

The Aspen Course

International Parkinson and Movement Disorder Society Pan American Section

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Comprehensive Review of Movement Disorders for the Clinical Practitioner

# The Diagnosis and Treatment of Myoclonus

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# Disclosures

- Advisor for AbbVie, AFFiRis, Alector, Amylyx, Aprinoia, Biogen, BioAdvance, Biohaven, BioVie, BlueRock, BMS, Cavion, CoA Therapeutics, Denali, Janssen, Jazz, Lilly, Novartis, Paladin, Pharma 2B, PsychoGenetics, Roche, Sun Pharma, and UCB.
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Nothing relevant to this lecture

# Special thanks to

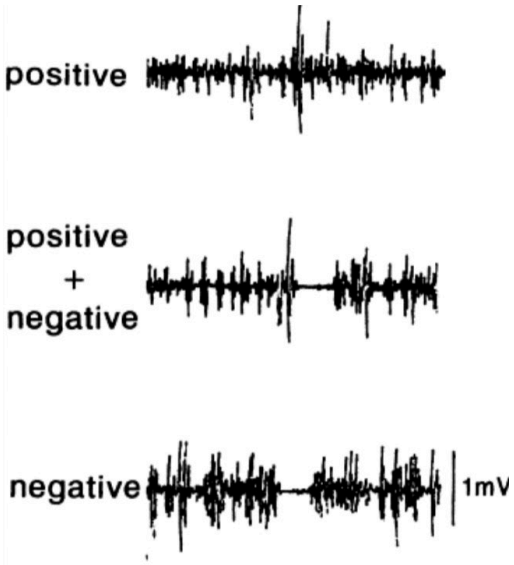

- Talyta Cortez (UHN, Toronto)
- Arturo Abundes-Corona (UHN, Toronto)
- Mark Hallett (NIH, Bethseda)

# Myoclonus

Derivation: Gr: Myo : “Muscle”.Klónos: “Turmoil”

**Definition**

Sudden, brief, lightning- or shock-like muscle *contractions* (“positive myoclonus”), or *contraction inhibition* (“negative myoclonus”)



# Myoclonus
## Differential Diagnosis of Jerky Movements

- Simple tics
- Chorea
- Fast jerky dystonic movements (previously “Myoclonic dystonia”)
- Tremor
- Peripheral disorders
  - Fasciculations
  - Minipolymyoclonus (can look like tremor)
  - Myokymia
  - Hemifacial Spasm

**Table 1** | Mimics of myoclonus

| Hyperkinetic movement disorder | Clinical characteristics | Electrophysiological characteristics |
|---|---|---|
| Functional (psychogenic) jerks | Inconsistent<br>Reduces with distraction<br>Entrainment | Variation in muscle involvement<br>Variation in muscle recruitment order<br>Variation in burst duration and/or amplitude<br>Pre-movement potential on back-averaging |
| Chorea | Dance-like movements<br>Non-patterned<br>Integrated with normal movement | Variation in burst duration<br>Variation in muscle recruitment order |
| Motor tics | Stereotypic or repetitive movements<br>Onset in childhood<br>Coexistence of other tics<br>Can be voluntarily suppressed<br>Premonitory sensations (urge)<br>Relief after movement | Burst duration >100 ms<br>Pre-movement potential on back-averaging |
| Dystonic jerks | Jerks together with dystonia<br>Sensory tricks (geste antagoniste) can alleviate | Co-contraction agonist and antagonist<br>Burst duration >100 ms<br>Overflow (unintentional muscle contractions that accompany jerks, but is anatomically distinct from the primary dystonic movements) |
| Tremor | Sinusoidal and rhythmic | Alternating contractions of antagonistic muscles<br>Steady frequency on accelerometry |

Zutt, R. *et al. Nat. Rev. Neurol.* **11**, 687–697 (2015)

# Myoclonus

## Clinical Classification

- Arrhythmic, Rhythmic, Oscillatory
- Focal, Segmental, Multi-focal, Generalized
- Asynchronous, Synchronous
- Spontaneous, Reflex, Action

# Myoclonus
## Neurophysiological Considerations

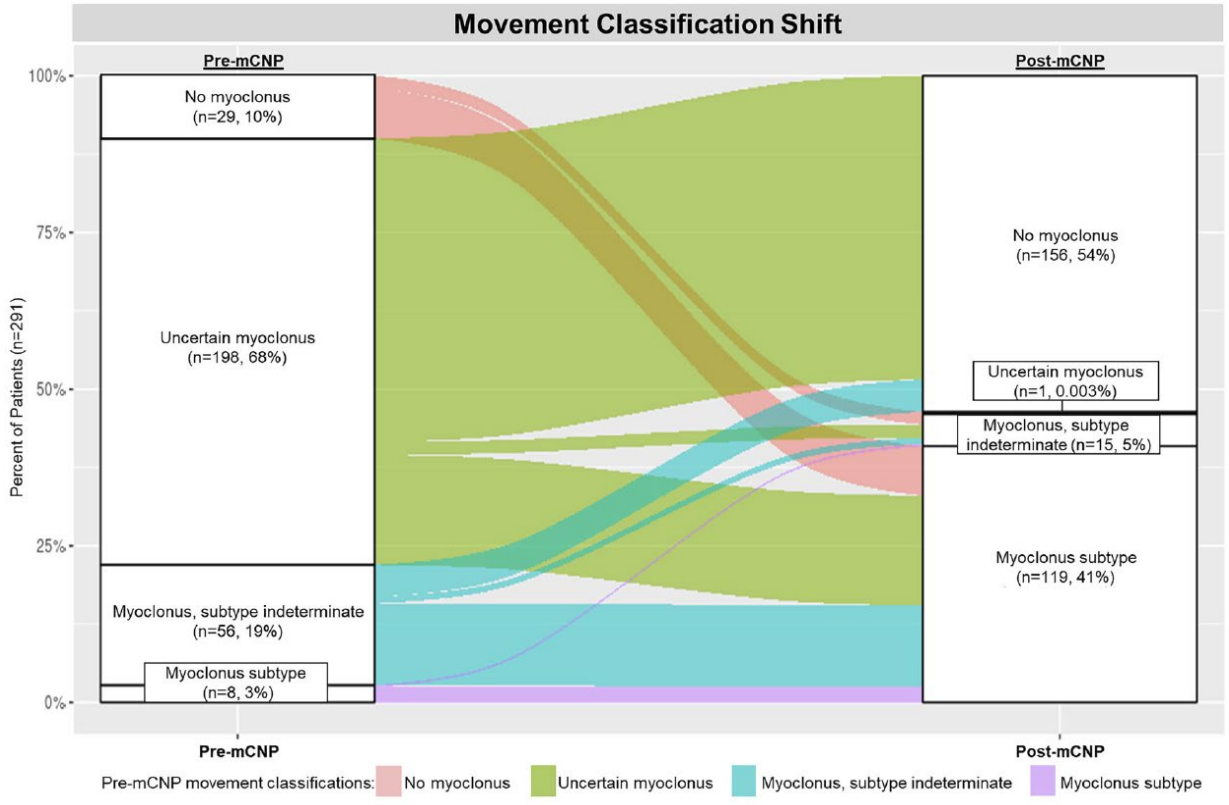
- EMG burst length
- Muscles involved in single jerk
- Timing of muscle activation
- Back-averaged EEG correlate
- Somatosensory evoked potentials
- C reflex
- Other: e.g. conduction times, latency from stimulus

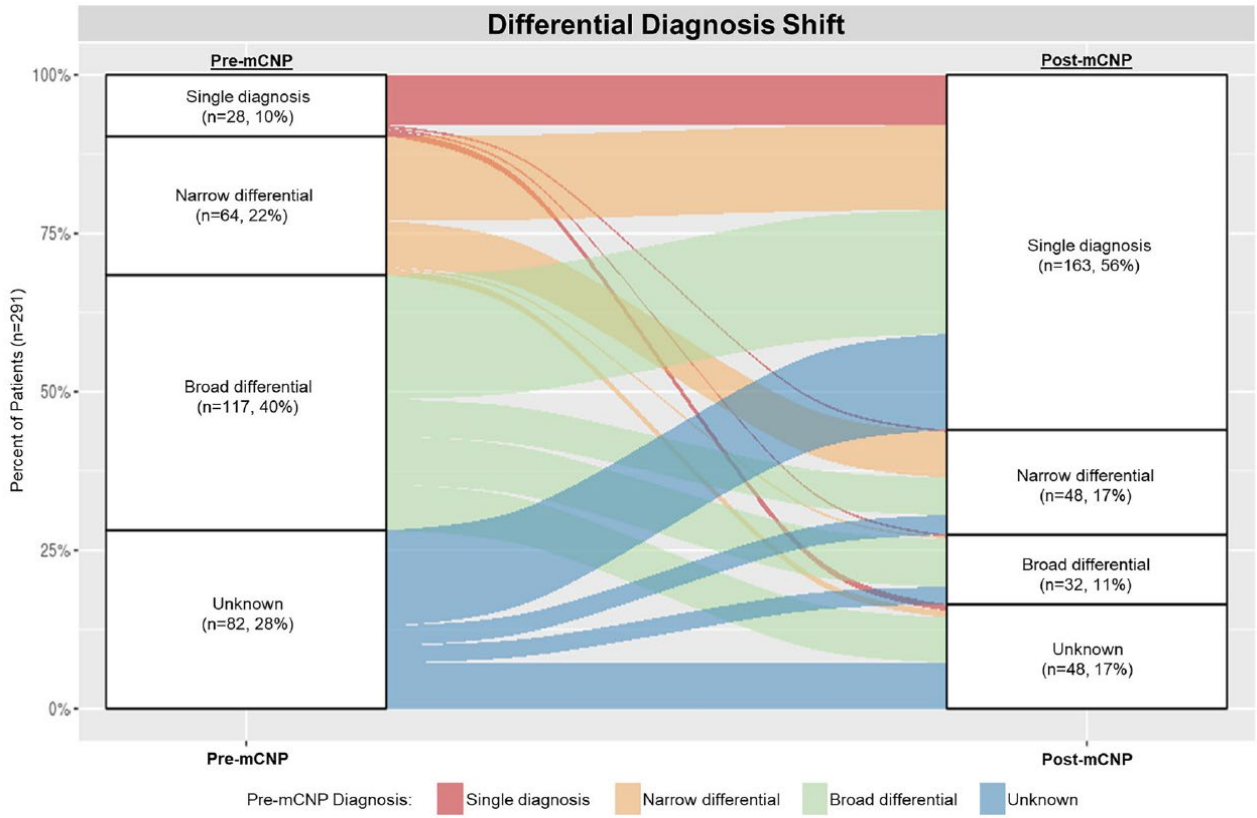
RESEARCH ARTICLE

*Movement* Disorders, Vol. 39, No. 12, 2024

# Clinical Utility of Neurophysiologic Classification (and Declassification) of Myoclonus

Marcus N. Callister, MD,[1,2*] Molly C. Klanderman, PhD, MS,[3] Alyssa Stockard, BS,[4] Charles Van Der Walt, BS,[3] Ashley B. Pena, MD,[1,5] and John N. Caviness, MD[1]



# Myoclonus
## Neurophysiological Classification

- Cortical
- Cortical-Subcortical
- Subcortical, Brainstem
- Spinal
- Propriospinal
- Peripheral
- Functional Jerks

**Table 2** | Characteristics that differentiate anatomical subtypes of myoclonus

| Subtype of myoclonus | Clinical characteristics | Electrophysiological characteristics |
|---|---|---|
| Cortical | (Multi)focal or generalized<br>Affects face, distal limbs<br>Spontaneous, action-induced or stimulus-sensitive<br>Negative myoclonus | Burst duration <100 ms<br>Positive back-averaging<br>Positive coherence<br>Giant somatosensory evoked potentials<br>C reflex |
| Subcortical: | | |
| Brainstem | Generalized or synchronous<br>Axial<br>Affects proximal limbs<br>Spontaneous or stimulus-sensitive | Burst duration >100 ms<br>Simultaneous rostral and caudal muscle activation<br>Habituation |
| Myoclonus dystonia | (Multi)focal<br>Axial, affects proximal limbs<br>Spontaneous or action-induced | Burst duration >100 ms |
| Spinal: | | |
| Segmental | Focal or segmental<br>Spontaneous (sometimes action-induced) | Burst duration >100 ms<br>Distribution of bursts depends on the affected segment |
| Propriospinal | Fixed pattern<br>Affects axial muscles<br>Spontaneous or stimulus-sensitive (lying down can be a provoking factor) | Burst duration >100 ms<br>Initiation in midthoracic segments followed by rostral and caudal activation<br>Slow propagation velocity (5–10 m/s) |
| Peripheral | Focal<br>Affects distal limbs<br>Spontaneous or action-induced<br>Can be accompanied by weakness and/or atrophy | Burst duration <50 ms<br>Large motor unit action potentials<br>Minipolymyoclonus<br>Fasciculations/myokymia |

Zutt, R. *et al. Nat. Rev. Neurol.* **11**, 687–697 (2015)

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

Anna Latorre, MD, PhD,[1,*] Christos Ganos, MD,[2] Masashi Hamada, MD, PhD,[3] Nicolas Phielipp, MD,[4] Lorenzo Rocchi, MD, PhD,[5] Shabbir Merchant, MD,[6] Marina A. Tijssen, MD, PhD,[7,8] Sterre van der Veen, MD, PhD,[7,8] and Robert Chen, MBBChir, MSc, FRCPC[9,*]

MOVEMENT DISORDERS CLINICAL PRACTICE 2025; 12(3): 272–284.

