myoclonus may be reserved for atonias affecting limbs, rather than the trunk or head.

**DISTINGUISHING MYOCLONUS FROM OTHER MOVEMENT DISORDERS**

The distinction between myoclonus and other movement disorders is not always clear, and some writers consider all manner of sudden involuntary jerks to be myoclonus. Nevertheless, differentiation of epileptic from nonepileptic myoclonus and of different varieties of jerks of presumed subcortical origin from one another is obviously important.

**Simple partial seizures with motor manifestations**

As previously discussed, EEG differences exist between simple partial seizures and myoclonic epilepsies, even though the jerks of the latter can be unilateral or focal. However, consistent focality, unilaterality, or Jacksonian spread strongly suggests simple partial seizures. Some varieties of myoclonus, such as cortical reflex or reticulospinal reflex myoclonus (discussion follows) (4), may involve sequential activation of cranial nerve and spinally innervated muscles in different orders, but this phenomenon occurs rather quickly (i.e., within a few seconds). Jacksonian spread across the motor cortex is usually relatively slow, taking many seconds or even minutes. Motor simple partial seizures often involve the upper extremities but, unlike myoclonic seizures, also commonly involve the lower extremities, alone or with the upper extremities. Some authors note that the jerks of simple partial seizures, especially the long-continuing movements of the EPC syndrome, are rhythmic, while myoclonic jerks are arrhythmic (11). However, motor jerks that occur with simple partial seizures are not always strictly rhythmic, and they are not always constant in amplitude or unidirectional. At the bedside, distinguishing among EPC, segmental myoclonus, or even psychogenic jerking (pseudoseizure) may be difficult or impossible.

**Tics**

Although many tics are visibly indistinguishable from myoclonus, some differences are diagnostically helpful (Table 2). Focal tics may resemble segmental myoclonus. Tics are usually facial or vocal, but segmental myoclonus is most often thoracic and is more continuous and rhythmic. The multifocal tics of Tourette’s syndrome resemble the small-amplitude myoclonus seen in PMEs, including the exacerbation by voluntary movement. The presence of vocal tics suggests Tourette’s syndrome, which can be useful in differentiation.

Tics must be differentiated from myoclonic disorders (or other myoclonic disorders if one classifies tics as myoclonus). Drugs for the treatment of myoclonus, whether epileptic (cortical) or nonepileptic (subcortical), are not usually effective for tic disorders, and neuroleptics used for tics, such as haloperidol or pimozide, may occasionally make seizures worse.

**Chorea**

Similar problems are encountered when differentiating chorea from myoclonus. However, chorea usually coexists with athetoid movements, which are not a feature of myoclonic disorders. Also, the patient with chorea often attempts to incorporate choreiform movements into voluntary actions, which is rare in patients with myoclonus.

**Fasciculations**

Fasciculations may be misidentified as myoclonus. In fact, the term “minipolymyoclonus” was first used to describe the fasciculations caused by the denervation of spinal muscular atrophy (23). Confinement of the twitches to single muscle fascicles versus larger units suggests local neuromuscular pathology. An EMG and the presence of other clinical features of denervating diseases should allow easy differentiation between fasciculations and myoclonus.

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**TABLE 2. Characteristics of myoclonus versus those of tic**

<table>
<thead>
<tr>
<th>Myoclonus</th>
<th>Tic</th>
</tr>
</thead>
<tbody>
<tr>
<td>No preceding urge to move</td>
<td>Urge to move</td>
</tr>
<tr>
<td>Simple movement</td>
<td>Simple or complex movement</td>
</tr>
<tr>
<td>Often bilateral upper</td>
<td>Multifocal (facial) or lateralized, variable, never bilateral extremities</td>
</tr>
<tr>
<td>extremities, little</td>
<td></td>
</tr>
<tr>
<td>variation in location</td>
<td></td>
</tr>
<tr>
<td>No vocalization</td>
<td>Vocal tics 5–30% (Tourette’s syndrome)</td>
</tr>
<tr>
<td>Nonpurposeful</td>
<td>May appear purposeful</td>
</tr>
<tr>
<td>Nonsuppressible</td>
<td>Temporarily suppressible</td>
</tr>
</tbody>
</table>

