Movement Disorders
CLINICAL PRACTICE
REVIEW

Diagnostic Utility of Clinical Neurophysiology in Jerky Movement Disorders: A Review from the MDS Clinical Neurophysiology Study Group

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Abstract: Background: Myoclonus and other jerky movement disorders are hyperkinetic disorders, the diagnosis of which heavily relies on clinical neurophysiological testing. However, formal diagnostic criteria are lacking, and recently the utility and reliability of these tests have been questioned.

Objective: The aim of this review was to assess the utilization of clinical neurophysiology testing to identify possible gaps and boundaries that might guide the development of new methods for a more precise diagnosis and in-depth understanding of myoclonus.

Methods: We reviewed electrophysiological features of cortical myoclonus, subcortical myoclonus (ie, myoclonus associated with dystonia, brainstem myoclonus), excessive startle reflex, spinal myoclonus (ie, spinal segmental and propriospinal myoclonus), peripheral myoclonus and mimics of myoclonus of peripheral origin (hemifacial spasm, minipolymyoclonus, myokymia), functional jerky movements, chorea, and tics.

Results: Electrophysiological features that support the recognition of myoclonus subtypes, such as muscle burst duration, muscle pattern of activation, measures of cortical excitability, or movement-related cortical potentials, have been identified. These significantly contribute to the diagnosis of jerky movement disorders, but their reliability is uncertain. Despite the significant advancements, several unresolved questions persist. Factors contributing to this include the absence of systematic neurophysiological assessment and standardized methods, alongside the limited number of patients investigated using these techniques.

Conclusion: Although clinical neurophysiology remains the "gold standard" for defining and diagnosing myoclonus, our review highlighted the need to enhance the quality and reliability of neurophysiological testing in jerky movement disorders. Further studies including larger cohorts of patients recruited from different centers, employing standardized and optimized electrophysiological techniques, are warranted.

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Myoclonus and other jerky movement disorders are hyperkinetic disorders, the diagnosis of which heavily relies on clinical neurophysiology (CN) testing.[1–3] This includes techniques such as surface poly-electromyographic (EMG) recording of myoclonic jerks, long-latency EMG responses to mixed or cutaneous nerve stimulation (long-latency reflex [LLR]), electroencephalography (EEG), EEG–EMG polygraphy using back-averaging (including Bereitschaftspotential [BP]), and cortico-muscular coherence analysis, as well as somatosensory evoked potentials (SEP).[4,5] These tests not only aid the differential diagnosis between myoclonus and other jerky movement disorders, and in certain cases help identify their underlying causes (eg, BP for functional jerky movement disorders), but can also identify the anatomical source of the myoclonus within the nervous system. According to this principle, four main myoclonus subtypes can be distinguished: cortical, subcortical (including myoclonus associated with dystonia, brainstem myoclonus), spinal (including segmental and propriospinal), and peripheral. An alternative classification of myoclonus has been proposed,[6] which, apart from cortical and peripheral, comprises the categories of cortical–subcortical, subcortical nonsegmental myoclonus, and segmental.[7] In this review we used the first classification as it is more applicable to clinical practice and more accurately reflects the pathophysiology of myoclonus and the neurophysiological findings associated with this disorder.

Beyond the classification, there is also a need to establish definitive CN diagnostic criteria for myoclonus. Despite being deemed the "gold standard," mainly to differentiate cortical from noncortical myoclonus,[2,5,8] the diagnostic utility of CN has been called into question, due to several limitations.[9,10] For instance, retrospective studies reported that CN testing revealed a cortical origin only in a minority of patients presumed to have cortical myoclonus clinically,[9,11] whereas the diagnostic accuracy of CN remains inadequately investigated.[10] Moreover, there is a lack of consensus on CN criteria, which are inconsistently applied across studies.

To elucidate the diagnostic value of CN in myoclonus, we conducted a thorough review of the electrophysiological features utilized to diagnose and differentiate various myoclonus subtypes, including mapping key milestones in the application of neurophysiological techniques to this disorder. Furthermore, we reviewed the application of CN for the differential diagnosis of myoclonus versus other jerky movement disorders, including excessive startle, mimics of myoclonus of peripheral origin, functional jerky movements, chorea, and tics, which often pose diagnostic challenges for clinicians.

Our aim was to identify possible gaps and boundaries that might guide the development of new methods for a more precise diagnosis and in-depth understanding of these disorders.