## *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 | | | | | | | |
| | 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 |

# Myoclonus

## 1982 Marsden, Hallett and Fahn Etiological Classification

- **Physiological myoclonus**
  - several types: sleep, anxiety, exercise, hiccough
- **Essential myoclonus**

  - hereditary (?relationship with hereditary myoclonus dystonia), sporadic
- **Epileptic myoclonus** (seizures dominant, no encephalopathy at least initially)

  - fragments of epilepsy, childhood myoclonic epilepsies, progressive myoclonic epilepsy, familial cortical myoclonic tremor with epilepsy
- **Symptomatic myoclonus** (progressive or static enecephalopathy dominates)

  - many causes: storage disorders, degenerative diseases, mitochondrial encephalopathies, viral encephalitis, metobolic, toxins and drugs, physical encephalopathies (anoxia), focal CNS damage

Progressive myoclonic epilepsy vs Progressive myoclonic ataxia

# The nosology and pathophysiology of myoclonus: C.D. Marsden, S. Fahn, M. Hallet

| | | |
|---|---|---|
| Physiologic myoclonus | | Hypnic jerks |
| | | Anxiety-induced |
| | | Exercise-induced |
| | | Hiccough (singultus) |
| | | Benign infantile myoclonus with feeding |
| Essential myoclonus | | Hereditary |
| | | Sporadic |
| Epileptic myoclonus | Fragments of epilepsy | Isolated epileptic myoclonus |
| | | Epilepsia partialis continua |
| | | Idiopathic stimulus sensitive myoclonus |
| | | Photosensitive myoclonus |
| | | Myoclonic absenses |
| | Childhood myoclonic epilepsy | |
| | Progressive myoclonic epilepsy | Infantile spasms |
| | | Severe myoclonic epilepsy of infancy (Dravet syndrome) |
| | | Myoclonic astatic epilepsy (Doose syndrome) |
| | | Cryptogenic myoclonus epilepsy (Aicardi syndrome) |
| | | Benign myoclonic epilepsy of infancy |
| | | Juvenile myoclonic epilepsy |
| | Familial cortical myoclonic tremor with epilepsy | |

Essential myoclonus:
Myoclonus without other neurological deficits and without a secondary cause

| | | |
|---|---|---|
| Symptomatic myoclonus | Storage disease | Lafora body disease |
| | | GM2 gangliosidosis |
| | | Tay-Sachs disease |
| | | Gaucher disease |
| | | Krabbe leukodystrophy |
| | | Ceroid-lipofuscinosis |
| | | Sialidosis types 1 and 2 |
| | Spinocerebellar degeneration | Progressive myoclonus ataxia |
| | | Friedreich ataxia |
| | | Ataxia telangectasia |
| | | Other spinocerebellar degeneration |
| | Basal ganglia degeneration | Wilson disease |
| | | Torsion dystonia |
| | | Neurodegeneration with brain iron accumulation (NBIA) |
| | | Progressive supranuclear palsy |
| | | Huntington's disease |
| | | Parkinson's disease |
| | | Multiple system atrophy |
| | | Corticobasal degeneration |
| | | Dentatorubropallidoluysian atrophy (DRPLA) |
| | Dementias | Creutzfeld-Jakob disease |
| | | Alzheimer's disease |
| | | Dementia with Lewy bodies |
| | | Frontotemporal dementia |
| | | Rett syndrome |
| | Infectious/ Postinfectious | Subacute sclerosing panencephalitis |
| | | Viral encephalitis (Herpes simplex, arbovirus, etc) |
| | | Human immunodeficiency virus |
| | | Malaria |
| | | Cryptococcus |
| | | Lyme disease |
| | | Syphilis |
| | | Whipple's disease |
| | | Progressive multifocal leukoencephalopathy |
| | | Other postinfectious encephalitis |
| | Inflammatory/ Paraneoplastic | Opsoclonus-myoclonus syndrome |
| | | Connective tissue disease |
| | | Steroid-responsive autoimmune encephalopathy with autoimmune thyroiditis |
| | | Rasmussen encephalitis |

| | | |
|---|---|---|
| Symptomatic myoclonus | | Anti-neuronal nuclear antibody |
| | | Voltage-gated potassium channel antibody |
| | | N-methyl-D-aspartate receptor antibody |
| | | Glutamic acid decarboxylase antibody |
| | | Glycine receptor antibody |
| | | Celiac disease |
| | Metabolic | Renal failure |
| | | Dialysis syndrome |
| | | Hepatic failure |
| | | Hypoglycemia |
| | | Hyperglycemia |
| | | Hyponatremia |
| | | Hyperthyroidism |
| | | Multiple carboxylase deficiency |
| | | Hypoxia |
| | | Metabolic alkalosis |
| | | Vitamin E deficiency |
| | | Biotin deficiency |
| | Toxic | Opioids |
| | | Anti-epileptic medications (carbamazepine, phenytoin, pregabalin, lamotrigine) |
| | | SSRIs |
| | | Lithium |
| | | Heavy metals |
| | | Anesthetics |
| | | Levodopa |
| | | Antiarrhythmic medications |
| | | Medication withdrawal |
| | Physical encephalopathies | Posthypoxic injury |
| | | Post-traumatic |
| | | Heat stroke |
| | | Electric shock |
| | | Decompression injury |
| | Focal nervous system damage | Post-stroke |
| | | Post-thalamotomy |
| | | Neoplasm |
| | | Trauma |
| | | Inflammatory (e.g. multiple sclerosis) |
| | | Developmental (e.g. dysplasia) |
| | Exaggerated startle syndrome | Hereditary |
| | | Sporadic |
| | Multiple system degeneration | Mitochondrial disorders |
| | | Allgrove syndrome |
| | | DiGeorge syndrome |

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Clinical Parkinsonism & Related Disorders 14 (2026) 100457

Special Section: Tribute to Mark Hallett, scientist and humanitarian

# Recent advances in clinical neurophysiology of myoclonus☆

Talyta Grippe [a], Benedetta Angeloni [b], Amitabh Bhattacharya [c], Robert Chen [b,c,*]

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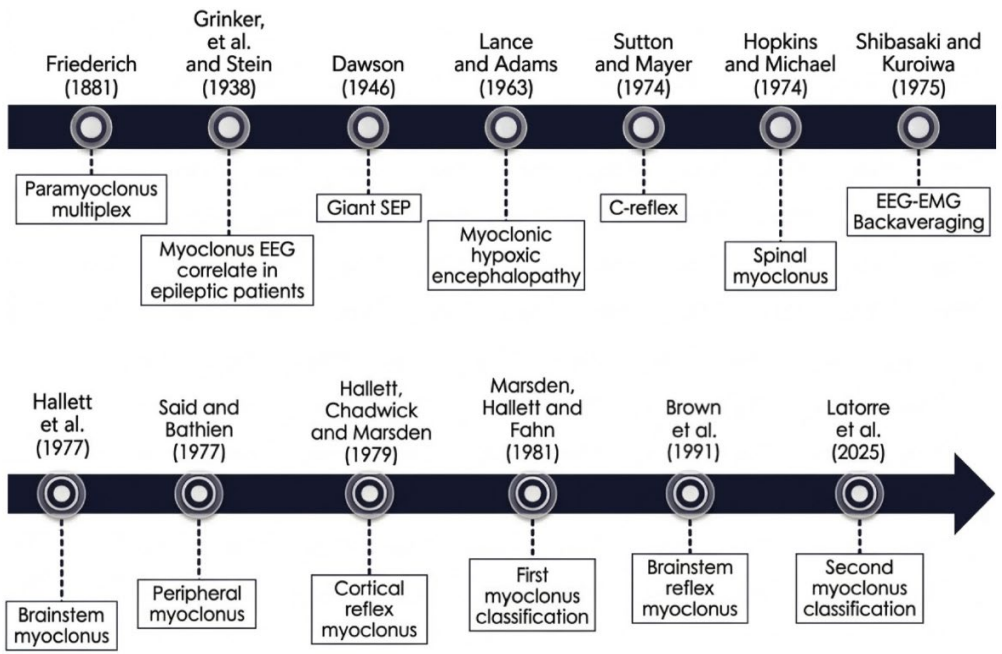



**Fig. 1.** Key historical milestones in myoclonus.

Parkinsonism and Related Disorders 132 (2025) 107216

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journal homepage: www.elsevier.com/locate/parkreldis

# IAPRD new consensus classification of myoclonus

Anna Latorre [a,1], S. van der Veen [b,1], Ashley Pena [c,1], Daniel Truong [d,1], Roberto Erro [e,1], Steven Frucht [f,1], Christos Ganos [g,1], Mark Hallett [h,1], Belen Perez-Duenas [i,1], Malco Rossi [j,1], Emmanuel Roze [k,1], Marie Vidailhet [l,m,1], Marina AJ. de Koning-Tijssen [n,1], John N. Caviness [o,1,*]

- Axis Ia. Clinical features: Historical Features, Myoclonus Characteristics, Diagnostic Evaluation
- Axis Ib. Clinical Neurophysiology Features
- Clinical Myoclonus Syndromes (from Axis Ia and Ib)
- Axis II. Etiology: Genetic, Acquired, Functional, Idiopathic, Physiological

# Myoclonus: Axis Ia – Historical features

| | |
|---|---|
| Age of onset | 1. Infancy (birth-2 years)<br>2. Childhood (3–12 years)<br>3. Adolescence (13–20 years)<br>4. Early adulthood (21–50 years)<br>5. Late adulthood (>50 years) |
| Temporal course | 1. Stable course<br>2. Progressive course<br>3. Improving course |
| Temporal onset | 1. Gradual onset<br>2. Sudden onset |
| Co-morbid medical or neurological conditions | |
| Medication | |
| Family history | |

Latorre et al,2025

# Myoclonus: Axis Ia – Myoclonus Characteristics

| | |
|---|---|
| Anatomical distribution | 1. Focal |
| | 2. Multifocal |
| | 3. Generalized |
| | 4. Hemi |
| | 5. Distal |
| | 6. Proximal limb |
| | 7. Axial |
| Activation state | 1. Rest/spontaneous |
| | 2. Action/intention |
| | 3. Stimulus induced (Tactile) |
| | 4. Stimulus induced (Visual) |
| | 5. Stimulus induced (Auditory) |
| | 6. Stimulus induced (Startle) |
| | 7. State-specific (Sleep) |
| | 8. State-specific (Sleep transitions) |
| Temporal profile | 1. Constant |
| | 2. Paroxysmal |
| | 3. Rhythmic |
| Other neurological features | 1. Isolated |
| | 2. Combined |

Latorre et al,2025

# Myoclonus: Axis Ia – Diagnostic Evaluation

Laboratory studies (non-genetic)

1. Electrolytes
2. Organ function
3. Toxins/drugs
4. Infections
5. Antibodies

Genetic testing

Neuroimaging

Electrodiagnostic testing

1. Surface Electromyography (sEMG)
2. Electroencephalography (EEG)
3. Evoked potentials
4. Corticomuscular coherence
5. Reflex testing
6. Back-averaging for fast or slow potential (jerk-locked or EMG discharge)

