Myoclonus

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What is Myoclonus?

- *"a long-standing source of confusion and debate" (Gastaut, 1968)*
- **Definitions:**
  - "quick muscle jerks, either irregular or rhythmic"
  - "sudden, brief involuntary movement"
  - "any brief muscle contraction"
  - " sudden, brief, shock-like muscle contraction arising from the CNS"
  - "abrupt, jerky, involuntary movements"

Other movement disorders

- Tics
- Simple partial seizures with motor dysfunction
- Chorea
- Startle syndromes
- epileptic vs. non-epileptic myoclonic disorders

Myoclonus ←→ Tics

Myoclonus	Tic
No preceding urge to move	Urge to move
Simple movement	Simple/Complex movement
Often bilateral upper extremities, little variation	Midline (facial) or lateralized – never bilateral
No vocalization	Vocal tics (5-30%) – Tourette's
Non-suppressible	Temporarily suppressible

Difference in treatment!

- Treatment of myoclonus → not effective for Tics
- Treatment of Tics → may worsen myoclonus (epileptic)

Myoclonus ←→ simple partial seizure (motor)

- EEG to differ!
- Phenotype of simple partial seizure (motor):
  - **Consistent focality**
  - **Unilaterality**
  - **Jacksonian spread**
  - Also lower extremities

Myoclonus ←→ Chorea

- Chorea + athetoid *(writhing)* movements
- Patients with Chorea often attempt to incorporate choreiform movements into volunatary actions

Myoclonus ←→ startle syndromes

- stiff baby syndrome: exaggerated startle to tactile or acoustic stimuli with no loss of consciousness
- Generalized stiffness after startle
- Absence of habituation ←→ normal startle reflex
- *+ cognitive deficiency / + cerebral palsy*

Myoclonus - Definition

Myoclonus - Definition

- **Sudden, brief, shock-like involuntary** movement
- burst of muscular activity (**positive** myoclonus) OR silencing of muscular activity (**negative**)
- At rest / during voluntary movement (action-induced) / due to provoking stimuli (sensory, visual, auditory, emotional)
- **Short (10-50 ms), non-rhythmic**
  - Exceptions: CJD (> 100 ms – "dystonic myoclonus"), familial cortical myoclonus, progressive myoclonic epilepsies, CBD, spinal segmental myoclonus ("rhythmic")

Cortical	Subcortical	Segmental	Peripheral
Focal discharge from M1 / S1 cortex	A) Cortical-Subcortical Thalamus-cortex network impaired B) Subcortical-nonsegmental myoclonus manifests far beyond the segments near to the originating site	Particular Segment(s) of brainstem/spinal cord	PNS lesion → hyperactive discharge to muscle
Cortical reflex myoclonus, neurodegenerative disease	A) Primary generalized epileptic syndromes (JME), Absence B) Essential	Palatal myoclonus, spinal segmental myoclonus	Hemifacial spasm
EEG: variable EMG: Bursts < 75 ms	EEG: Generalized spike and wike EMG: Bursts < 100 ms	EEG: normal EMG: Bursts > 100ms	EEG: normal EMG: variable

Etiologies - Overview

- Physiologic
- Essential
- Epileptic
- Secondary / Symptomatic

Etiologies

Physiologic:

- Jerk during **sleep** or sleep transition, **anxiety**-induced myoclonus, **exercise**-induced myoclonus, singultus, benign infantile myoclonus with feeding
- Nocturnal Myoclonus (period limb movements of sleep):
  - Stereotyped repetitive dorsiflexion of toes and feet (see 'RLS')
  - → sleep disturbance / excessive daytime sleepiness

Etiologies

Essential I:

- Myoclonus = **most prominent** or only finding
- Mild disability / slow or absent progression / normal cognition
- Sporadic ←→ hereditary (A-D: arms and axial muscles)
- Palatal Myoclonus:
  - Often secondary due to brainstem lesion – but also essential
  - Contractions of tensor veli palatini – roof of the mouth
  - + clicking/popping in the ear

Etiologies

Essential II:

- Myoclonus-Dystonia:
  - Dystonia as a common feature of hereditary essential myoclonus *(involunatary, repetitive or twisting movements)*
  - **Cervical / limb dystonia** + short **jerks**
  - Onset: > 6 years (f > m)
  - DYT11 gene
  - little or no functional disability

Etiologies

Epileptic I:

- = myoclonus in the setting of epilepsy – **seizures** dominate
- **Infantile spasms** (West syndrome):
  - Triad: infantile spasms + interictal EEG hypsarrhythmia + mental retardation
  - → ACTH, steroids, vigabatrin
- **Severe myoclonic epilepsy of infancy (Dravet syndrome):**
  - Severe seizures triggered by hot temperature and fever
  - + ataxia, psychomotor delay

Etiologies

Epileptic II:

- Lennox-Gastaut-Syndrome:
  - + mental retardation + regression
  - Multiple seizure types: absence / tonic / atonic / tonic-clonic
- Benign myoclonic epilepsy of infancy
- Myoclonic astatic epilepsy (Doose syndrome)
- Cryptogenic myoclonus epilepsy (Aicardi):
  - = agenesis of corpus callosum + retinal abnormalities + seizures
  - X-linked (in girls or in boys with Klinefelter syndrome)

Etiologies

Symptomatic:

- Drug-induced syndrome
- Neurodegenerative disease
- Encephalopathies, including hypoxia
- Progressive myoclonus ataxia
- Infectious and postinfectious disorders
- Autoimmune inflammatory disorders (opsoclonus-myoclonus syndrome)
- Metabolic disorders
- Mitochondrial disorders
- Storage diseases
- Exaggerated