Patients and Methods

We identified 6 topics for literature search: (1) cortical myoclonus, (2) subcortical myoclonus (including myoclonus associated with dystonia, brainstem myoclonus) and excessive startle reflex, (3) spinal myoclonus (including spinal segmental and propriospinal myoclonus), (4) peripheral myoclonus and mimics of myoclonus of peripheral origin (such as minipolymyoclonus, myokymia, hemifacial spasm), (5) functional jerky movements, and (6) tics and chorea. Each of these topics was assigned to 2 members of the *myoclonus and other jerky movements group* of the Movement Disorders Society CN Study Group for conducting literature review. The findings were presented to the entire group for discussion and analysis. Considering the broad topic, we opted for a narrative, because the definition of a strict search strategy would have limited our findings. Nevertheless, the key words primarily used to select studies on Medline database were cortical, subcortical, brainstem, spinal, propriospinal, peripheral myoclonus, myoclonus dystonia, excessive startle reflex, tics, chorea, functional jerky movements together with neurophysiology, EMG, EEG, back-averaging, SEP, giant SEP, cortico-muscular coherence, and BP. Review articles were checked to include relevant articles and information. All types of original articles were included with the following exclusion criteria: written language other than English, use of noninvasive brain stimulation techniques, or other neurophysiological techniques not for diagnostic purpose.

Results

Cortical Myoclonus

Professor Friedreich in 1881[12] first published a case of a man affected by pneumonia, who exhibited brief, arrhythmic, stimulus-sensitive, multifocal twitches that he called paramyoclonus multiplex. Grinker, Serota, and Stein[13] observed that EEG abnormalities were related to specific jerky movements in epileptic patients, and Dawson[14] reported the first recordings of enlarged SEP in patients with myoclonic epilepsy, evoked by tapping tendons or electrical stimulation. Halliday[15] further characterized the cortical involvement in what he called "pyramidal" myoclonus. In 1975, Shibasaki and Kuroiwa[16] introduced the EEG back-averaging technique using the brief muscle twitch as a trigger event, showing that a cortical transient preceding the muscle burst even with an initial unremarkable EEG. Hallett and colleagues[17] described enhanced cortical(C-) reflex in patients affected by cortical myoclonus. Reviewing this literature and adding their own observations, Obeso and colleagues[18] outlined the clinical and neurophysiology spectrum of cortical myoclonus, with neurophysiology comprehensively reviewed by Shibasaki.[19] Brown and colleagues[20,21] described abnormal cortico-muscular and intermuscular coupling in patients affected by high-frequency rhythmic myoclonus. The main components of cortical myoclonus have been reported from retrospective[9,22,23] or cross-sectional[11,20,21,24–29] case series, and a systematic review,[10] which includes some of the case series referenced before. This literature includes 227 cases in which the clinical features of cortical myoclonus and its physiology correlates have been described (Table 1). Features of negative cortical myoclonus, which refers to a brief and sudden occurrence of EMG silence when holding a posture, have been illustrated[30] and suggest a cortical origin,[31] as it can be induced by median nerve stimulation, the same stimulation that can elicit enhanced SEP and C-reflex in

TABLE 1 *Clinical neurophysiological studies in cortical myoclonus*

Technique	Subjects studied over a total sample of 227 (%)	Subjects studied showing positive findings (n) and percentage (%)
Jerk locked back-averaging	138 (60%)	70 (50%)
SEP	144 (63%)	67 (46%)
C-reflex	68 (29%)	49 (72%)
Cortico-muscular coherence[a]	49 (21%)	19 (38%)

Abbreviation: SEP, somatosensory evoked potentials.
[a]Note that this technique can be used only when studying events with a frequency of >3 Hz.

cortical myoclonus. However, most of the published results relate to positive cortical myoclonus (ie, presence of brief muscle contractions). Clinical features of cortical myoclonus include brief movements, focal or more frequently multifocal anatomical distribution, arrhythmic and rarely rhythmic, spontaneous or induced by sensory stimulus or movement, sporadic or familial, primary or secondary. In parallel, the following neurophysiological features have been described for cortical myoclonus: short EMG burst duration, presence of enlarged or giant SEP, enhanced C-reflex, presence of EEG discharges time locked to individual myoclonic jerks detected with jerk-locked back-averaging (JLBA), and enhanced cortico-muscular and intermuscular coherence. Regarding EMG burst duration, most case series reported durations of ≤50 ms. However, some groups reported cortical myoclonus exceeding this duration up to 200 ms.[18,22,23] SEPs were studied in 144 of the patients reported (63% of the whole sample), and they were enlarged in 67 subjects (46%). The threshold amplitude to consider SEP to be enhanced was in some studies >12 μV for median nerve stimulation at the wrist, 5.5 μV for finger stimulation, and >2 μV for toe stimulation.[18,32,33] However, this is laboratory dependent. Case series reviewed usually report higher amplitudes in the patients studied, namely >10 μV measured between P1 (P25) and N2 (N35) in the somatosensory areas. C-reflex or LLR was studied in 68 subjects (29%), and exaggerated responses were present in 49 subjects (72% of the sample studied). JLBA[16] was studied in 138 subjects (60%) and was present in 70 subjects (50% of the sample studied). Finally, coherence studies (cortico-muscular and intermuscular coherence)[11,21] have been reported to be helpful in patients with rhythmic cortical myoclonus (cortical tremor) with frequency >3 Hz. Cortico-muscular coherence was studied in 49 patients of the discussed sample and was present in 19 of the patients studied (38%). It is sometimes considered helpful to demonstrate cortical involvement when JLBA does not show positive findings or cannot be applied because of the high frequency of muscle jerks.[21]