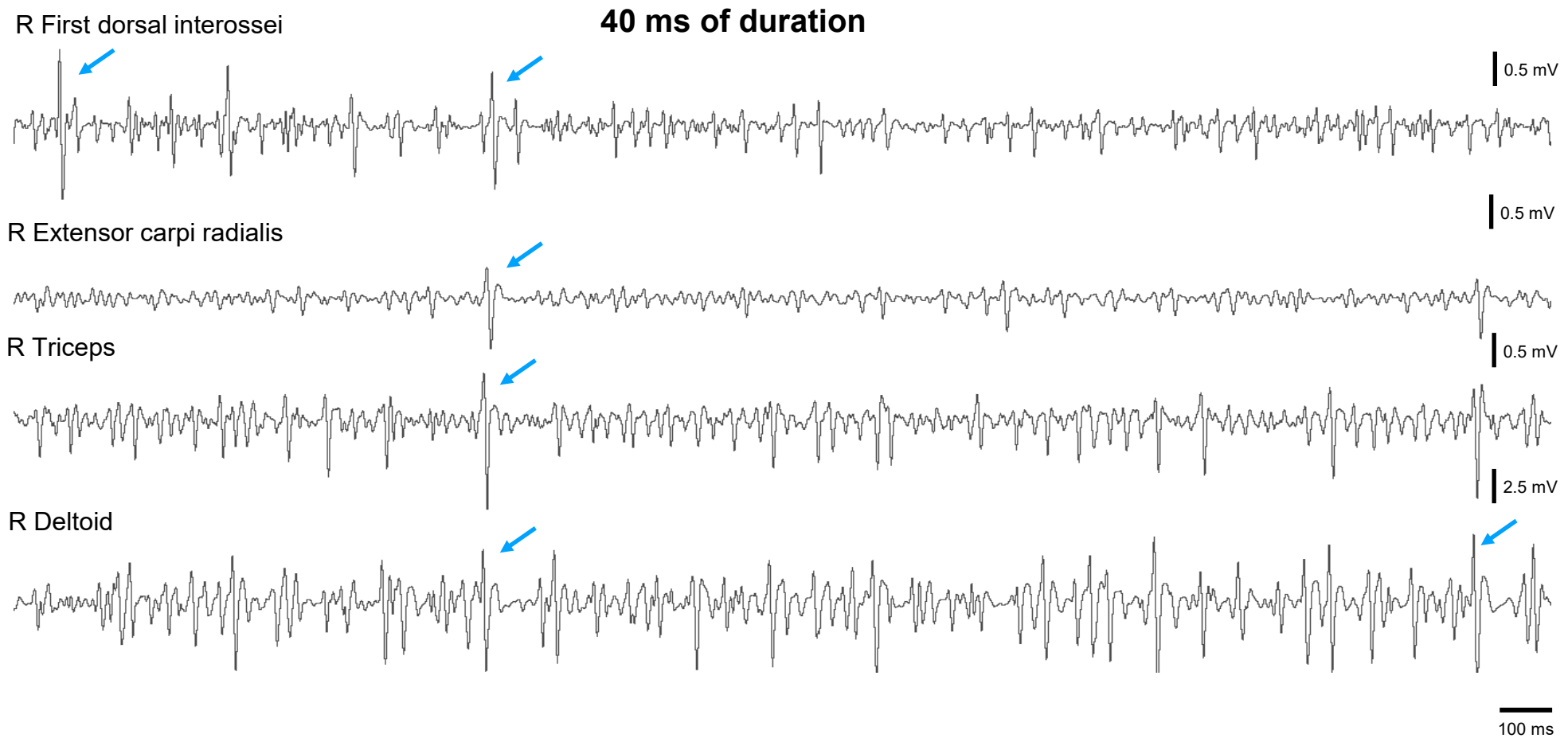
Latorre et al,2025

# Myoclonus: Axis Ib – Clinical Neurophysiology Features
## Cortical Myoclonus

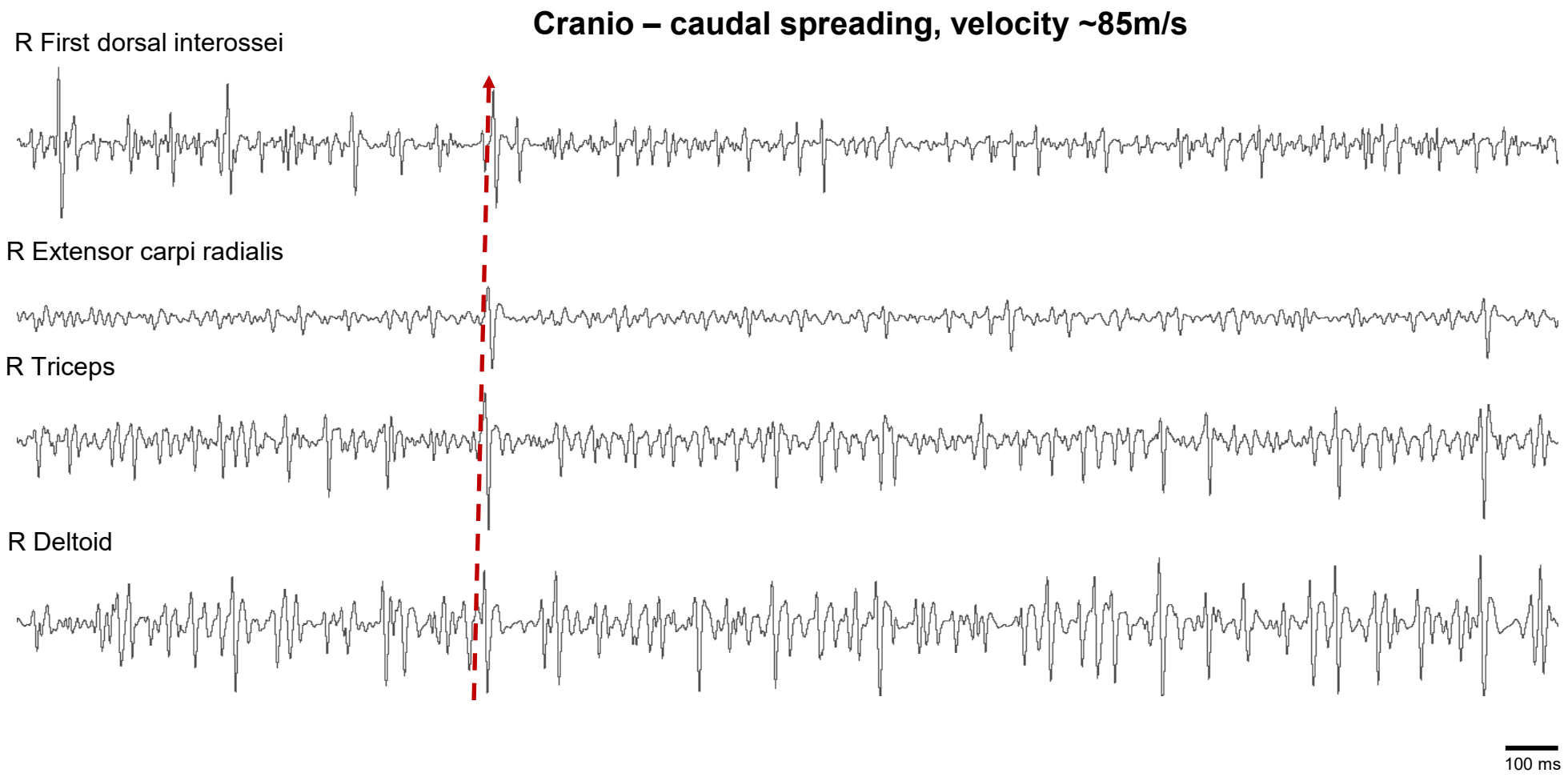
| | |
|---|---|
| Duration | 1. sEMG discharges <100 ms (ms) (usually <50 ms) |
| | 2. Negative myoclonus corresponding to a silent period of 100–400 ms within a tonic sEMG discharge |
| Muscle recruitment pattern | 1. Often focal or multifocal |
| | 2. Co-contracting sEMG discharges among agonist-antagonist muscle groups; cranial-caudal progression may be seen |
| EEG | 1. Time-locked cortical sharp wave on EEG corresponding to a sEMG discharge in a corresponding anatomical distribution |
| | 2. Cortical sharp wave precedes the onset of the sEMG myoclonus discharge (with 15–22 ms latency in upper extremity, ~40 ms in lower extremities) |
| Other | 1. Presence of long latency reflex type I |
| | 2. Presence of enlarged somatosensory evoked potential (SEP) |

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# Cortical myoclonus

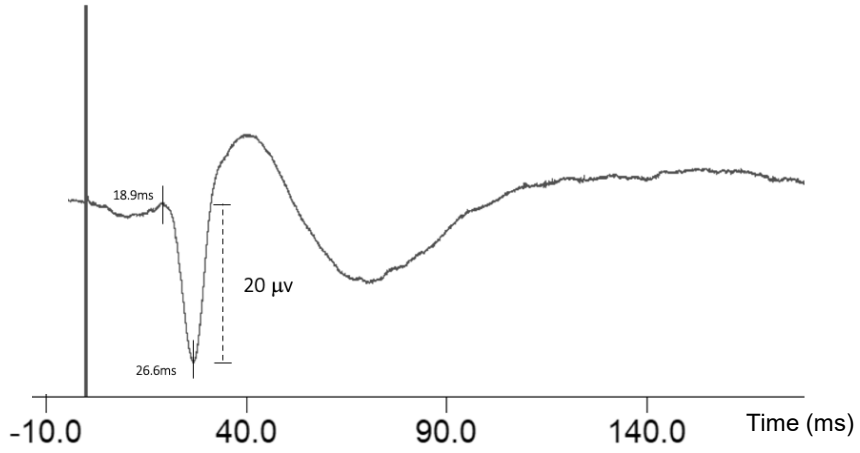


# Cortical myoclonus

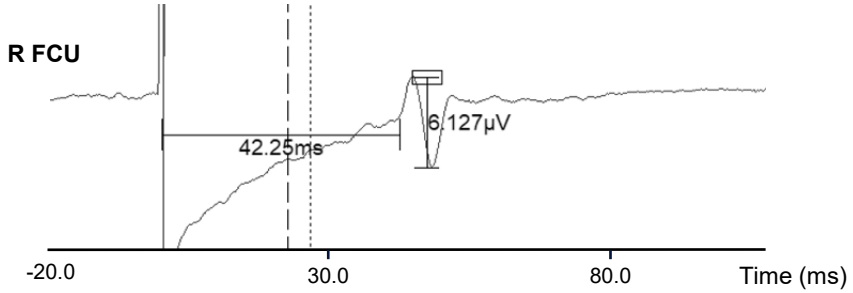


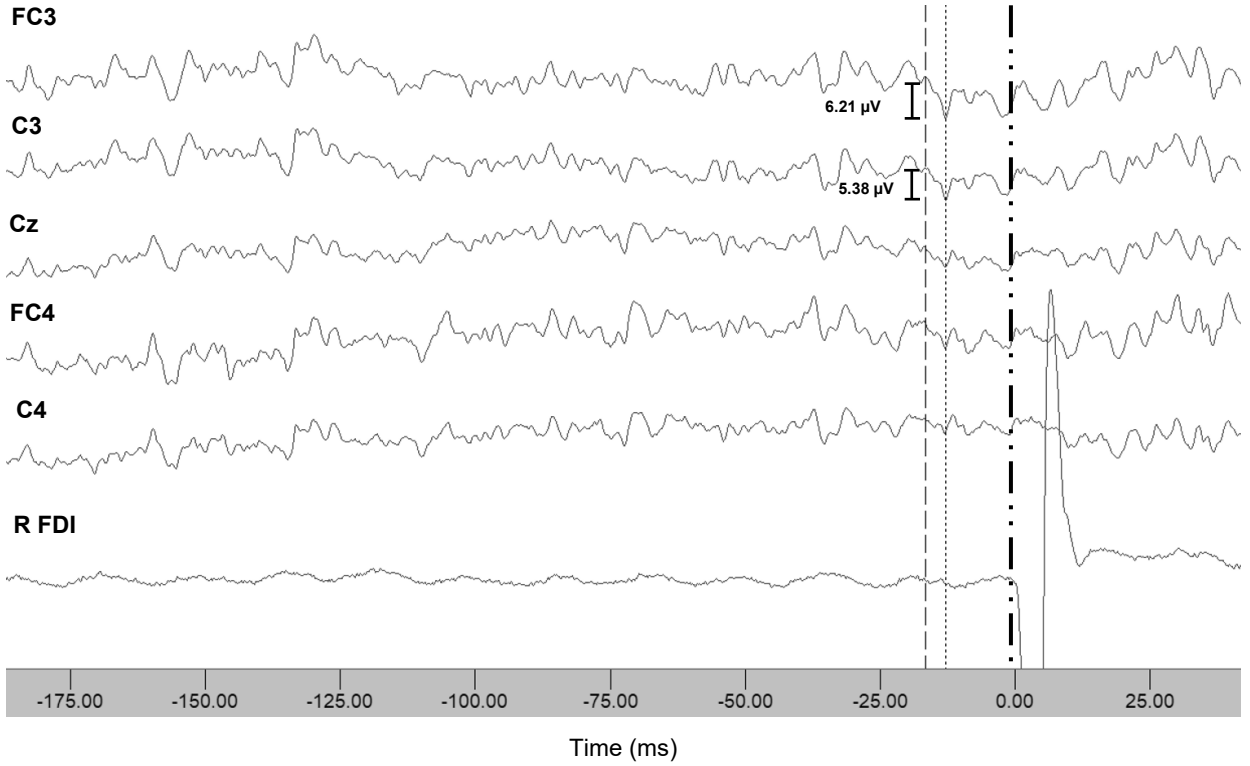
# Cortical myoclonus

**Giant SEP**




**C reflex**



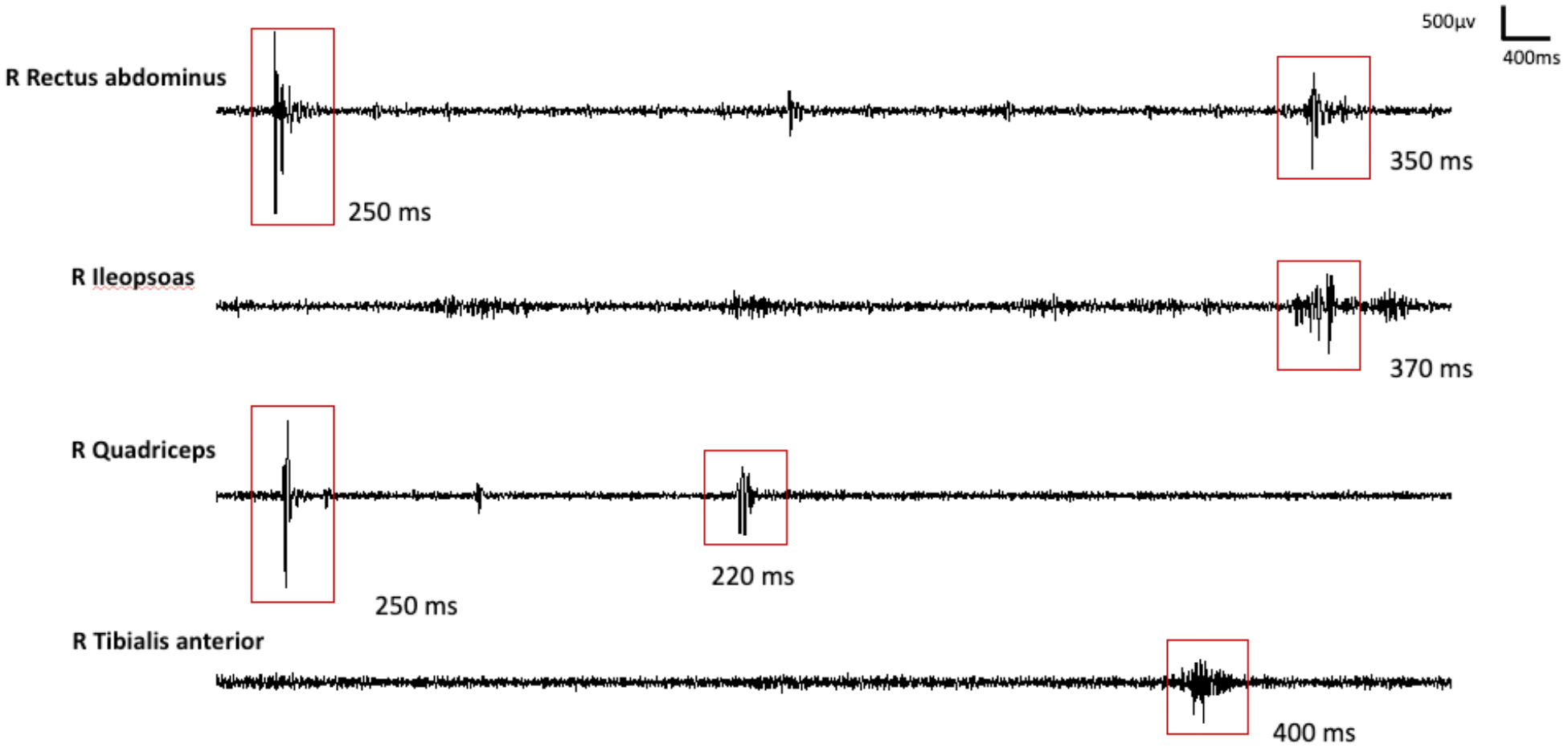
# Myoclonus: Axis Ib – Clinical Neurophysiology Features
## Cortical-Subcortical & Subcortical Myoclonus

| | |
|---|---|
| Duration | sEMG discharges of 50–100 ms |
| Anatomical distribution | Generalized bilateral synchronous |
| EEG patterns observed | 1. EEG correlate is polyspike, polyspike and wave (4–6 Hz spike and wave), with variable EEG-EMG latency<br>2. sEMG discharges time-locked with generalized spike and wave discharges on EEG (e.g. absence seizures with myoclonus)<br>3. EEG correlate is bifrontal/fronto-central/bifrontal negativity to myoclonus EMG discharge. |

| | |
|---|---|
| Duration | Normally >100 ms, but could be 50–100 ms |
| Muscle recruitment | Variable |
| EEG | Absence of time-locked cortical potential |
| Other | Absence of giant SEP/Absence of long latency reflex type I |

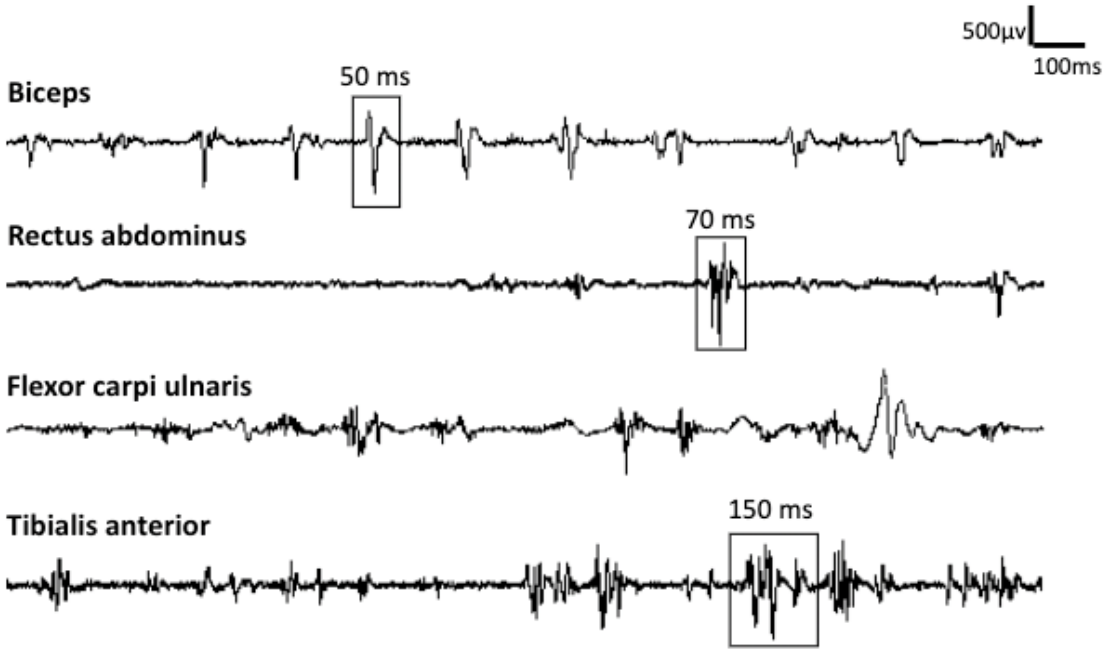
Latorre et al,2025

# Subcortical myoclonus




Patient with Turner syndrome

# Sucortical myoclonus




Fearon C, Grippe TC, Chen R, Lang AE. Early-Onset Neurodevelopmental Movement Disorder Secondary to Novel Mutation in KCNN2. Mov Disord Clin Pract. 2022 Sep 11;9(Suppl 2):S9-S12.