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**FHM**
Startle syndromes

This category encompasses “startle epilepsy,” which usually occurs as an auditory reflex epilepsy, hyperekplexias, and culturally conditioned excessive startle responses (24). Startle epilepsy is commonly of frontal lobe or midline hemispheric origin and is often (but not always) associated with cognitive deficiency or cerebral palsy. The initial tonic axial movement was asymmetrical in 16 of 19 patients in one series (25). It often converts quickly to a versive or fencing movement of the head and body and sometimes to a generalized tonic-clonic seizure. The exaggerated startle responses seen in the nonepileptic startle syndromes are usually axial, upper limb, and bilateral, but the EEG is normal. An exception is the abnormal periodic sharp-wave EEG pattern of Creuzfeldt-Jakob disease, but the sharp waves do not necessarily coincide with spontaneous or startle-induced myoclonic jerks.

EPILEPTIC VERSUS NONEPILEPTIC MYOCLONIC DISORDERS

The distinction commonly made between epileptic and nonepileptic myoclonus is often considered synonymous with the presence or absence of EEG epileptiform discharges time-locked to the jerks. Unfortunately, the pathophysiology is not that simple. In many diseases that involve the cortex, including the PMEs, Creuzfeldt-Jakob disease, Alzheimer’s disease, posthypoxic brain damage, and many other metabolic encephalopathies, myoclonus is a prominent or occasional feature but there may be no EEG discharge associated with the jerks. In a series of 81 patients with Alzheimer’s disease, 10% had seizures or myoclonus, but they never occurred together (26). Perhaps there is also some subcortical pathology to explain the myoclonus in these disorders. Other possible explanations are that the cortex participates in a nonepileptic fashion or that epileptiform cortical discharges are so spatially restricted that they do not reach the scalp.

Hallett and others (4,5,7) distinguished no fewer than three categories of “epileptic” myoclonus that involve the cortex. However, in two of these categories, cortical involvement is not the first event. In cortical reflex myoclonus, considered in this schema to be a fragment of partial epilepsy, there is somatosensory precipitation and a giant somatosensory-evoked potential, followed by activation of cranial nerve and segmental myotomes in numeric (rostral to caudal) order. In reticular reflex myoclonus, which seems to originate within the brainstem (but in this schema is considered to be a fragment of a generalized epilepsy), the cranial nerves are activated caudally to rostrally, in reverse numeric order, with cortical involvement occurring last. Only in primary generalized epileptic myoclonus (which is considered to be a fragment of primary generalized epilepsy) is the cortex the prime mover of the jerk, with no discernible sequential activation. One can argue which among these physiological sequences should be called epilepsy. Other anatomic-physiological subvisions of myoclonic disorders based on correlations of EMG with EEG, duration of EMG discharges, action or reflex precipitation, and anatomy can also be made (4,7).

Less ambiguously, there are several quick-movement syndromes often referred to as myoclonus that are definitely of subcortical and nonepileptic origin. These include palatal myoclonus, probably better described as clonus since it is rhythmic (at 0.5–3 Hz) and uniphasic, and segmental myoclonus, which is probably better described as segmental tremor since it is relatively rhythmic and biphasic. There is a syndrome of “essential myoclonus,” which is familial or sporadic and is associated with a normal EEG and no other movement disorder (27). Asterixis may be considered a type of nonepileptic negative myoclonus. Combinations of myoclonic movements with other disordered movements, such as dystonia or ballism are also seen; this combination is a good indication of a nonepileptic, subcortical origin. However, a Parkinsonism-myoclonus combination is a feature of some PMEs, including a rare adult-onset autosomal dominant form of neuronal ceroid lipofuscinosis (28).

POSTANOXIC MYOCLONUS

Three very different phenomena are referred to as postanoxic myoclonus. The first two may be considered epileptic; they are seen soon after rather severe anoxic cortical insult during coma. The third is a late complication in survivors and may originate subcortically.