In summary, myoclonus characterized by multifocal, arrhythmic, stimulus-sensitive, and brief movements with EMG burst durations of <50 ms is highly probable to be of cortical origin. However, longer EMG bursts or rhythmic/focal phenomenology does not rule out cortical myoclonus and necessitates additional assessments such as SEP, C-reflex, and JLBA. Coherence studies for rhythmic myoclonus exceeding a frequency of 3 Hz are recommended. Regarding the averaging techniques, there is no consistent recommendation for the number of events that need to be averaged, with multiple series reporting >100 events for C-reflex or JLBA, but ranging between 17 and 200 or more. Despite positive findings in approximately 48% to 72% of cases, the sensitivity of SEP, C-reflex, and JLBA remains relatively low (Table 1). Uncertainty persists regarding the inconsistent presence of neurophysiological markers across patients with similar clinical presentations, warranting further investigation into the underlying pathophysiology of different cortical myoclonus phenomena and the applied methodologies to capture them. Additionally, discrepancies between clinical and neurophysiological assessments may exist, potentially leading to misclassification. Although individual test sensitivity may be limited, combining tests may improve overall sensitivity.[34] Finally, further exploration of negative myoclonus is necessary to elucidate the role of the motor cortex in its generation.

Subcortical Myoclonus

The term "subcortical myoclonus" is employed to differentiate it from cortical myoclonus, which exhibits neurophysiological markers indicative of a cortical origin. Subcortical myoclonus refers to forms of myoclonus where the presumed generator lies between the basal ganglia and the medulla. Following this definition, two primary subtypes can be identified: myoclonus associated with dystonia and brainstem (reticular) myoclonus. Exaggerated startle reflex will also be discussed. Due to the ambiguity surrounding the terms "palatal tremor" and "palatal myoclonus" in the literature, and its current classification as palatal tremor given the rhythmicity of palate movements,[35] this topic has not been included in this review.

Myoclonus Associated with Dystonia

According to several reviews, subcortical myoclonus related to myoclonus dystonia has prolonged burst duration, no stimulus sensitivity, and lack of electrophysiological cortical features compared to cortical myoclonus. Nevertheless, only a few studies have performed myoclonus recording in these patients.[1,4,7,36] The first study investigating the electrophysiological features of myoclonus dystonia was performed before the discovery of genes associated with this condition.[37] In 10 patients, EMG, SEP, and EEG were recorded. The findings showed EMG burst durations between 50 and 250 ms, but up to 500 ms, and when the EMG bursts were prolonged, they

always produced visible muscle jerks that were distinct from dystonic spasms. The jerks involved one muscle and its synergists or showed co-contraction of agonist–antagonist muscle groups; they could be rhythmic at time with a frequency of 3 to 4 Hz. Negative myoclonus was observed in some cases. Its duration normally varies from 50 to 500 ms,[30,38] but in a recent study on progressive myoclonus ataxia, it was found to be from 88 to 194 ms in 6 patients, including 2 with cortical negative myoclonus.[39] SEP was normal in all myoclonus-dystonia subjects, except 1 case that showed an amplitude of ~13 μV for the P26-N35 component contralateral to the affected arm. No EEG activity time locked to the jerks was found in the 8 patients studied using back-averaging.

Other studies on different myoclonus dystonia syndromes showed similar findings (45 patients in total, but not all underwent all the tests).[40–44] EMG burst durations were between 15 and 250 ms (1 study reported up to 750-ms burst duration, likely related to dystonia[40]). The EMG bursts were mostly irregular but sometimes rhythmic[42] or associated with tremor.[41] SEP was not enlarged, JLBA was negative (subcutaneous single-use needle recording in 1 study[42] and average of 24 epochs in another study[44]), and LLR (recorded under muscle activation[40,42] and/or at rest) was normal or not found. Only one study investigated EMG–EEG and EMG–EMG coherence in 20 patients (5 of whom were asymptomatic) with myoclonus dystonia caused by *SGCE* gene mutation.[45] High EMG–EEG coherence was found only in patients with predominant dystonia, but not in patients in whom the predominant feature was myoclonus, whereas there was no EMG–EMG coherence (between the neck muscles, between several arm muscles, and between the arm and neck muscles) at rest and during weak (25% maximum voluntary contraction) isometric contraction when rotating the head or extending the wrist.