Patient with KCNN2

# Myoclonus: Axis Ib – Clinical Neurophysiology Features

## Brainstem Myoclonus

| | |
|---|---|
| Reticular | 1. Contiguous sequential activation of brainstem innervated structure |
| | 2. Stimulus sensitivity |
| | 3. If EEG potential exists, it begins after beginning sEMG discharge |
| Startle | 1. Contiguous sequential activation of brainstem innervated structures |
| | 2. Stimulus sensitivity |
| | 3. Early auditory blink response |
| Focal | Localized activation brainstem innervated structures at 1–3 contiguous levels |

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# Myoclonus: Axis Ib – Clinical Neurophysiology Features

## Spinal (focal distribution) Myoclonus

| | |
|---|---|
| Duration | >100 ms sEMG discharges |
| Muscle recruitment | 1. sEMG discharges localized to 1–3 contiguous levels of the spinal cord<br>2. Co-contracting |
| EEG | Absence of time-locked cortical potential |
| Other | Absence of giant SEP/Absence of long latency reflex type I |

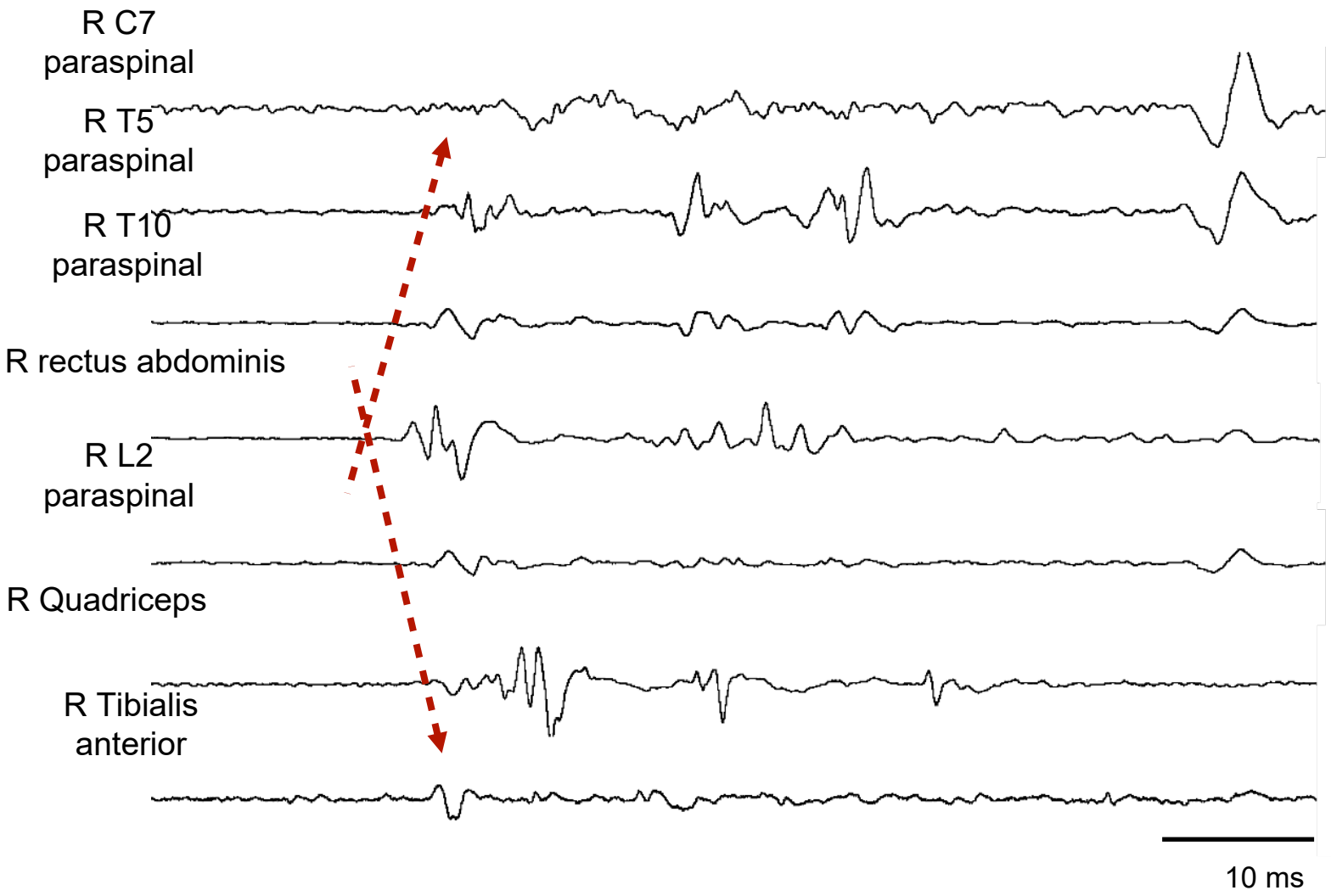
Latorre et al,2025

# Myoclonus: Axis Ib – Clinical Neurophysiology Features
## Propriospinal Myoclonus

| | |
|---|---|
| Duration | >100 ms |
| Muscle recruitment | sEMG discharges arising from trunk muscles followed by rostral and caudal activation through propriospinal pathways (slow conduction velocity) |
| EEG | Absence of time-locked cortical potential |
| Other | Absence of giant SEP/Absence of long latency reflex type I |

Latorre et al,2025

# Propriospinal myoclonus




Velocity: 15 m/s

Functional

# Myoclonus: Axis Ib – Clinical Neurophysiology Features
## Peripheral Myoclonus

| | |
|---|---|
| Duration | Variable, 50–100 ms |
| Muscle recruitment | 1. sEMG discharges localized to muscles innervated by single peripheral nerve or nerve root<br>2. sEMG co-contracting discharges across a specifical peripheral nerve distribution |
| EEG | Absence of time-locked cortical potential |
| Other | Absence of giant SEP/Absence of long latency reflex type I |

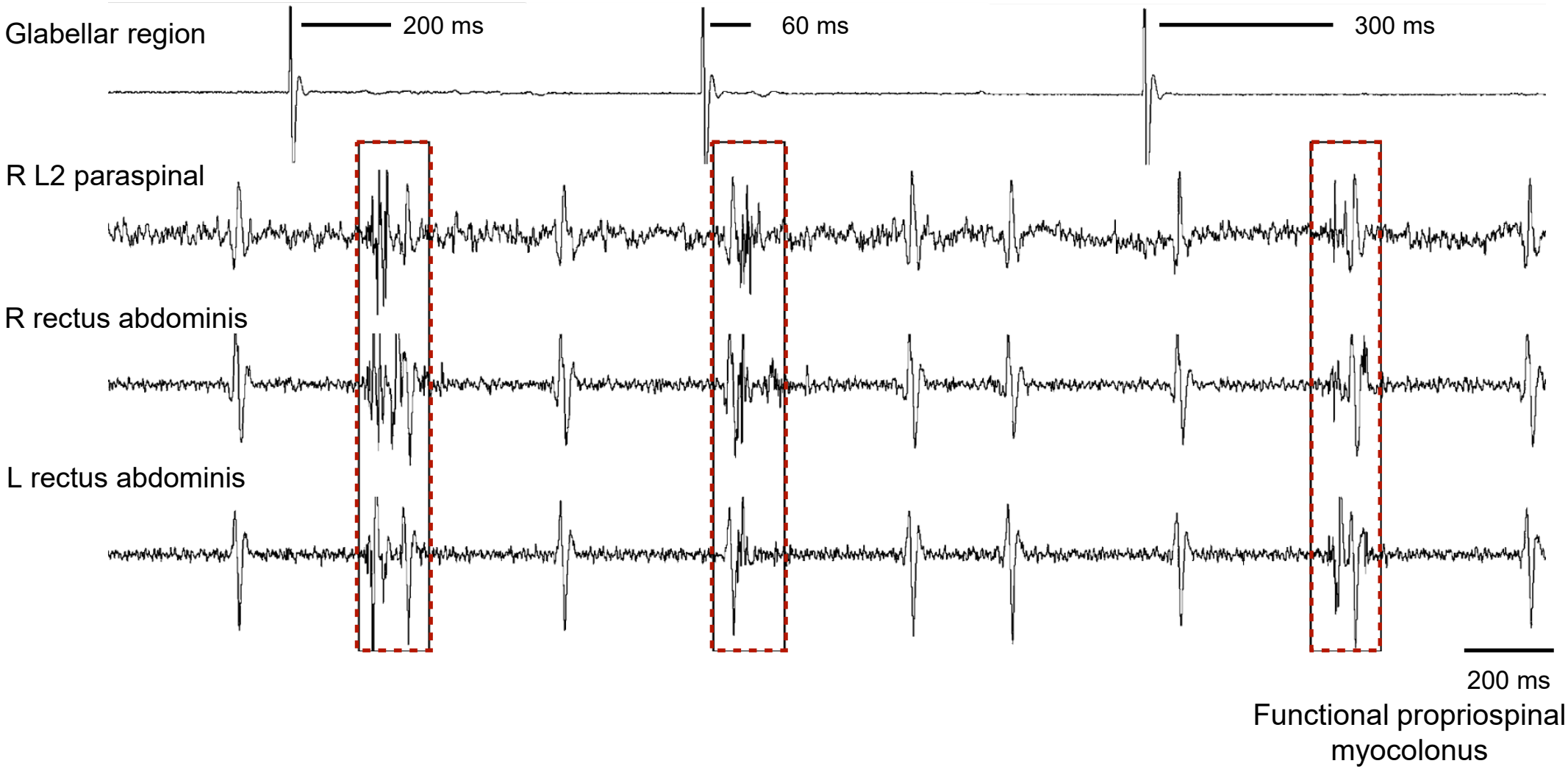
Latorre et al,2025

# Myoclonus: Axis Ib – Clinical Neurophysiology Features
# Functional Jerk Features

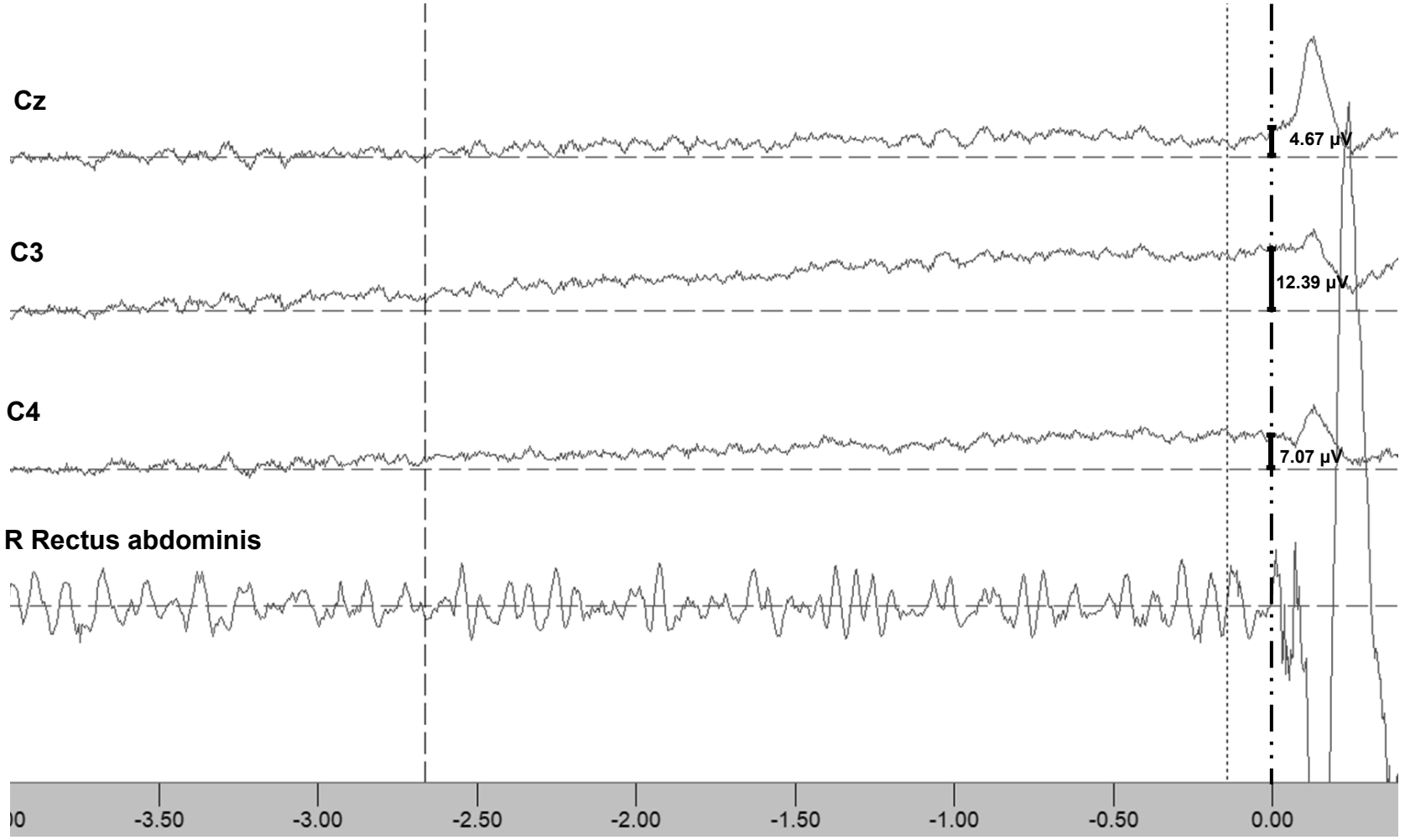
| | |
|---|---|
| Duration | Most of the times >200 ms sEMG burst duration |
| Muscle recruitment commonly shows variable pattern | |
| EEG | 1. Bereitschaftspotential present on EEG-EMG back averaging<br>2. Event-related desynchronization in broad beta band with reduction of beta and low gamma oscillations prior to cued and self-paced movement |
| Other | 1. Distractible<br>2. Entrainable<br>3. Non-physiologic stimulus latency |

Latorre et al,2025

# Latency variability after stimulus



# Premotor potential




Functional propriospinal myocolonus

# Myoclonus: Syndromes and Etiology

| Clinical Myoclonus Syndromes (derived from Axis Ia and Ib) |
| --- |
| 1. Myoclonus-Dystonia |
| 2. Progressive myoclonus epilepsy |
| 3. Progressive myoclonus ataxia |
| 4. Cortical myoclonus tremor |
| 5. Juvenile myoclonic epilepsy |
| 6. Opsoclonus-myoclonus-ataxia |
| 7. Functional jerks |

| Axis II. Etiology[a] |
| --- |
| **Genetic** |
| Prominent myoclonus |
| Combined myoclonus with other movement disorders |
| Disorders that usually present with other phenotypes but can present with prominent myoclonus |
| **Acquired** |
| Metabolic (non-genetic) |
| Toxic- and drug-induced |
| Neurodegenerative disease |
| Nervous system lesions |
| Static |
| Progressive |
| Infections/post-infectious |
| Inflammatory/paraneoplastic (autoimmune) |
| Other medical (systemic) disorders |
| **Functional neurological disorder** |
| **Idiopathic** |
| Familial (genetic basis undetermined) |
| Sporadic |
| **Physiological** |
| Hypnic jerks |
| Fragmentary (sleep) |
| Exercise-induced |
| Hiccup |
| Anxiety-induced |