Symptomatic Myoclonus

Drug-Induced

- Levodopa
- TCA, SSRI, MAO inhibitors, lithium
- Antibiotics *(penicillins, cephalosporins, quinolones)*
- Anticonvulsants
- CCB
- Drug withdrawal (e.g. sedatives)

→ Myoclonus typically resolves upon withdrawal

Metabolic

- Hyperthyroidism
- Hepatic failure
- Renal failure
- Electrolyte disturbances
- Hypoxia: Lance-Adams-Syndrome
  - Posthypoxic myoclonus, days after successful CPR
  - Triggered by intentional actions or external stimuli
  - ←→ acute posthypoxic seizure: + comatose state

Neurodegenerative diseases

- Alzheimer‘s, PD, FTD, LBD
- Wilson‘s
- Huntington‘s disease
  - Autosomal-dominant, CAG repeats
  - **Chorea** (involuntary, irregular, nonrepetitive, arrhythmic)
  - Oculomotor disorders (nystagmus)
  - Hyperreflexia, sensory deficits, autonomic dysfunction
  - → hypokinetic (dystonia), akinetic mutism, **myoclonus**

CNS damage

- Post-stroke
- Post-thalamotomy
- Tumor
- Trauma
- Infection *(Cryptococcus, HIV, Lyme, Malaria, PML, SSPE, Syphilis)*
- Inflammation *(paraneoplastic, postinfectious)*
- idiopathic

Tay-Sachs disease

- Autosomal-recessive, more common in Ashkenazi Jews
- Hexosaminidase A deficiency → GM2 ganglioside buildup → neurodegeneration
- Developmental delay, regression, "cherry-red" spot on macula
- Dx: lysosomes with "onion skin" appearance

Gaucher disease

- Autosomal-recessive
- Glucocerebrosidase deficiency → glucocerebroside buildup → brain, liver, spleen, bone marrow
- Hepatosplenomegaly, osteoporosis, pancytopenia, neurodegeneration with myoclonus
- Dx: reduced glucocerebrosidase activity in leukocytes
- Th: recombinant glucocerebrosidase

Progressive myoclonic epilepsy (Unverricht-Lundborg)

- Age: 6-16 years, prevalent in Scandinavia
- Autosomal-recessive
- **Progressive** myoclonus
- + cognitive decline
- + lifespan: middle-age
- Cave: Phenytoin – seriously exacerbates this condition

Lafora disease

- autosomal-recessive, fatal condition
- Lafora bodies in multiple organs *(glycogen storage disorder)*
- Myoclonic seizures + ataxia + hallucinations + rapid dementia

Myoclonic epilepsy with ragged red fibres (MERRF)

- **Mitochondrial** disease
- Myoclonic seizures + cerebellar ataxia + myopathy
- → dementia, optic atrophy, WPW syndrome
- Dx: ragged red fibres on muscle biopsy
- Th: Coenzyme Q10, B complex, L-Carnitine

Dentatorubralpallidoluysian atrophy

- Autosomal-dominant *(CAG repeats)*: spinocerebellar degenaration
- *Naito-Oyanagi-disease*
- + ataxia, choreoathetosis, dementia

Creutzfeld-Jakob disease

- **Rapid** progression
- Motor symptoms:
  - **Myoclonus** + hypokinesia + ataxia
- Neuro**psychiatric** features:
  - Mutism, sleep disorders, anxiety, paranoia, dementia
- Dx: EEG *(periodic sharp wave complexes)*, CSF *(14-3-3 protein)*

Malabsorption

- Celiac disease *(HLA-DQ8)*:
  - Chronic and recurring **diarrhea** + extraintestinal manifestations:
    - vitamin deficiency, **dermatitis herpetiformis**
    - Neuropsychiatric (**myoclonus**, neuropathy, ataxia)
    - Etc.
  - Dx: transglutaminase antibody, gliadin peptide, endomysial antibody
- Whipple's disease:
  - Tropheryma whipplei infection
  - **Malabsorption** + arthritis + myoclonia + ataxia+ **cardiac** symptoms
  - Dx: PAS-positive macrophages → Th: ceftriaxone

Opsoclonus-Myoclonus Syndrome

- Paraneoplastic: *SCLC, Ovarian, Breast, Neuroblastoma*
- Antibodies against fastigial nucleus →
  - Opsoclonus = rapid, involuntary, multivectorial, conjugate fast eye movements

Hashimoto's encephalopathy

- Encephalopathy + Hashimoto's **thyroiditis**
  - hypothyroidism
  - Neuropsychiatric features: personality changes, delusion, amnesia, myoclonus *(65% cases)*, ataxia, sleep disorder
- Responsive to steroids
- Dx: anti-TPO, anti-Tg

MELAS

- = **m**itochondrial **e**ncephalopathy, **l**actic **a**cidosis and **s**troke-like episodes
- → brain + muscles affected
  - Muscle weakness, pain, exercise intolerance
  - myoclonus
  - Short stature, diabetes mellitus
  - Stroke-like episodes before age 40 – temporary hemiparesis, AMS
- Dx: blood lab *(lactic acids, CK)*, genetic testing

Myoclonus - Summary

- Myoclonus is **not a diagnosis**
- Physical sign seen in diseases of **many different pathologies** and in **normal physiological** situations
- Effort of diagnosis is not trivial
- **A good understanding of the features associated with other neurological disorders that resemble myoclonic disorders, is the best aid to accurate diagnosis**