In summary, about 50 patients with myoclonus dystonia have been investigated using clinical electrophysiological techniques (Table 2). EMG recording of the myoclonus showed variable burst duration, which could be <50 to 100 ms and up to 500 ms (which might reflect dystonic spasms). SEP, JLBA, and LLR (exact number of patients not available) were negative, apart from 1 patient who showed enlarged SEP. In all patients EMG–EMG and EEG–EMG analyses did not show coherence related to myoclonus.

Brainstem (Reticular) Myoclonus

Brainstem or reticular myoclonus is thought to originate from the lower brainstem or reticular formation, in view of its typical muscle pattern of activation. It was first described by Hallett and colleagues in 1977,[46] who presented a single case of post-hypoxic "reticular reflex myoclonus" showing, on clinical electrophysiological studies, a short duration of the EMG bursts (~10–30 ms), with earlier activation of trapezius and sternocleidomastoid (SCM) followed by a rostral and caudal progression; activation of the arms tended to precede the legs, and the cranial nerve musculatures (at least those supplied by the lower cranial nerves) seemed to be activated in ascending order, with a latency that was compatible with the distance of the muscles from the neuraxis. SEP was normal and JLBA was negative. The other recordings were performed on single cases (7 in total) with different etiologies[47–52] but showed similar EMG pattern, namely short EMG burst duration (from 10 to 100 ms, except 1 case up to 150 ms[49]) and early activation of muscles innervated by the accessory nerve followed by the orbicularis oculi and then upper- and lower-limb muscles (with a proximal–distal gradient). In 2 cases, C-reflex was found.[48] Interestingly, the conduction velocity through the spinal cord was rapid, differentiating brainstem myoclonus from excessive startle reflex.[46,52]

In conclusion, brainstem myoclonus was recorded only in a small number of patients (Table 3). The EMG recording showed short burst durations and a typical pattern of muscle activation. The C-reflex was found in 2 cases. The conduction velocity through the spinal pathway was measured in 2 patients (80 and 40 m/s, respectively),[46,52] but in 1 study the methods were not detailed.[52]

TABLE 2 *Clinical neurophysiological findings of myoclonus associated with dystonia*

EMG burst duration (range)	Enlarged SEP	JLBA, LLR, EMG–EMG/EMG–EEG coherence
15–750 ms	2 subjects	None

Notes: Total subjects studied are 50; exact number for each test is not available.
Abbreviations: EMG, electromyography; SEP, somatosensory evoked potential; JLBA, jerk-locked back-averaging; LLR, long-latency reflex; EEG, electroencephalography.

Excessive Startle

Startle is a physiological reflex to unexpected auditory and somesthetic stimulation. It is deemed pathological, known as excessive startle, when certain criteria are met: shorter onset latencies of EMG responses, longer burst durations, persistent responses with repeated stimuli but not strictly reduced habituation, and more consistent activation of limbs and lumbar spinal muscles. Importantly, the pattern of muscle activation in excessive startle is similar to the physiological startle response.[53,54] Excessive startle reflex has been investigated in several studies for 58 patients[53–59] but using different methods. Whereas auditory stimulation was used in all studies, other forms of stimulation to elicit the reflex were used only in some, such as peripheral electrical stimulation of sensory and mixed nerves[53,54,59] and taps to the body with a tendon hammer.[53,54,57] Regarding auditory stimulation, different protocols have been applied with various sound intensities and stimulation frequencies (ie, randomly about once every 20 min,[54] every 45 to 60 s for 20 trials,[53] every 10 or 60s,[55,56] either unexpected or at 10-s intervals,[58] at random intervals of 2 to 5–10 min[57,59]). Despite the diverse protocols, the evoked responses were consistent, with an early auditory blink reflex response followed by activation of the SCM muscle, and then rostro and caudal progression based on the distance of segmental innervations from the caudal brainstem.[60] The conduction velocity in spinal efferent pathways is considered moderately slow.[53,54] In cases with excessive startle response, when compared to the physiological startle reflex, no habituation to repeated stimuli was found.[53,54,58] However, according to

TABLE 3 *Clinical neurophysiological findings of brainstem myoclonus*

EMG burst duration	Pattern of muscle activation	C-reflex	Rapid conduction velocity
10–100 ms (150 ms in 1 case)	Early-onset activation of the SCM and trapezius muscles followed by rostral and caudal activation, with onset latencies compatible with the distance from the lower brainstem	Found in 2 subjects	Measured in 2 subjects: 80 and 40 m/s

Note: Total subjects studied are 8.
Abbreviations: EMG, electromyography; SCM, sternocleidomastoid muscle.