REVIEW

*Movement* Disorders, Vol. 34, No. 11, 2019

# Nomenclature of Genetically Determined Myoclonus Syndromes: Recommendations of the International Parkinson and Movement Disorder Society Task Force

Sterre van der Veen, BSc,[1] Rodi Zutt, MD, PhD,[1,2] Christine Klein, MD,[3] Connie Marras, MD, PhD,[4]
Samuel F. Berkovic, MD,[5] John N. Caviness, MD, PhD,[6] Hiroshi Shibasaki, MD, PhD,[7]
Tom J. de Koning, MD, PhD,[1,8] and Marina A.J. Tijssen, MD, PhD[1*]

67 genes divided into 3 groups

1. Prominent myoclonus syndromes, 35 genes
2. Prominent myoclonus syndromes combined with another prominent movement disorder, 9 genes
3. Disorders usually presenting other phenotypes but can manifest a prominent myoclonus syndrome, 23 genes

REVIEW

*Movement* Disorders, Vol. 34, No. 11, 2019

# Nomenclature of Genetically Determined Myoclonus Syndromes: Recommendations of the International Parkinson and Movement Disorder Society Task Force

Sterre van der Veen, BSc,[1] Rodi Zutt, MD, PhD,[1,2] Christine Klein, MD,[3] Connie Marras, MD, PhD,[4] Samuel F. Berkovic, MD,[5] John N. Caviness, MD, PhD,[6] Hiroshi Shibasaki, MD, PhD,[7] Tom J. de Koning, MD, PhD,[1,8] and Marina A.J. Tijssen, MD, PhD[1*]

## Prominent myoclonus syndromes

| | |
|---|---|
| MYC-*CLN3*[11] | CLN3 disease |
| MYC-*CLN5*[12] | CLN5 disease |
| MYC-*CLN6*[13] | CLN6 disease |
| MYC-*CLN8*[15] | CLN8 disease |
| MYC-*DNAJC5*[16] | CLN4 disease |
| MYC-*GLRA1*[17]; MYC-*SLC6A5*[18]; MYC-*GLRB*[19] | Hyperekplexia |
| MYC-*KCNC1*[20] | MEAK |
| MYC-*PRICKLE1*[21] | EPM 1B |
| MYC-*SAMD12*,[c] | FCMTE |
| MYC-*RAPGEF2*[22] | |
| MYC-*SCARB2*[24] | AMRF syndrome |
| ATX/HSP-*FOLR1*[25] | Cerebral folate transport deficiency |
| *CARS2*[27] | CARS2 |
| *CHD2*[29] | CHD2 encephalopathy |
| CUX2[31] | Myoclonic DEE |
| *GLDC*[32]; *AMT*[33] | Classic non-ketotic hyperglycinemia |
| mt-*MTTK*[34d] | MERRF |
| *PIGA*[36] | MCAHS2 |
| *POLG*[37] | POLG-related disorders |
| *SCN1A*[38e] | Dravet syndrome |
| *SERPINI1*[39,40] | FENIB |
| *SLC6A1*[41] | Doose syndrome |
| *TBC1D24*[42] | TBC1D24-related disorders |

## Combined myoclonus syndromes

| | |
|---|---|
| MYC/ATX-*CSTB*[44] | Unverricht-Lundborg |
| MYC/ATX-*EPM2A*[46] | Lafora disease |
| MYC/ATX-*GOSR2*[48] | North Sea PME |
| MYC/ATX-*KCTD7*[49] | EPM 3 |
| MYC/ATX-*NEU1*[51] | Sialidosis |
| MYC/ATX-*NHLRC1*[53] | Lafora disease |
| MYC/ATX-*TPP1*[54] | CLN2 disease |
| MYC/DYT-*SGCE*[55] | Myoclonus-dystonia |
| MYC/DYT-*KCTD17*[56] | Myoclonus-dystonia |

*Epilepsia*. 2025;66:1804–1823.

# Updated classification of epileptic seizures: Position pape of the International League Against Epilepsy

Sándor Beniczky[1,2,3] | Eugen Trinka[4,5,6] | Elaine Wirrell[7] | Fatema Abdulla[8]
Raidah Al Baradie[9] | Mario Alonso Vanegas[10] | Stéphane Auvin[11,12,13] |
Mamta Bhushan Singh[14] | Hal Blumenfeld[15] | Alicia Bogacz Fressola[16] |
Roberto Caraballo[17] | Mar Carreno[18,19] | Fernando Cendes[20,21] |
Augustina Charway[22] | Mark Cook[23] | Dana Craiu[24,25] | Birinus Ezeala-Adikaibe[26,
Birgit Frauscher[28,29] | Jacqueline French[30] | M. V. Gule[31,32] |
Norimichi Higurashi[33] | Akio Ikeda[34] | Floor E. Jansen[35] | Barbara Jobst[36]
Philippe Kahane[37] | Nirmeen Kishk[38] | Ching Soong Khoo[39,40,41] |
Kollencheri Puthenveettil Vinayan[42] | Lieven Lagae[43] | Kheng-Seang Lim[44] |
Angelica Lizcano[45,46] | Aileen McGonigal[47] |
Katerina Tanya Perez-Gosiengfiao[48,49,50] | Philippe Ryvlin[51] | Nicola Specchio[52]
Michael R. Sperling[53] | Hermann Stefan[54] | William Tatum[55] |
Manjari Tripathi[56] | Elza Márcia Yacubian[57] | Samuel Wiebe[58] |
Jo Wilmshurst[59] | Dong Zhou[60] | J. Helen Cross[61]

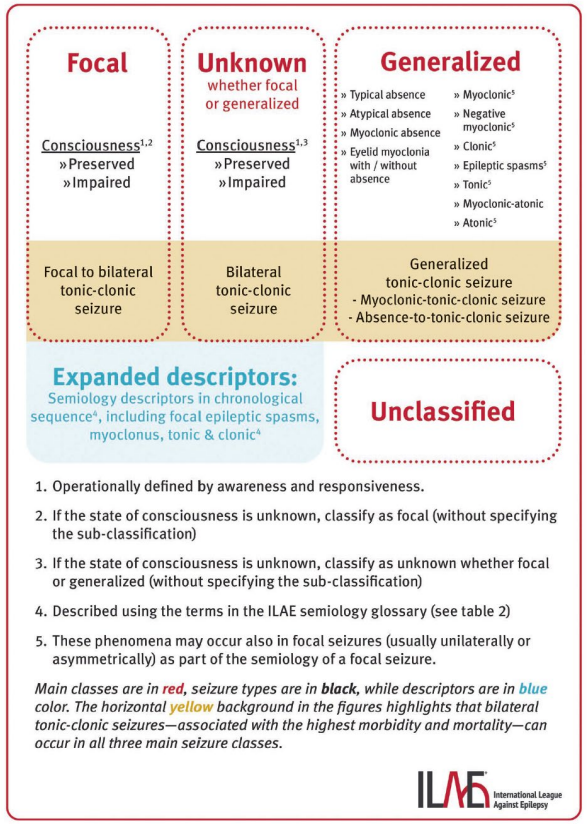



**TABLE 1** Taxonomic hierarchy of epileptic seizure classification.

**1. Focal (F)**
- 1.1. Focal preserved consciousness seizure (FPC)
- 1.2. Focal impaired consciousness seizure (FIC)
- 1.3. Focal-to-bilateral tonic-clonic seizure (FBTC)

Don't forget EPC!

***Descriptors***
- *Basic:*
  - *With observable manifestations*
  - *Without observable manifestations*
- *Expanded:*
  - *Semiology descriptors in chronological sequence: Semiology (glossary[a]) + Somatotopic modifiers*

**2. Unknown whether focal or generalized (U)**
- 2.1. Unknown whether focal or generalized - preserved consciousness seizure (PC)
- 2.2. Unknown whether focal or generalized - impaired consciousness seizure (IC)
- 2.3. Unknown whether focal or generalized - bilateral tonic-clonic seizure (BTC)

***Descriptors***
- *Basic:*
  - *With observable manifestations*
  - *Without observable manifestations*
- *Expanded:*
  - *Semiology descriptors in chronological sequence: Semiology (glossary[a]) + Somatotopic modifiers*

**3. Generalized (G)**
- 3.1. Absence seizures (AS)
  - 3.1.1. Typical absence seizure (TA)
  - 3.1.2. Atypical absence seizure (AA)
  - 3.1.3. Myoclonic absence seizure (MA)
  - 3.1.4. Eyelid myoclonia with / without absence (EMA)
- 3.2. Generalized tonic-clonic seizure (GTC)
  - 3.2.1. Myoclonic tonic-clonic seizure
  - 3.2.2. Absence-to-tonic-clonic seizure
- 3.3. Other generalized seizures[b]
  - 3.3.1. Generalized myoclonic seizure (GM)
  - 3.3.2. Generalized clonic seizure (GC)
  - 3.3.3. Generalized negative myoclonic seizure (GNM)
  - 3.3.4. Generalized epileptic spasms (GES)
  - 3.3.5. Generalized tonic seizure (GT)
  - 3.3.6. Generalized atonic seizure (GA)
  - 3.3.7. Generalized myoclonic-atonic seizure (GMA)

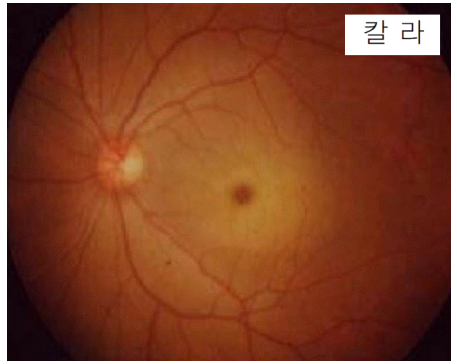
**4. Unclassified**

# Progressive Myoclonic Epilepsies

**Table 1.** The most common PMEs with their associated genes and gene products.

| PME (Acronym) | Affected Genes | Protein Function |
|---|---|---|
| Unverricht-Lundborg disease (ULD) | *CSTB* | Cystatin B/Stefin B, a cathepsin B lysosomal protease inhibitor |
| Lafora disease (LD) | *EPM2A, EPM2B* | Laforin, a glycogen phosphatase; malin, an E3-ubiquitin ligase |
| Neuronal ceroid lipofuscinosis (NCLs) | Several *CLN* genes | Cln1/Ppt1, lysosomal palmitoyl protein thioesterase;<br>Cln2/Tpp1, lysosomal tripeptidyl peptidase 1;<br>Cln3, a lysosomal membrane protein; others |
| Sialidosis (ST-1) | *NEU1* | Neu1, lysosomal α-N-acetylneuraminidase |
| North Sea PME | *GOSR-2* | Golgi SNAP receptor 2 |
| Acid ceramidase deficiency (Farber disease/SMA-PME) | *ASAH1* | Asah1, acid ceramidase |
| Myoclonic epilepsy with ragged red fibers (MERRF) | *MT-TK* | Mitochondrial lysine transfer tRNA |

Zimmern V, Minassian B. Progressive myoclonus epilepsy. Genes 2024: 15:171




**Cherry-red spot**
**Myoclonus**

# Progressive Myoclonic Epilepsies

**Table 2.** A table of rare PMEs with their associated gene names, gene products and function.

| Gene | Protein Function |
|---|---|
| *KCNC1* | A member of the integral membrane proteins that mediates the voltage-dependent potassium ion permeability of excitable membranes |
| *NEXMIF* | Neurite extension and migration factor |
| *SEMA6B* | Semaphorin 6B, member of the semaphorin family, a group of proteins characterized by the presence of a conserved semaphoring domain, which typically play a role in axon guidance |
| *GALC* | Galactosylceramidase, a lysosomal protein that hydrolyzes the galactose ester bonds of galactosylceramide; associated with Krabbe disease |
| *SCARB2* * | Scavenger receptor class B member 2, a type III glycoprotein found mostly in limiting membranes of lysosomes and endosomes; it may participate in membrane transportation |

Zimmern V, Minassian B. Progressive myoclonus epilepsy. Genes 2024: 15:171

**And many more!**

* Action Myoclonus Renal Failure Syndrome
(may not have renal failure or develop myoclonus long after renal transplantation)

# EPM1 Treatment

- Avoid phenytoin!

  …and lamotrigine
- Use valproate with possible supplementation with clonazepam, levetiracetam, topiramate and zonisamide
- Consider perampanel (for all types of EPM)
  - Inhibits postsynaptic AMPA receptors

# Familial Adult Myoclonus Epilepsy (FAME)*

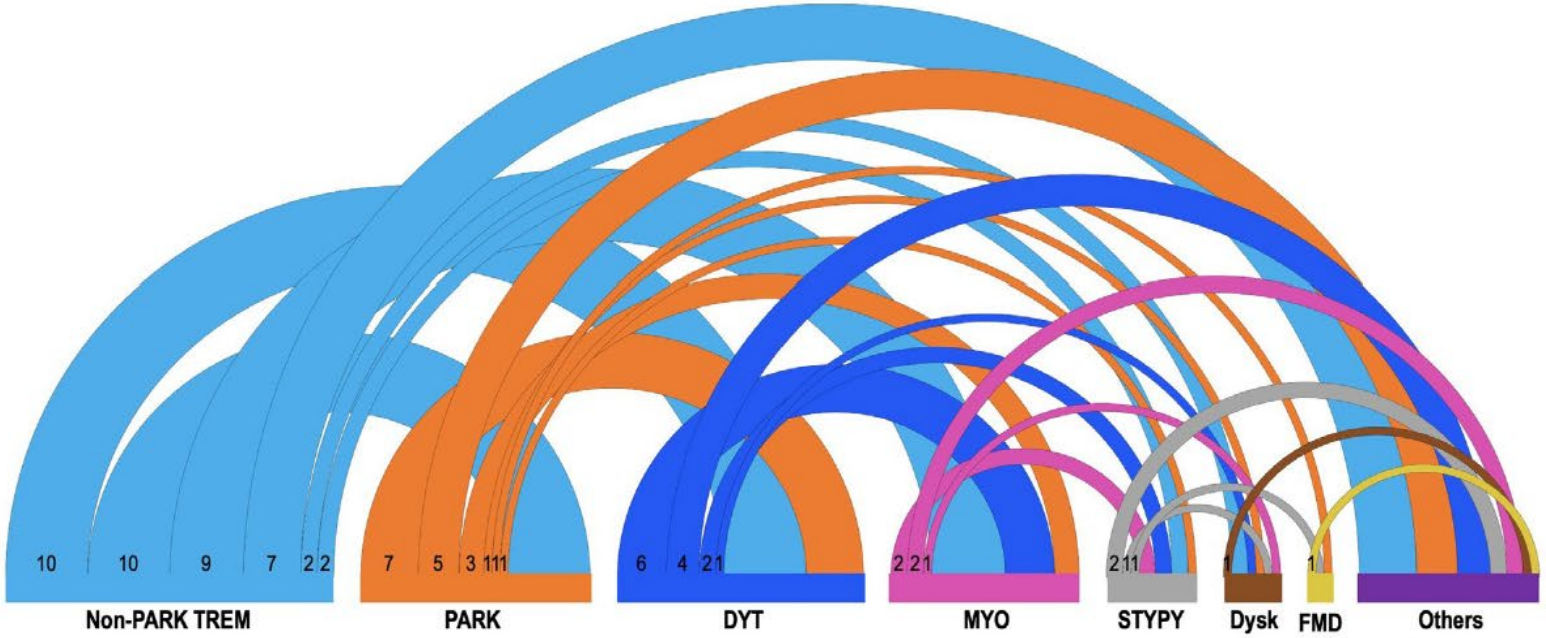
- Other names
  - Familial adult myoclonic epilepsy, Adult familial myoclonic epilepsy (BAFAME), Autosomal dominant cortical myoclonus and epilepsy (ADCME), Familial cortical myoclonic tremor with epilepsy (FCMTE)
- Etiology – the same pentanucleotide TTTTA repeat expansion containing a TTTCA insertion (absent in healthy populations) in 7 different genes: SAMD12 (FAME1/BAFME1), STARD7 (FAME2/FCMTE2/ADCME), MARCHF6 (FAME3/FCMTE3), YEATS2 (FAME4/BAFME4), TNRC6A (FAME6/BAFME6), RAPGEF2 (FAME7/BAFME7), and RAI1 (FAME8/BAFME8).