Early focal/multifocal postanoxic myoclonus

Close observation of comatose patients often reveals subtle, low-amplitude facial twitching, eye jerks or rhythmic nystagmus, tonic eye deviation, or low-amplitude multifocal twitches. The EEG of such patients very frequently reveals irregular generalized or bilateral but asymmetric spike-wave activity on a slow background. This phenomenon is considered by some to be a form of “non-convulsive” or “myoclonic” status epilepticus, but may more accurately be termed subtle generalized convulsive status (29). It most frequently occurs after an anoxic brain insult but may also develop from other causes (30). It can occur as a late stage of convulsive status epilepticus from any etiology, or as an initial form of status epilepticus after other severe causes of widespread cortical dysfunction (29).

Not all multifocal, low-amplitude postanoxic myoclonus is associated with an epileptiform EEG. In such cases, the myoclonus may be subcortical, and antiepileptic drug (AED) treatment is unlikely to be beneficial. This distinction may not be possible at the bedside, and an emergent EEG must be obtained.
Early bilateral flexor postanoxic myoclonus

This form of myoclonus is also seen soon after an anoxic event but implies even more severe cortical damage than the lower-amplitude postanoxic myoclonus. It consists of sudden flexion movements of the trunk, sometimes involving the head or extremities, and is sometimes stimulus induced. This form of myoclonus should be distinguished from decorticate or decerebrate posturing. The EEG shows a burst-suppression pattern, and unlike the subtle postanoxic jerks, the bursts coincide with the flexion spasms. This form of myoclonus has an extremely poor prognosis. Disagreement persists as to whether this phenomenon should be considered status epilepticus or simply an agonal brain rhythm, and whether or not drug treatment is of any use.

Late postanoxic intention myoclonus

This syndrome, often called the Lance-Adams syndrome (31), occurs in survivors of anoxic brain injuries and consists of interruptions of voluntary movements by positive jerks or brief negative atonias, both of which are considered myoclonus. The jerks are not associated with EEG discharges, are probably of subcortical origin, and do not improve after treatment with standard AEDs. However, improvement in this condition associated with piracetam and levetiracetam use has been reported (32).

MYOCLONUC STATUS EPILEPTICUS

If the term “subtle generalized convulsive status epilepticus” is used for the phenomenon described previously, then myoclonic status epilepticus is extremely rare. Gastaut divided myoclonic status epilepticus into three types: Type 1 in idiopathic generalized epilepsy, Type 2 in secondary generalized epilepsy, and Type 3 as part of an encephalopathy (33). He did not consider Type 3 to be true status epilepticus. Arguably, the existence of Type 2 is questionable, and Type 1 is rare.

Patients with JME sometimes have very frequent jerks or a series of jerks immediately preceding a tonic-clonic seizure, but the myoclonic seizures are almost never sufficiently continual or prolonged to warrant a designation as status epilepticus. There are only four well-described cases of JME in which the jerks recurred continually (every 1–15 s) over a long enough time period (1–24 h) to be designated as status epilepticus (34–36). In some cases, what is described as myoclonic status epilepticus is probably either subtle generalized convulsive status epilepticus or subcortical encephalopathic myoclonus (Gastaut’s Type 3) (36). The presence of eye or facial twitches sometimes seen in patients with absence status epilepticus or motor movements caused by involvement of motor areas during complex partial status epilepticus does not constitute a sufficient reason to rename the status event “myoclonic.”

CONCLUSION

Myoclonus is not a diagnosis. It is a physical sign seen in diseases of many different pathologies and in normal physiological situations. Myoclonus is universally understood to be a quick, involuntary movement, but opinions diverge as to the boundaries of the term. A narrower definition that excludes rhythmic movements aids in differentiating myoclonic disorders from tremors and clonus, including clonic seizures. However, there is no way to construct a strictly phenomenological definition of myoclonus since many movements generally agreed to be myoclonic are clinically indistinguishable from tics, chorea, startle disorders, and other phenomena. In conclusion, one must rely mostly on convention, with the rather circular conclusion that myoclonus occurs in myoclonic disorders. Nevertheless, the effort of diagnosis is not trivial and has major therapeutic and prognostic implications. A good understanding of the features associated with myoclonic disorders, particularly the myoclonic epilepsies, and the features associated with other neurological disorders that resemble myoclonic disorders, is the best aid to accurate diagnosis.

REFERENCES