2 studies, habituation depends on severity of the startle response and may be less prominent than in control cases.[55,56] Two patients with excessive startle reflex were found to have enlarged or giant SEP.[54]

In conclusion, excessive startle reflex is characterized by a reproducible response, elicited by auditory stimulation or other sensory stimuli. Different from brainstem myoclonus, the early response is an auditory blink reflex, and there is a relatively slow recruitment of caudal muscles, indicating moderate conduction velocity in spinal efferent pathways, and longer EMG burst duration.[61] Additionally, startle reflex is stimulus induced, whereas brainstem myoclonus may occur spontaneously. However, studies have been conducted on a limited number of patients with varying methodologies. Not all studies confirm reduced habituation of excessive startle reflex. Furthermore, enlarged/giant SEP has been found in 2 patients.[54]

Spinal Myoclonus

Propriospinal Myoclonus

Propriospinal myoclonus is a rare form of myoclonus, characterized by jerks of spinal origin.[62,63] The first description of propriospinal myoclonus in 3 cases was given by Brown and colleagues.[62] Flexor arrhythmic jerks of the axial muscles were the typical presentation, often accompanied by jerks of proximal limb muscles. Typically, they are stimulus sensitive and increase in the supine position. The EMG discharge lasted from 50 to 300 ms, rarely 1000 ms or longer. The characteristic pattern of muscle activation can be detected by measuring latencies of recruited muscles, showing that the discharge slowly spread (5–15 m/s) up and down the origin in the spinal cord to involve the rostral and caudal segments, presumably via propriospinal pathway. Neither corresponding EEG discharge nor giant SEP was noted.

Although there are some reports in which spinal cord lesions were present in the case of propriospinal myoclonus,[64–69] suggesting that they are symptomatic (ie, secondary), most patients who presented with propriospinal myoclonus are considered to have a functional movement disorder mainly because of the absence of spinal cord lesions and the presence of BP in many cases.[63,70–72] However, it is still controversial whether idiopathic propriospinal myoclonus exists.[73] We conclude that propriospinal myoclonus is rare,[22,63,70] and many cases are likely caused by a functional movement disorder.

Segmental Myoclonus

This type of myoclonus is considered extremely rare. Segmental myoclonus is the result of abnormal spontaneous discharges of motor neurons in a limited area of the spinal cord, inducing involuntary rhythmic or semirhythmic (usually 1–3 Hz, ranging 2–600 contractions per min[74]) jerks in a muscle or group of muscles innervated by the affected spinal segment. The durations of EMG discharge varied but were usually between 100 and 500 ms.[75–78] Segmental myoclonus is generally not stimulus sensitive, but some cases with stimulus sensitivity have been reported.[77,79] EEG and SEP were normal. Various possible causes have been reported, including autoimmune,[80–82] Chiari malformation,[83] cervical spondylosis/myelopathy,[74,84–86] cervical transforaminal epidural steroid injection,[87] demyelination,[88] drug,[89] infection,[90,91] paraneoplastic,[92] postinfectious,[93] tumor,[94,95] spinal surgery,[96] and vascular diseases.[97,98]

Peripheral Myoclonus

The term "peripheral myoclonus" indicates rhythmic or semirhythmic jerk secondary to plexus, nerve, root lesion, or, rarely, anterior horn cell disease. Compared to myoclonus from other generators, it presents with specific electrophysiological features, such as long EMG bursts (100–400 ms) and a pseudorhythmic/rhythmic pattern (1–3 Hz).[99–101] It is interesting to note that long EMG bursts and rhythmicity are commonly found in spinal segmental myoclonus as well.[102] Consistent with this finding, it has been hypothesized that peripheral and spinal segmental myoclonus may share a common pathophysiology, represented by disinhibition of spinal motor circuits, caused by deafferentation in peripheral myoclonus and direct spinal cord damage in spinal myoclonus.[99–101]

These physiological features make this form of peripheral myoclonus substantially different from hemifacial spasm that is considered the most common form of peripheral myoclonus. It is typically caused by arterial compression of the facial nerve at its exit site from the pons but has also been reported in multiple sclerosis with or without a unilateral pontine demyelinating lesion.[103,104] In hemifacial spasm motor units fire in bursts of up to 40 at frequencies of 200 to 300 Hz. There may be synchronicity between different facial muscles that is consistent with ephaptic transmission between neighboring motor axons.[105]

In summary, although peripheral myoclonus might be difficult to distinguish from spinal segmental myoclonus clinically, its most common form, that is, hemifacial spasms, is easily recognized using needle EMG.

Mimics of Myoclonus from Peripheral Disorders

The main peripheral myoclonus mimic is myokymia, in which a "true" peripheral origin can be identified. Myokymia classically results from radiation plexopathy or demyelination within either the spinal cord or the peripheral nervous system[106,107] and manifests as continuous, irregular quivering of muscles. With needle EMG, myokymic discharges are characterized by motor unit action potentials occurring as doublets, triplets, and multiplets, at inter-burst frequencies of 2 to 10 Hz and intra-burst spike frequency commonly between 5 and 62 Hz.[108,109] Therefore, the diagnosis of myokymia can be easily confirmed using needle EMG.