* May have cortical myoclonus (including action /exercise induced myoclonus) without epilepsy

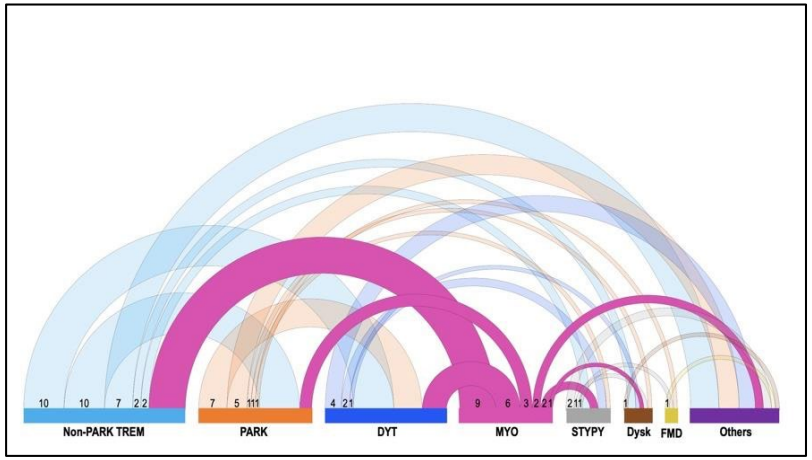
*European Journal of Neurology*, 2025; 32:e70256
https://doi.org/10.1111/ene.70256

# Dissecting the Phenotypic Spectrum and Complexity of Movement Disorders in 22q11.2 Deletion Syndrome

Nikolai Gil D. Reyes[1,2,3,4] | Talyta Grippe[1,4] | Marcus Callister[1,4] | Tarig Abkur[1,4] | Emilio Q. Villanueva III[5] | Tracy Heung[2,3] | Robert Chen[1,4,6] | Erik Boot[2,7,8] | Anne S. Bassett[2,3,9] | Anthony E. Lang[1,4,6]



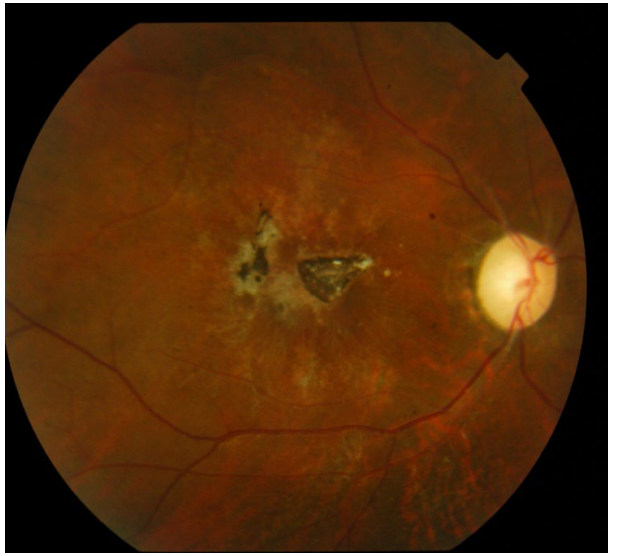

Co-occurring movement disorder phenotypes in 22q11.2 deletion syndrome (n = 24/31, 77% of the cohort).




Interaction between myoclonus and other movement disorder phenotypes

# Viral Encephalopathies

- Herpes simplex encephalitis
- Subacute sclerosing panencephalitis (SSPE)
  - Therapy (Garg et al. 2019 Rev Med Virol 29:e2058)
    - Immunomodulatory therapy with interferon and isoprinosine have had some success
    - Carbamazepine can be useful symptomatically
- AIDS-dementia complex
- Chikungunya meningoencephalitis
- Nipah virus
- SARS-CoV-2 (including opsoclonus-myoclonus)



**Chorioretinitis/maculopathy and optic atrophy in SSPE**

# Metabolic Encephalopathies / Endocrine Disorders

- Hepatic failure
- Renal failure
- Hyponatremia
- Hypoglycemia
- Non-ketotic hyperglycinemia
- Hyperthyroidism
- Biotin (vitamin H) deficiency

Note: These are frequent causes of asterixis and are generally treatable!

# Autoimmune disorders

- Opsoclonus-myoclonus syndrome
- Progressive encephalomyelitis with rigidity and myoclonus (PERM) (“jerky stiff-man”)
  - Anti-glycine receptor (GlyR) antibodies (males; often presents with brainstem involvement)
  - Also anti-GAD, anti-amphiphysin, and anti-NMDAR; 20% paraneoplastic
- Celiac disease
  - Stimulus sensitive foot myoclonus
- Anti-IgLON5 disease (also myorhythmia)
- Hashimoto’s encephalopathy (SREAT)

# Focal Stimulus Sensitive Leg Myoclonus in Celiac Disease



# Opsoclonus-Myoclonus Syndrome

- Associated with a distinctive pattern of serum IgM and IgG binding to neural tissues and antigens

Etiology:

- Children: often associated with neuroblastoma
- Adults:
  - Paraneoplastic (most common antibody, antineuronal nuclear antibody type 2, anti-Ri)
  - Idiopathic
  - Parainfectious (often HIV; COVID-19)
  - Toxic/metabolic
  - Autoimmune (anti-NMDA-R antibody)

EXPERT REVIEW OF NEUROTHERAPEUTICS, 2016
VOL. 16, NO. 6, 641–648
http://dx.doi.org/10.1080/14737175.2016.1176914

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PERSPECTIVE

# Childhood opsoclonus-myoclonus syndrome: diagnosis and treatment

Franz Blaes[a,b] and Backialakshmi Dharmalingam[b]

Table 1. Causes of opsoclonus–myoclonus syndrome.

| Causes | Reference |
|---|---|
| **Infectious** | – |
| Mumps | [9] |
| Coxsackie B3 | [10] |
| Rotavirus | [11] |
| Epstein–Barr virus | [12] |
| West Nile virus | [13] |
| Streptococci | [14] |
| Mycoplasma pneumonia | [15] |
| Dengue virus | [16] |
| Human herpes virus type 6 | [17] |
| HIV | [18] |
| Hepatitis C | [19] |
| **Paraneoplastic** | – |
| Neuroblastoma | [2] |
| Ganglioneuroma | [20] |
| Hepatoblastoma | [21] |
| SCLC (adults) | [8] |
| Breast cancer (adults) | [22] |
| Ovarian teratoma, nasopharyngeal | – |
| Carcinoma, non-SCLC (adults), esophagus | – |
| Carcinoma | [23–26] |
| **Toxic** | – |
| Thallium | [27] |
| Strychnine | [28] |
| Cocaine | [29] |
| **Drugs** | – |
| Amitryptiline | [30] |
| Lithium | [31] |
| Phenytoine | [32] |

SCLC: small-cell lung cancer.

Infectious

Paraneoplastic

Toxic

Drugs

# Opsoclonus-Myoclonus Syndrome: Treatment

- Treat the underlying cause if possible
  - For example, remove the underlying tumor
- Treat the autoimmune aspect for symptomatic treatment with ACTH, steroids or plasmapheresis
- More aggressive and effect approach with rituximab, ACTH and IVIG
- Autologous stem cell transplantation

# Opsoclonus Myoclonus 10 Days post SARS-CoV-2




Video Challenge 2021
Maziar Emamikhah
Iran University of Medical Sciences, Tehran

# Medications and Toxic Agents Causing Myoclonus

| *Prescription drugs* | |
|---|---|
| Anticonvulsants | Phenytoin, carbamazepine, sodium valproate, gabapentin, pregabalin, lamotrigine, phenobarbital, vigabatrin, oxcarbazepine, levetiracetam |
| Antipsychotics | Haloperidol, chlorpromazine, sulpiride, clozapine, olanzapine, metoclopramide |
| Antidepressants | Lithium, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants, fluoxetine, imipramine |
| Antihypertensives | Verapamil, caverdilol, furosemide |
| Cardiovascular drugs | Propafenone, flecainide, diltiazem, nifedipine, buflomedil, veratramine, amiodarone |
| Antiparkinson drugs | Levodopa, bromocriptine, amantadine, entacopone, selegiline |
| Antibiotics | Quinolones, penicillin, cefepime, ceftazidime, moxalactam, ciprofloxacin, imipenem, carbenicillin, ticarcillin, piperacillin, cefuroxime, β-lactam antibiotics, gentamicin |
| Other anti-infective drugs | Piperazine, isoniazid, acyclovir |
| Antineoplastic drugs | Chlorambucil, prednimustine, busulphan plus cyclophosphamide, ifosfamide |
| Opiates | Morphine, tramadol, fentanyl, methadone, pethidine, norpethidine, hydrocodone |
| Anxiolytics | Buspirone, lorazepam, midazolam, zolpidem, zopiclone, carisoprodol, benzodiazepine withdrawal |
| Antidementia drugs | Cholinesterase inhibitors |
| Anaesthetic agents | Enflurane, etomidate, propofol, choralose |
| Others | Bismuth salts, contrast media, domperidone, omeprazole, antihistamines, prednisolone, ketoprofene, physostigmine, tryptophan, diclofenac, cobalamine supplementation, cimetidine, salicylates, tetanus toxin, dextromethorphan, tacrolimus |
| *Toxic agents* | |
| Psychoactive substances | Alcohol, cannabis, amphetamine, cocaine, ecstasy, toluene, intoxicating inhalants (for example, gasoline), heroin |
| Heavy metals | Aluminium, manganese, bismuth, mercury, tetra-ethyl lead |
| Insecticides | Methyl bromide, dichlorodiphenyltrichloroethane |
| Others | Baking soda, carbon monoxide, chloralose, colloidal silver |

Zutt, R. *et al. Nat. Rev. Neurol.* **11**, 687–697 (2015)

*Systematic Review*

*Medicina* **2025**, *61*, 131

## Drug-Induced Myoclonus: A Systematic Review

Jamir Pitton Rissardo [1,*], Ana Letícia Fornari Caprara [1], Nidhi Bhal [2], Rishikulya Repudi [3], Lea Zlatin [4] and Ian M. Walker [1,5]

# Myoclonus in Hereditary Dystonias

- Any type of dystonia, including DYT1
- Fast, jerky dystonic movements – may need electrophysiology to distinguish
- **Myoclonus Dystonia**
  - Epsilon sarcoglycan (*SGCE*) mutations commonest cause; considerable intrafamilial variability
    - Paternal transmission with maternal imprinting
    - Recent studies supporting a role of the cerebellum in several aspects
    - ETOH responsive; THX, clonazepam, zonisamide, levodopa, ?TBZ, DBS (esp Gpi) (excellent long-term responses)

*Movement* Disorders, Vol. 40, No. 10, 2025

**Deep Brain Stimulation in Children and Adolescents with ε-Sarcoglycan Myoclonus Dystonia Causes a Sustained Improvement in Motor Functionality and Quality of Life**

Ainara Salazar-Villacorta, MD,[1,2] Ana Cazurro-Gutiérrez, MSc,[3,4] Lucy Dougherty-de Miguel, MD,[1,3] Julia Ferrero-Turrión, MD,[1,3] Anna Marcé-Grau, PhD,[3] Marta Folch-Benito, MD,[1,3] Álvaro Lucero-Garófano, MSc,[3,4] Alfons Macaya, MD, PhD,[1,3,4,5] Antonio Moreno-Galdó, MD, PhD,[1,4,6] Maria I. Vanegas, MD, PhD,[7] Marta Correa-Vela, MD, PhD,[8] María Victoria González, MD, PhD,[1,3] Gemma Español-Martín, MD,[1,3,4,9] Martha Loredo,[1] Ignacio Delgado, MD,[1,3] Esther Toro-Tamargo, MD,[1] Margarita Figueroa, MD,[1] Dolores Vilas, MD, PhD,[10] Manel Tardáguila, MD,[10] Jorge Muñoz, MD,[10] Lourdes Ispierto, MD, PhD,[10] Ramiro Álvarez, MD,[10] Agustí Bescós, MD, PhD,[1] and Belén Pérez-Dueñas, MD, PhD[1,3,4,5,6*]

  - Mutations also in *KCTD17*, *CACNA1B*, *RELN*, *ANO3*, *SCN8A*, *ADCY5*, *TITF1*, *TUBB2B*, *KCNN2*, *GNB1*, *KCTD17*, 47 XXX, *CAPN3* (some questionable)
    - Subtle differences between *SGCE* and non-*SGCE* MD on FDG PET suggest distinct endophenotypes.

**Myoclonus-dystonia: classification, phenomenology, pathogenesis, and treatment**

**Curr Opin Neurol** 2018, 31:484–490

*Emmanuel Roze*[a,b], *Anthony E. Lang*[c], *and Marie Vidailhet*[a,b]

**Table 2.** Diagnostic criteria for the syndrome of myoclonus-dystonia

| |
|---|
| **Major criteria** |
| Myoclonus isolated or predominating over dystonia |
| Prominence of the motor manifestations in the upper body |
| Absence of truncal dystonia |
| Positive family history |
| Onset before age 18 years |
| **Minor criteria** |
| Obsessive compulsive disorder, anxiety related disorder or alcohol dependence |
| Spontaneous remission of limb dystonia during childhood or adolescence |
| Alcohol responsiveness |
| **Exclusionary criteria** |
| Other neurologic manifestation in addition to myoclonus and/or dystonia |
| Abnormal brain MRI |
| Neurophysiological findings that do not support the diagnosis (see text) |

# Myoclonus in Later-Onset Neurodegenerative Diseases

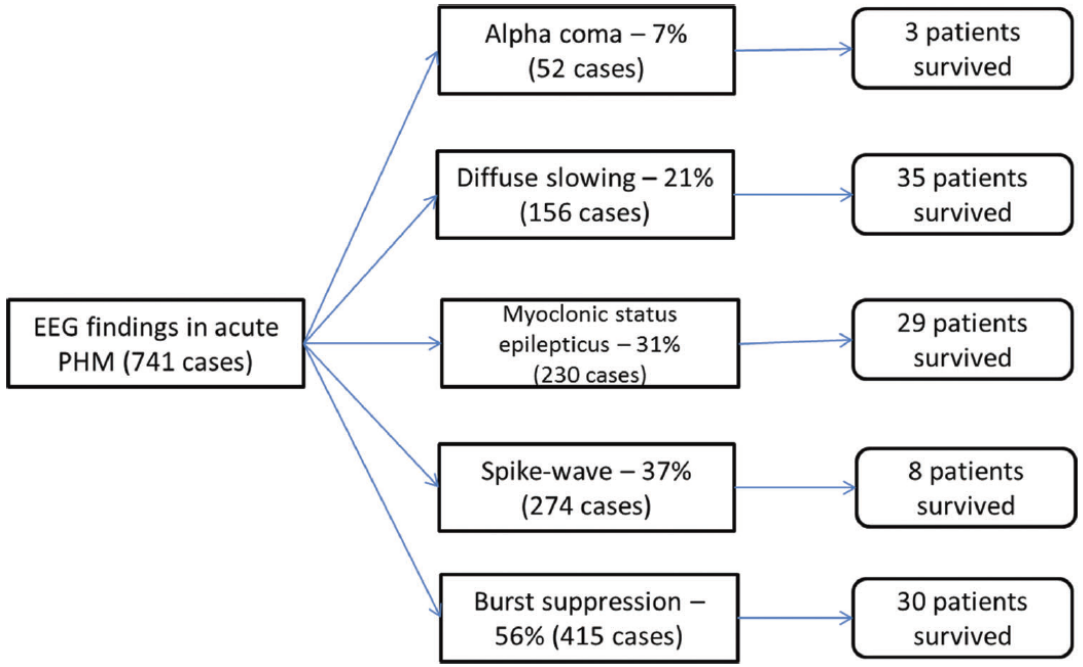
- Parkinsonisms:
  - PD – typically PDD; LID (rare), amantadine (distinct phenotype: cranial action myoclonus)
  - MSA (including minipolymyoclonus)
  - CBS/CBD (PSP rare)
- Dementias
  - AD
  - DLB (PDD)
  - FTDs
  - CJD
- Others
  - Huntington’s
  - DRPLA (typically early-onset)

# Focal CNS Damage and Physical Encephalopathies

- Focal lesions: Tumors, Angiomas, etc
- Encephalitis
- Trauma
- Heat stroke
- Electric shock
- Decompression injury
- Post-hypoxic Myoclonus
  - Acute
  - Chronic (Lance-Adams Syndrome)

# Acute Post-Hypoxic Myoclonus

- Generalized or multifocal
- Status myoclonicus / myoclonic status epilepticus
- Onset usually within 1 day of hypoxia
- A poor prognostic sign (esp generalized)
- Therapeutic hypothermia may improve outcome




Gupta & Caviness, 2016

# Chronic Post-Hypoxic Action Myoclonus (Lance-Adams Syndrome)

- Typically follows respiratory arrests: anaesthesia/surgery, drug intoxication, status asthmaticus, cardiac arrest much less common
- Onset days-weeks after hypoxia as consciousness regained
- Action and stimulus-sensitive myoclonus; cortical and subcortical
- Positive and negative myoclonus (latter → bobbing truncal movements (postural lapses) often more resistant to Rx)
- Seizures and cognitive dysfunction may co-occur; usually not prominent
- Neuropathology has varied (varied etiology/duration) – exact pathogenesis uncertain
- Usually requires multiple medications: levetiracetam (? brivaracetam), VPA, clonazepam, others (5HTP + carbidopa), ? DBS

# Exaggerated Startle Syndromes

- Startle can be exaggerated by virtue of:
  - Increased magnitude of the startle
  - Lack of inhibition

# Exaggerated Startle Syndromes

- Hyperekplexia
  - Hereditary
  - Symptomatic
    - brain stem lesions, perinatal hypoxic-ischemic encephalopathy, thalamic lesions, schizophrenia, post-traumatic stress syndrome, Tourette syndrome, drugs (amphetamine, cocaine), idiopathic
- Startle epilepsy
- Culture-specific behavioral syndromes

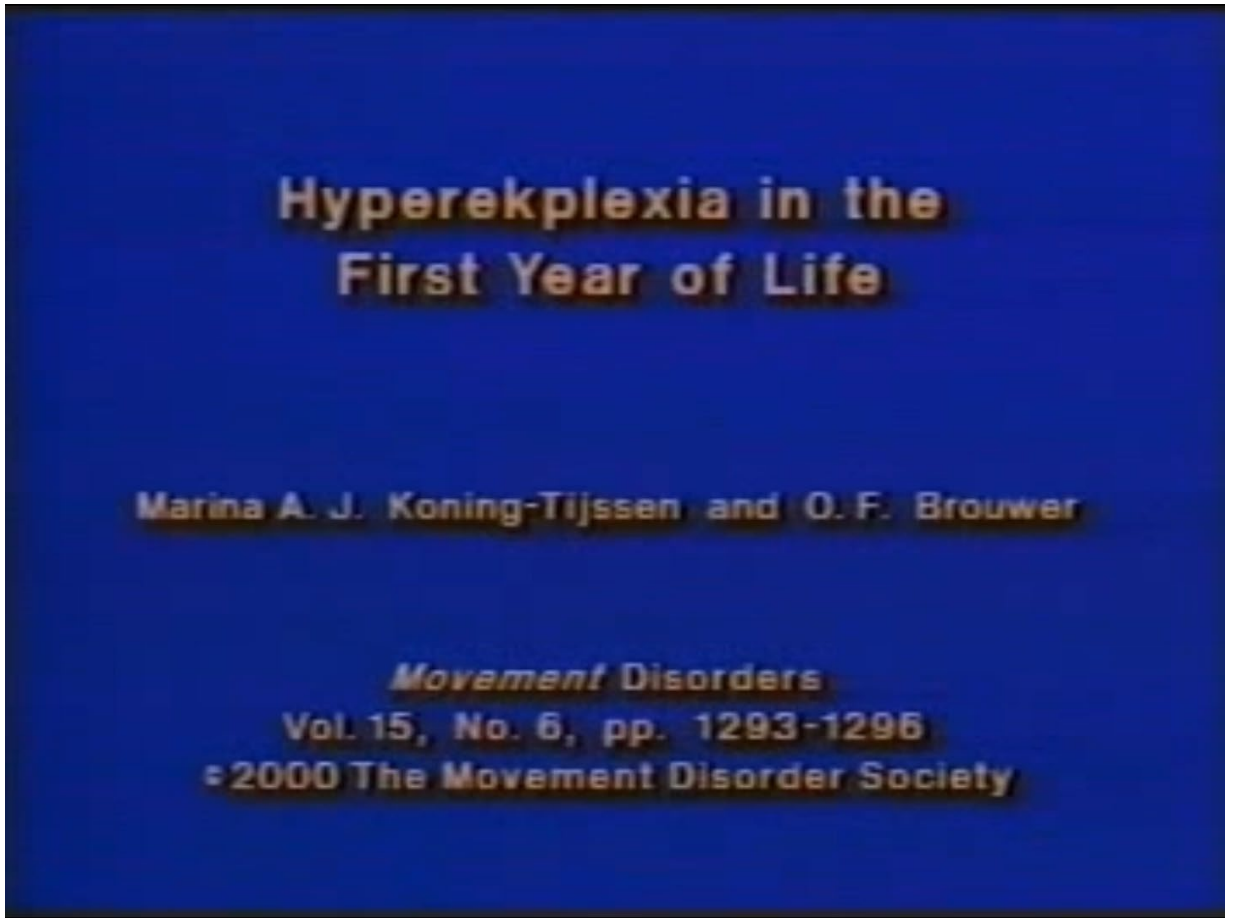
# Hereditary Hyperekplexia

- Genetic disorder due to several possible abnormalities of glycine transmission
- Commonly autosomal dominant, but can be recessive or Xlinked
- The alpha-1 subunit of the glycine receptor is most commonly affected (*GLRA1* – AD and AR), milder and later-onset phenotypes possible, neurodevelopmental issues (up to 1/3)
- Beta subunit also possible, or very rarely in related proteins gephyrin and collybistin
- Also the presynaptic glycine transporter 2 (GlyT2, specifically *SLC6A5*) can be affected

# Hereditary Hyperekplexia

- Characterized by excessive startle, then stiffening that can cause falls
- Babies are very stiff (stiff baby syndrome) and can have sudden infant death syndrome (SIDS)
- Treatment
  - Clonazepam is treatment of choice
    - 0.03 to 0.2 mg/kg/day

# Hyperekplexia in First Year of Life ("Stiff Baby Syndrome")



# Culturally-Specific Startle Syndromes

- Consists of a startle, secondary behavior such as striking out and an emotional response
- Patients also have echolalia and echopraxia

- Latah (Malaysia)
- Jumping (Jumping Frenchmen of Maine)
- Myriachit (Siberia)
- Yaun (Burma)
- Bah-tsche (Thailand)
- Mali-mali (Philippines)
- Lapp panic (Lapland)
- Imu (Japan)
- Goosey (Southern United States)
- Ragin’Cajuns (Louisiana)

# Spinal Myoclonus

- Rhythmic / Segmental
  - spontaneous, persistent rhythmic repetitive movements usually unaffected by sleep
  - etiologies: trauma, tumor, infection, disk herniation

# Segmental Spinal Myoclonus (and Camptocormia) due to CASPR2-autoimmunity



Video Challenge 2019
Sangeeta Scotton
Queen Elizabeth
University Hospital, UK

# Spinal Myoclonus

- Rhythmic / Segmental
  - spontaneous, persistent rhythmic repetitive movements usually unaffected by sleep
  - etiologies: trauma, tumor, infection, disk herniation

- Propriospinal
  - non-rhythmic: symmetric flexion (rarely extension) of neck, trunk, hips and knees
  - jerks can be spontaneous or stimulus-induced
  - myoclonus starts in mid-thoracic region and propagates at about 5 m/s both rostrally and caudally
  - usually functional

# Idiopathic Spinal Myoclonus: A Clinical and Neurophysiological Assessment of a Movement Disorder of Uncertain Origin

*Movement Disorders*
Vol. 24, No. 16, 2009, pp. 2344–2349
© 2009 Movement Disorder Society

Marcello Esposito, MD,[1] Mark J. Edwards, PhD,[2] Kailash P. Bhatia, MD,[2]
Peter Brown, MD,[2] and Carla Cordivari, MD[1]*

**TABLE 2.** *BP detection in OM, PM, and NK patients*

| Group | Definite BP | Possible BP | Absent BP |
|---|---|---|---|
| OM | 4 | 1 | 0 |
| PM | 1 | 6 | 3 |
| NK | 1 | 2 | 2 |

OM, organic myoclonus; PM, psychogenic myoclonus; NK, not known.

All patients Dx'd as Organic by both raters:
BP Definite or Possible

# Palatal tremor/myoclonus

## A type of segmental myoclonus – 2 types

1. Essential palatal tremor / myoclonus (“Isolated PT”)
   - Ear click
   - Tensor veli palatini muscle (trigeminal nerve)
   - Stops during sleep
   - Hypertrophy of inferior olive is NOT found
   - This is a functional movement disorder (distractible, entrainable)

# Essential Palatal Tremor – Voluntary Control



*Movement* Disorders, Vol. 30, No. 6, 2015

## Successful Treatment of Functional Palatal Tremor: Insights Into Pathogenesis and Management

Drew S. Kern, MD, MSc,[1] and
Anthony E. Lang, MD, FRCPC*[1]

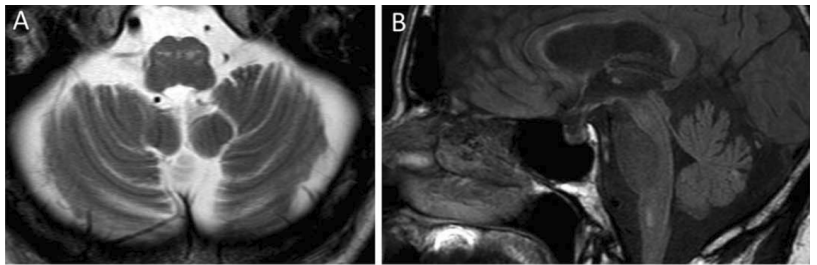
# Palatal tremor/myoclonus

## A type of segmental myoclonus – 2 types

2. Symptomatic palatal tremor
   - Levator veli palatini muscle (largely vagus n, also IX and XI)
   - May be accompanied by synchronous activity of adjacent muscles
   - Continues during sleep
   - Exerts remote effect on limb muscles
   - Hypertrophy of inferior olive (unilateral or bilateral)
   - Etiology:
     - Lesion in the ascending or descending limbs of the GM triangle
       - Associated with ipsilateral cerebellar dysfunction
     - Neurodegenerative disorder – Progressive Ataxia and Palatal Tremor (PAPT)
       - Sporadic: pure PAPT (tauopathy), “PAPT+”: PSP, others, ? IgLON5
       - Genetic: Alexander’s disease, SCA20, *POLG* mutations, GM2 gangliosidosis





# Functional (Psychogenic) Myoclonus

- Clinical features incongruous with other known type of myoclonus
- Inconsistency including improvement with distraction or placebo
- Clinical neurophysiology can support the diagnosis
  - EMG bursts longer than “organic” forms of myoclonus
  - Reflex myoclonus at voluntary reaction time latency
  - Inconsistent activation patterns, duration of m. activity
  - Presence of a Bereitschaftspotential in the backaveraged EEG

# Orthostatic Myoclonus

- Elderly patients – c/o shaky/wobbly legs, unsteadiness, early falls not uncommon (negative myoclonus may be associated with “drop attacks”)
- Absolute indication for clinical electrophysiology
- Leaning on object: as in OT - markedly reduces jerks; unlike OT - transmission to arms uncommon
- Typically very low amplitude movements seen in legs while standing – TA and MGs
- All have other neurological disturbances
  - 1/3 parkinsonism – PD, atypical park,; 1/3 severe microvascular disease; 1/3 multifactorial (CASPR2, irradiation, Hashimoto enceph, IgLON5, TCA, others)
  - Some of these may have atypical electrophysiological findings
- Management very challenging – clonazepam, levetiracetam; walker

# Classical Orthostatic Tremor (OT) vs Slow OT vs Orthostatic Myoclonus (OM) - I

**Comparison of Clinical, Electrophysiological, Imaging, and Treatment Features of Classical OT, slow OT, and OM.**

| | Classical OT | Slow OT | OM |
|---|---|---|---|
| Gender | Female predominant | Female predominant | No gender preference |
| Age of onset | Older adults | Older adults | Older adults |
| Coexistent ET | 25% | No | No |
| Coexistent parkinsonism | 11% | Unknown | 33% |
| Coexistent neurological disease | 40% | Unknown | 100% |
| Family history OT/OM | 5-7% | Unknown | No |
| Family history tremor | Up to 50% | Up to 37.5% | Unknown |
| Family history parkinsonism | 9% | Unknown | No |
| Leg shaking provoked by standing | 100% | 100% | 88% |
| Leg shaking improves with walking | 93.6% | Unknown | No |
| Leg shaking improves with leaning | 98.6% | Unknown | 100% |
| Difficulty with prolonged standing in line | Yes | Unknown | Yes |
| Falls | 24.1% | 37–50% | Frequent at onset |
| Progressive disorder | 91% | Unknown | Unknown |