Minipolymyoclonus

The term "minipolymyoclonus" or "polyminimyoclonus" refers to a hyperkinetic movement disorder characterized by intermittent, low-amplitude, arrhythmic movements of the hands, commonly involving several fingers, with amplitudes just sufficient to produce visible and palpable movements of the joints.[110] Minipolymyoclonus has been described in 3 main groups of neurological conditions: central neurodegenerative disorders, epilepsy, and diseases of spinal anterior horn cells. When associated with disorders causing cortical degeneration, minipolymyoclonus appears to have a similar pathophysiology to cortical myoclonus.[5,9,111–113] For instance, several studies[114–116] described patients affected by Parkinson's disease and multiple system atrophy presenting with minipolymyoclonus, which was characterized by variable combinations of brief EMG bursts (<100 ms), enhanced LLR, positive JLBA, and synchronous activation of agonist and antagonist muscles, with findings consistent with cortical myoclonus.[117] Exceptions are represented by studies, such as in Alzheimer's disease, where minipolymyoclonus was preceded by a bifrontal EEG negativity, a finding interpreted as more suggestive of a subcortical, rather than cortical, generator.[118]

Minipolymyoclonus has been described in neurological disorders associated with epilepsy. Its electrophysiological features have been less well studied than in degenerative disorders, possibly because its cortical origin has been postulated to be due to the coexistence of epilepsy. This assumption has been partly confirmed,[28,119] as shown by electrophysiological features compatible with cortical myoclonus. An exception is the EEG discharges, which in some patients were bifrontal and long lasting (100–250 ms) and precedes the EMG burst associated with minipolymyoclonus by a highly variable interval (5–500 ms), sometimes too long to be considered cortical myoclonus.

Disease affecting the spinal motor neurons[110,120–124] or conditions causing peripheral nerve hyperexcitability, such as anti-CASPR2-associated paraneoplastic Morvan syndrome,[125] have all been associated with minipolymyoclonus; however, accurate neurophysiological characterization in this context is lacking.

Inoue and colleagues[126] described minipolymyoclonus, induced by voluntary movement, in a small number of patients affected by amyotrophic lateral sclerosis and found that EMG discharges associated with the jerks were compatible with large fasciculation potentials, which are caused by irregular activation of single motor units, either at the spinal motor neuron level or its axon.[108] Another possibility, strengthened by the occurrence of minipolymyoclonus during movement, is that it may reflect unfused tetanus (sometimes named "contraction pseudotremor of chronic denervation"[127]). This can be observed when, as a result of chronic denervation, a reduced number of large motor units discharge at an abnormally high frequency.[110,127] Albeit not formally tested, the two entities should be easily discriminated by needle EMG: whereas fasciculations would show an irregular firing pattern and occur either spontaneously or during muscle activation, unfused tetanus would occur only during contraction and be associated with regular motor unit firing.

In conclusion, the term "minipolymyoclonus" does not indicate a single pathophysiological entity, and proposals have been made to use it only when its central origin is suspected, while resorting to "minipolyfasciculation" in the case of a peripheral origin.[123,128] Whereas the former would be sufficiently precise, the prefix "mini" in the latter term would likely be misleading, as the fasciculations causing minipolymyoclonus would necessarily be an expression of large motor unit discharges; therefore, "polyfasciculation" would likely be more appropriate. This phenomenon would still need to be distinguished from unfused tetanus, which may coexist but would represent a different entity.

Jerky Functional Movement Disorders

Various neurophysiological features have been investigated in the context of jerky functional movement disorders[10,129]; these include the inconsistency of the EMG pattern in relation to other types of myoclonus, the BP, event-related desynchronization (ERD), and the auditory startle reflex.

Seven case series, involving 170 patients diagnosed with functional jerks, described the polymyographic pattern observed. The majority of patients exhibited an axial body distribution, specifically involving propriospinal, idiopathic spinal, and startle-like reflex (n = 121), and the remainder palatal tremor/myoclonus (n = 9) or an unspecified presentation (n = 40).[22,70,71,130–134] The following findings were considered as "incongruent EMG": (1) inconsistent activation of the first muscle, (2) inconsistent spread of muscle recruitment (rostral and caudal propagation), (3) burst duration >1000 ms, (4) no synchronous activation of agonist and antagonist, and (5) presence of distractibility or entrainment; and these were observed in approximately 75% of patients with clinical functional jerks.