Hassan & van Gerpen, 2016

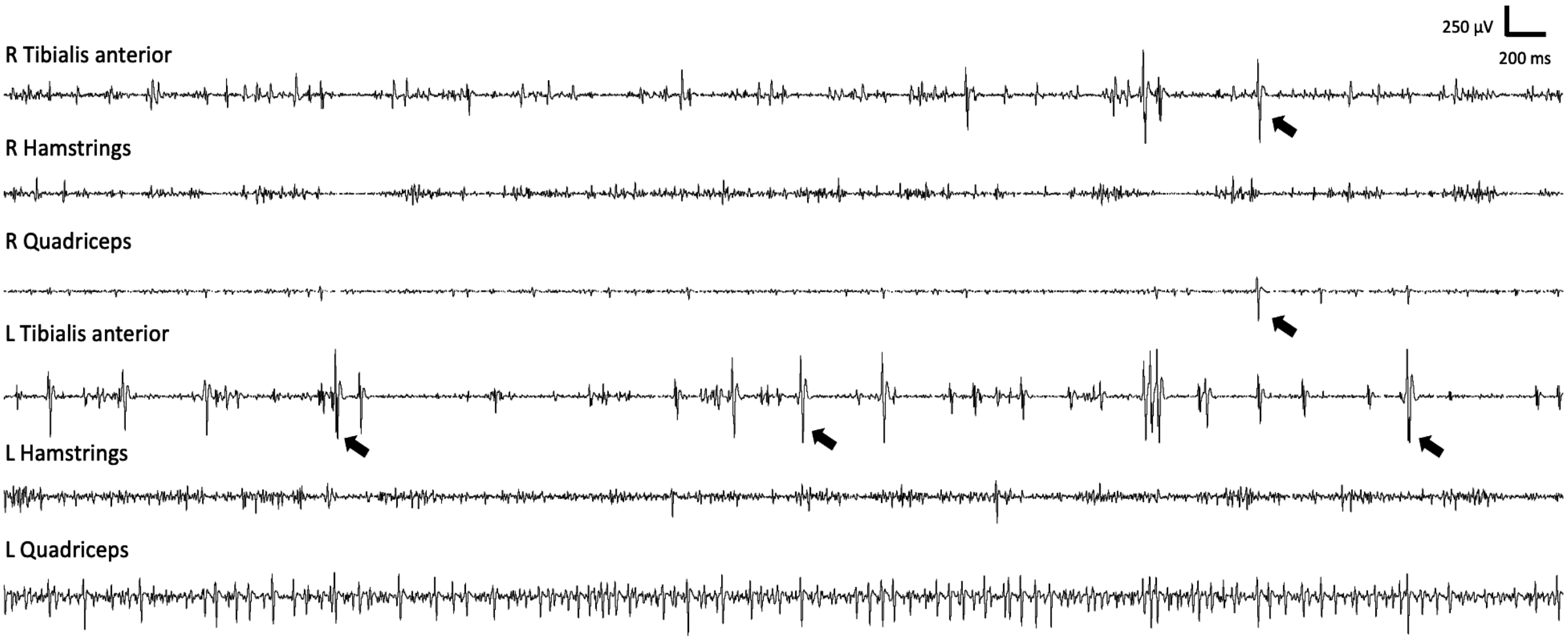
# Classical Orthostatic Tremor (OT) vs Slow OT vs Orthostatic Myoclonus (OM) - II

**Comparison of Clinical, Electrophysiological, Imaging, and Treatment Features of Classical OT, slow OT, and OM.**

| | Classical OT | Slow OT | OM |
|---|---|---|---|
| SEMG | Tremor bursts >13 Hz, (usually 15–16 Hz); shorter-duration discharges | Tremor bursts usually <10 Hz, longer-duration discharges | Myoclonic bursts 3–7 Hz, Very short burst duration (30–100 ms) |
| Synchronicity of bursts | Highly synchronous | Less synchronous | Synchrony of homologous muscles common |
| Transmits to arms on weight-bearing | Yes | Yes | Rare |
| Coexistent SEMG findings reported | Postural arm or leg tremor | Unknown | Coexistent arm myoclonus rarely |
| Medications of choice | Clonazepam, beta-blockers, gabapentin, valproate, primidone | Partial response – clonazepam, gabapentin, primidone, propranolol | Clonazepam, levetiracetam |
| Response to alcohol | Yes | Unknown | No |
| Response to DBS | Yes | Unknown | Unknown |
| Gait aid | Roller walker | Unknown | Roller walker |
| Imaging findings | Normal or age-related atrophy or leukoaraiosis | Unknown | Severe microvascular disease common |

Hassan & van Gerpen, 2016

# Orthostatic myoclonus



# Orthostatic Myoclonus—Clinical and Electrophysiological Features in a Large Retrospective Cohort

*Sai A. Nagaratnam, FRACP,[1,2] Niroshan Jeyakumar, MD,[1,2] Gobishan Jeyakumar, BE/BSc,[1] Florence Chang, PhD,[1,2] Duncan Wilson, PhD,[1] Paloma Becker, MD,[1,2] Hugo Morales-Briceno, FRACP,[1,2] Neil Mahant, PhD,[1,2] and Victor S.C. Fung, PhD[1,2,*]*

MOVEMENT DISORDERS CLINICAL PRACTICE 2026

**Abstract:** Background: Orthostatic myoclonus is characterized by irregular, lower limb myoclonic bursts during stance and is a major cause of postural instability and falls. However, studies are limited, and little is known about its pathophysiology.

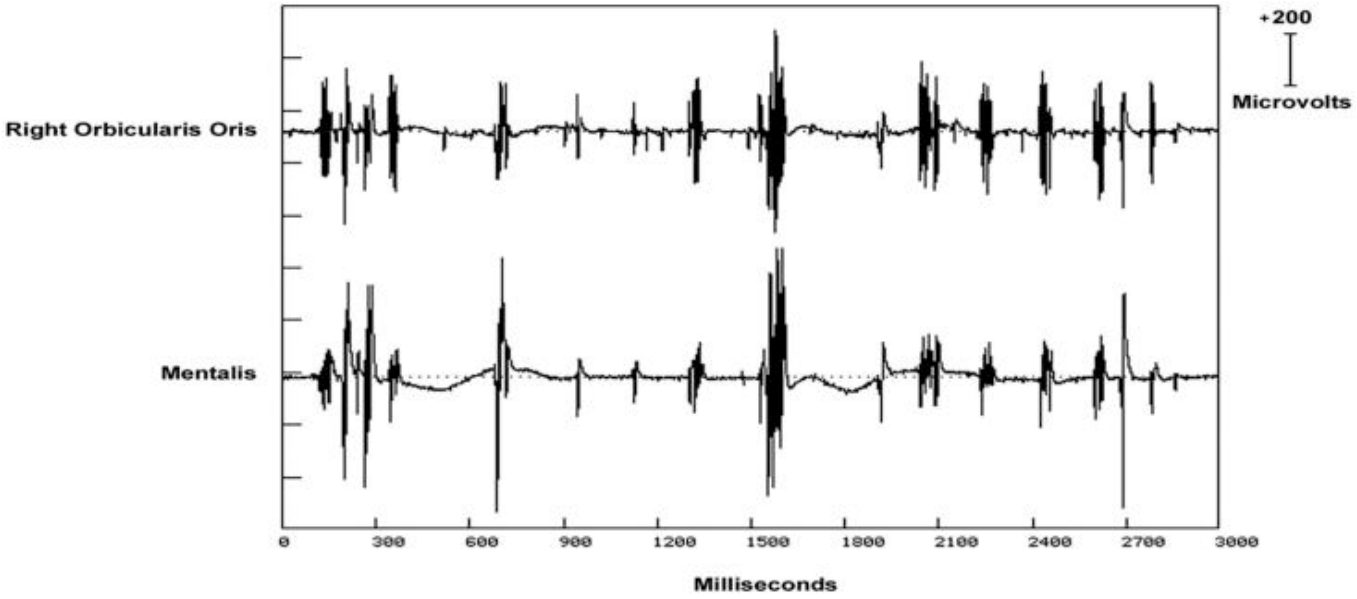
Objectives: We sought to define the clinical and electrophysiological features of orthostatic myoclonus in a large, single-center cohort.

Methods: We included 42 participants (24 males, 18 females) with a mean age of 74 years (range, 46–93) from Westmead Hospital presenting with orthostatic myoclonus from 2007 to 2023. Medical records were retrospectively reviewed for demographic details, symptoms, co-morbidities, and treatment. Lower limb surface electromyography (EMG) was analyzed using a custom-designed algorithm to automatically identify myoclonic bursts and measure their duration, synchronicity, and rhythmicity. Differences in burst parameters between muscles and associations between burst parameters and clinical characteristics were statistically evaluated.

Results: Mean burst durations during standing were 77 to 90 ms across lower limb muscles. Maximum burst activity and bilateral synchronicity occurred in tibialis anterior. Only 12% of participants exhibited any rhythmicity. A total of 79% of participants had a coexistent neurological disorder including 26% with parkinsonism. There was no significant association between parkinsonism and burst parameters. However, there was a significant, inverse correlation between the presence of neuropathy or radiculopathy and synchronous activity ($P = 0.02$).

Conclusions: We provide a computationally robust clinical and electrophysiological analysis of orthostatic myoclonus in a large cohort. Our findings support the theory of a subcortical generator arising from protean secondary causes and subject to peripheral modulation. Further work is needed to clarify treatment outcomes.

# Peripheral Myoclonus




Electromyographic (EMG) discharges have a highly variable duration of 25 to 100 ms, showing both synchronous and asynchronous discharge relationships between muscles, which gives a disorganized appearance to the EMG polygraphy recording.

van der Veen S, Caviness JN, Dreissen YEM, Ganos C, Ibrahim A, Koelman JHTM, Stefani A, Tijssen MAJ. Myoclonus and other jerky movement disorders. Clin Neurophysiol Pract. 2022

- Rhythmic or semi-rhythmic movements
- Secondary to injuries to the plexus, nerve, root, or, rarely, anterior horn cell disease
- Can persist in sleep

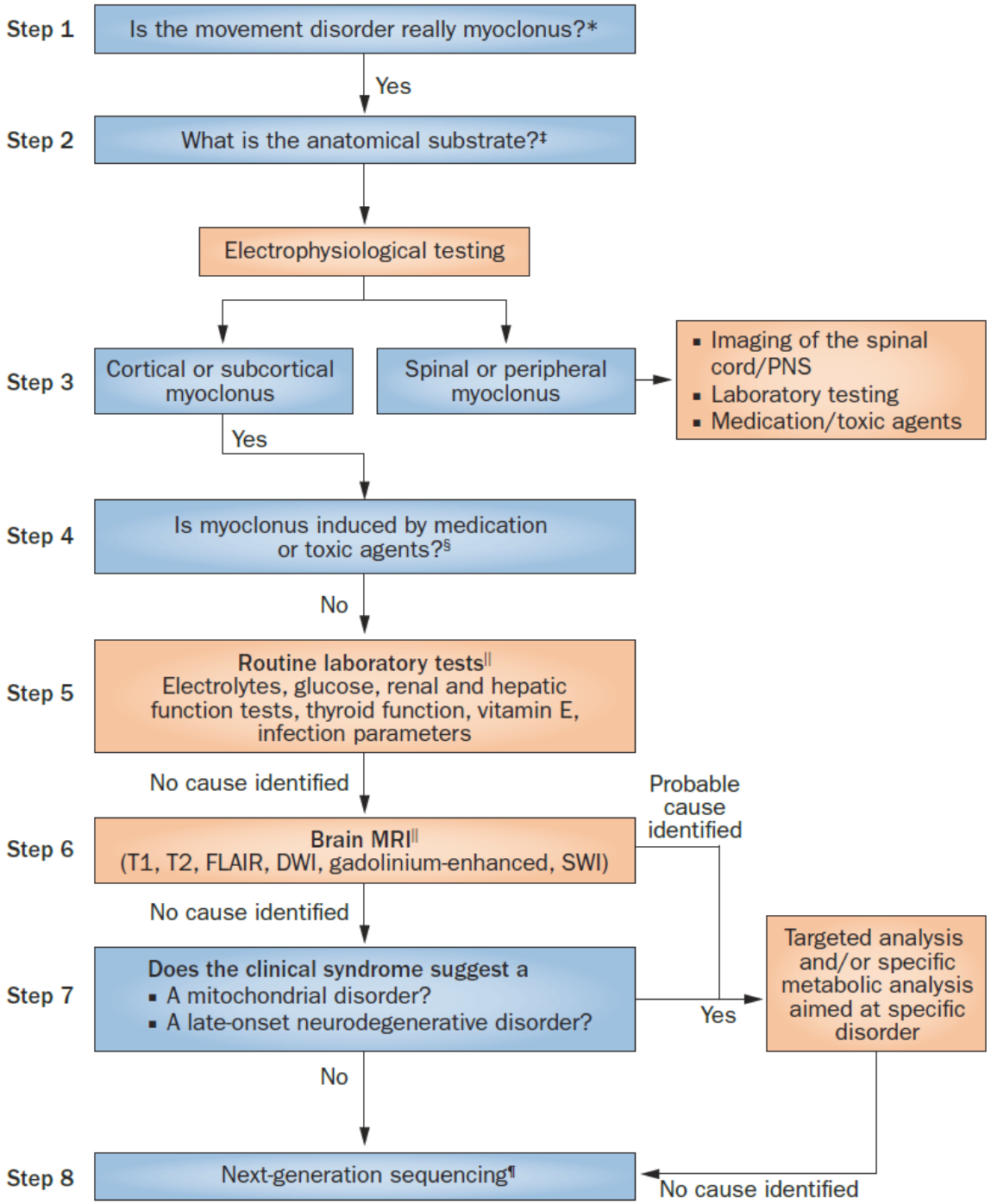
*J Vet Intern Med.* 2025;39:e17227.
https://doi.org/10.1111/jvim.17227

# Characteristics and clinical course of myoclonus in Cavalier King Charles Spaniels

Matthew James[1] | Mark Lowrie[2] | Clare Rusbridge[3]



# Approach to Myoclonus




Zutt, R. *et al. Nat. Rev. Neurol.* **11**, 687–697 (2015)

# Anticonvulsants used for myoclonus

| AGENT | DOSE (mg/day) |
|---|---|
| Clonazepam | 3 to 20 |
| Valproic acid | 1000 to 2000 |
| Levetiracetam | 1000 to 3000 |
| Primidone | 500 to 1000 |
| Phenobarbital | 60 to 180 |
| Zonisamide | 100 to 600 |
| Brivaracetam (?) | 50 to 150 (?) |
| Perampanel | 2 to 8 |

Avoid Phenytoin, Gabapentin and Carbamazepine

2 or 3 drugs in combination might be better than a single drug

# Summary

- Myoclonus is extremely common
- Multiple clinical and electrophysiological subtypes
- Clinical electrophysiology extremely useful in diagnosis and management
- Treatment needs to be tailored to the diagnosis

# Thank you!




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