The BP is the earliest movement-related cortical potentials, namely EEG potentials that manifest around the time of movement, offering insights into the cortical activity underlying actions. BP is observed prior to a self-paced movement and considered a signature of motor preparation[134,135]; it is a slowly

TABLE 4 *Summary of the main clinical neurophysiological findings for each myoclonus subtype*

	Cortical myoclonus	Myoclonus associated with dystonia	Brainstem (reticular) myoclonus	Excessive startle	Propriospinal myoclonus	Segmental myoclonus	Peripheral myoclonus	Jerky functional movement disorder
Pattern of muscle activation	Multifocal, arrhythmic (rarely rhythmic), stimulus sensitive	Jerks involving 1 muscle and its synergists, or co-contraction of antagonist muscles; can be rhythmic	Early activation of trapezius and SCM followed by a rostral and caudal progression	Like brainstem myoclonus, but with auditory blink reflex early response; elicited by sensory stimuli (mainly auditory)	Flexor arrhythmic jerks of the axial and proximal limb muscles	Rhythmic or semirhythmic jerks (usually 1–3 Hz) in muscles innervated by the affected spinal segment	Rhythmic or pseudorhythmic jerks (1–3 Hz)	Inconsistent activation/spread of muscle recruitment, no synchronous activation of antagonist muscles, distractibility, entrainment
EMG burst duration	Usually short (<50 ms)	50–100 ms (up to 500 ms, which might reflect dystonic spasms)	10–100 ms (1 case up to 150 ms)	Longer EMG burst duration compared to brainstem myoclonus	50–300 ms (rarely 1000 ms or longer)	100–500 ms	Long (100–400 ms)	Very long burst duration (>1000 ms)
SEP and C-reflex	Giant SEP and C-reflex present	Generally, no giant SEP and no C-reflex	C-reflex in 2 of 8 cases	Enlarged/giant SEP in 2 patients	No giant SEP	No giant SEP		
EEG–EMG	JLBA and EEG–EMG coherence present	No JLBA and no EMG–EMG/EEG coherence			No EEG discharge BP present in many cases	No EEG discharge		BP present in 25–86% of the cases; specificity of 100%
Others	Duration up to 200 ms has been reported		Conduction velocity through the spinal cord is rapid	Conduction velocity through the spinal cord is moderately slow	Discharge slowly spread (5–15 m/s) rostrally and caudally the origin in spinal cord		In HFS, motor units fire in bursts (up to 40) at 200–300 Hz. There may be synchronicity between different muscles	ERD present in 62–65% of the cases; specificity of 100%
	Comments							

(Continues)

TABLE 4 *Continued*

Cortical myoclonus	Myoclonus associated with dystonia	Brainstem (reticular) myoclonus	Excessive startle	Propriospinal myoclonus	Segmental myoclonus	Peripheral myoclonus	Jerky functional movement disorder
Uncertainty persists regarding the inconsistent presence of the above markers	Small number of patients studied, but no clear signs of cortical involvement found	Small number of patients studied, but consistent pattern of muscle activation	Reproducible response and consistent pattern of muscle activation	Controversial. It is maybe rare, and most of the cases are likely caused by FMD	Extremely rare, only a few evidence available	Rare, it can be like segmental myoclonus. HFS is easily recognized using needle EMG	BP and ERD are highly accurate, but evidence is limited

Abbreviations: SCM, sternocleidomastoid; EMG, electromyography; SEP, somatosensory evoked potentials; EEG, electroencephalography; JLBA, jerk-locked back averaging; BP, Bereitschaftspotential; HFS, hemifacial spasm; ERD, event-related desynchronization; FMD, functional movement disorder.

rising, negative cortical deflection started at least 1000 ms (early BP) or between 1000 and 500 ms (late BP) before the movement onset as measured using EMG.[10] It has been shown that BP is present in 25% to 86% of patients with functional jerky movements (n = 216) and has a specificity of 100% in differentiating functional from "organic" myoclonus and a specificity of 86% differentiating functional myoclonus from tics.[22,70,71,130,131,133,136–139]

ERD refers to reduction in amplitude of β and low γ EEG oscillations (13–45 Hz) prior to cued and self-paced movements. Studies showed that ERD was present in 62% to 65% of patients with functional myoclonus (n = 49) and has a specificity of 100% in differentiating functional from cortical myoclonus.[137,138] The combination of BP and ERD has a sensitivity of 75% to 80% and a specificity of 100% in differentiating functional (n = 29) from cortical myoclonus.[137]

The auditory startle response has been studied in the context of functional jerks.[4] A study showed increased response probability of the early and late phases of the startle reflex in patients with functional myoclonus (n = 17) compared to healthy controls.[131] Furthermore, variable muscle recruitment was observed in the late phase.[131]

In summary, although electrophysiological techniques seem to be highly accurate in discriminating myoclonus from functional jerks, the existing evidence primarily derived from case series and a limited number of case–control studies. Moreover, technical challenges, such as the variability of the muscles involved in the jerky movements, should be considered as these features may limit the possibility of performing these tests based on signal averaging.

Tics

Tics are brief and discrete movements that strongly resemble voluntary actions but occur repetitively and irregularly, and are not embedded in a discernible context.[140]

The variability in tic behaviors and their parallels to volitional motor behavior is also reflected in their physiological parameters as captured using surface EMG.[141] Both EMG burst duration and pattern of muscle activation during tic do not provide unique clues to distinguish them from voluntary actions.[141] Therefore, although surface EMG may be used to characterize tics, its application is not particularly useful for the purpose of diagnosis. Routine EEG recordings also do not provide reliable insights into the neural processes that underly tic generation.[142] However, the combination of surface EMG and EEG with back-averaging has been suggested to be useful in the distinction of tics from myoclonus, and in functional jerky movements that may resemble tics.[143,144] Several studies have used JLBA to demonstrate that some, but not all tics, may be preceded by BP.[136,145–147] Whereas the first study showed that tics were not preceded by BP,[146] later studies reported that tics can indeed be preceded by BP, albeit with a short duration falling within the range of late BP, or normal BP.[136,143,145,147] Crucially, the morphology of the premovement potentials that precede tics often differs from phenomenologically similar voluntary actions.[136,145–147] Another neurophysiological cortical marker that has been examined is event-related power changes, specifically ERD in the β frequency band. Several studies

have reported an absence of β ERD with some tics,[148–150] which is typically observed in volitional actions.[145] A study examined both the presence of premotor potentials and event-related β desynchronization preceding tics and reported a dissociation between the 2 phenomena in some cases.[145]

In conclusion, except for some clinico-electrophysiological features (including the distribution and pattern of activation, absence of very short burst duration and negative bursts), the use of EMG is limited for the diagnosis of tics. Conversely, combined EEG–EMG recording, with back-averaging technique (like BP) and event-related power changes, might be helpful to distinguish tics from jerky functional movement disorders.

Chorea

Although chorea is primarily characterized by a constant flow of movements that are randomly distributed across the body and over time, it is often described among jerky movement disorders.[151] This is due to the nature of individual movements, which may still have a jerky quality. Distinguishing chorea from myoclonus can sometimes be challenging. EMG recordings of chorea typically show subcontinuous, fluctuating muscle activities of variable duration but often longer than that seen in myoclonus.[152,153] However, the diagnosis relies mainly on clinical presentation rather than neurophysiological studies, as there are a few studies on the CN of chorea.[10]

Conclusion

Myoclonus is characterized by brief, jerky, shock-like involuntary movements, which can result from sudden muscle contractions, known as positive myoclonus, or from the abrupt cessation of ongoing muscle activity, termed "negative myoclonus."[154] This straightforward definition can be readily translated into electrophysiological terms, as EMG recordings of myoclonus typically reveal brief bursts or interruptions in muscle activities. These features serve to differentiate myoclonus from other movement disorders, as EMG discharges in the myoclonus are too arrhythmic to be considered a tremor, too fast and brief to be dystonic or choreic, and not stereotyped as tics. Although these hallmarks are widely recognized, they have never been formally established, and the exceptions (eg, rhythmic myoclonus) are rarely considered, making the diagnosis or characterization of myoclonus using electrophysiology difficult at times. Another level of complexity is related to a peculiar aspect of myoclonus: it can originate from different parts of the central and peripheral nervous system, leading to variable clinical presentations. Myoclonus can indeed be focal, multifocal, or generalized, based on body distribution, and more or less brief based on the duration of EMG bursts; it is mostly arrhythmic, but it can be semirhythmic or rhythmic, and spontaneous, reflex, or action-induced, depending on the provoking factors.[5,61,155] Although these features depend on the source of its generation, a definitive clinico-pathophysiological correlation remains elusive.

Our review showed that efforts to define myoclonus and jerky movement disorders using CN techniques have been made, but limitations persist due to a lack of systematic assessments and standardized methodologies. Only a small number of patients with jerky movement disorders assessed using CN techniques have been reported in the literature,[8,34] and conventional criteria for diagnosing myoclonus lack uniformity. For instance, whereas some techniques such as SEP are applied according to international guidelines,[156] others, including JLBA, C-reflex, and startle reflex, lack established methodologies, thereby hindering the comparison of results across different laboratories.[34] A summary of the main clinical neurophysiological findings for each myoclonus subtype is presented in Table 4.

The aforementioned limitations strongly warrant further studies to establish the sensitivity and specificity of each test, taking into consideration that the combination of these tests may increase the sensitivity.[34] Moreover, standardization of both advanced and basic technical aspects, such as the number of epochs to record and average, EEG montage, EMG threshold for back-averaging, automated process, and criteria for EMG burst, should be implemented.

In conclusion, CN may be regarded as the "gold standard" for defining myoclonus and at least some of its subtypes, significantly contributing to the diagnosis of jerky movement disorders. However, to enhance the quality and reliability of these tests, further research is warranted. This should encompass various myoclonus subtypes and other jerky movement disorders, involving larger cohorts of patients recruited from diverse centers. Standardized and optimized CN techniques should be employed to ensure consistency and validity across studies.

Author Roles

1. Review: A. Conception, B. Organization, C. Execution
2. Manuscript preparation: A. Writing of the first draft, B. Review and critique

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Data sharing is not applicable to this article as no new data were created or analyzed in this study. ■

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