Tunis, Tunisia
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International Parkinson and Movement Disorder Society

Myoclonus

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Definition

Myoclonus is a sudden brief (20–250 ms) contraction (positive myoclonus) or interruption of tonic muscle contraction (negative myoclonus) inducing a simple jerky movement of body part

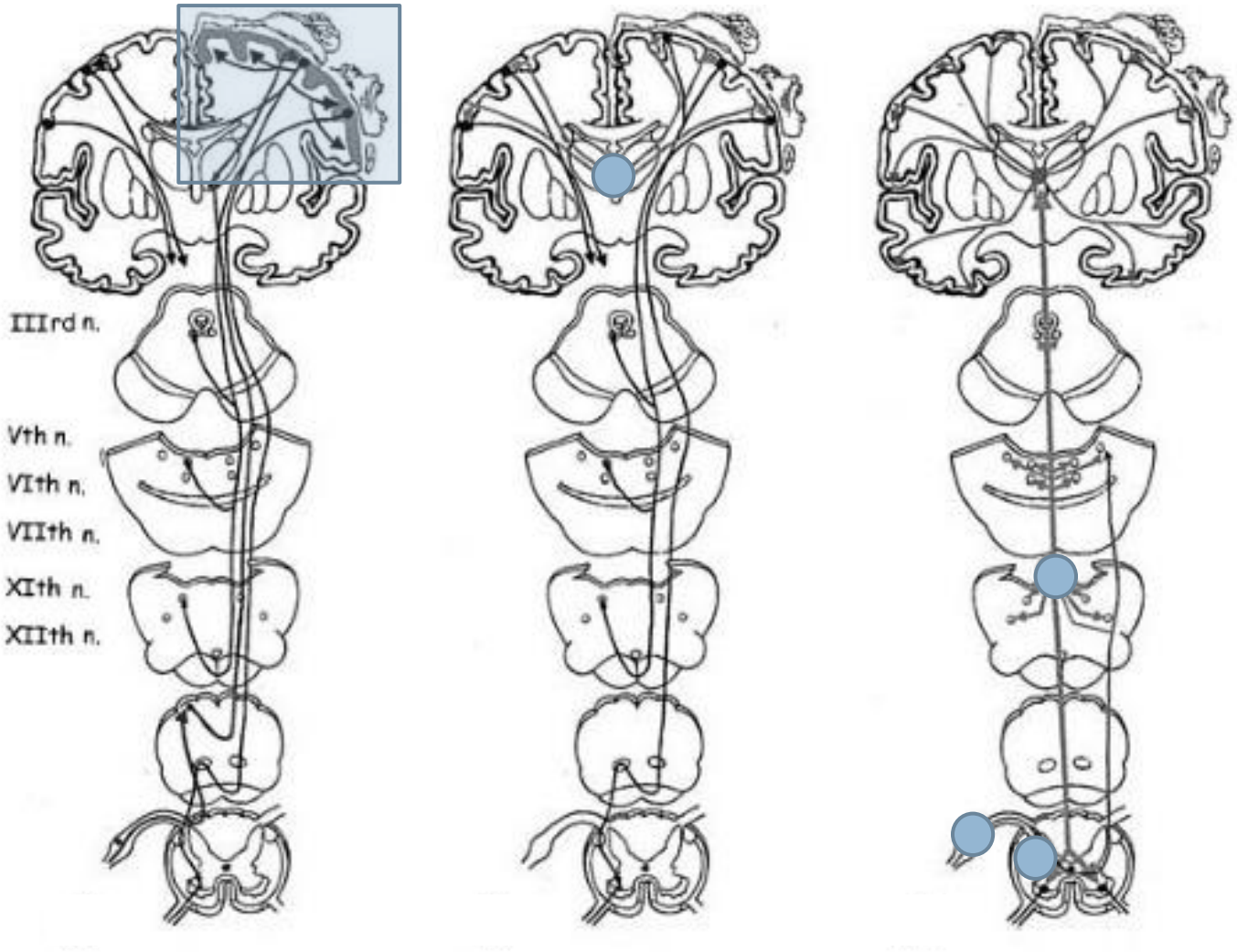
Myoclonus

- Pathological myoclonus has a lifetime prevalence of 8·6 cases per 100 000 population

- Symptom of a broad range of neurological and systemic diseases

Djik et al, 2015

Myoclonus Generators

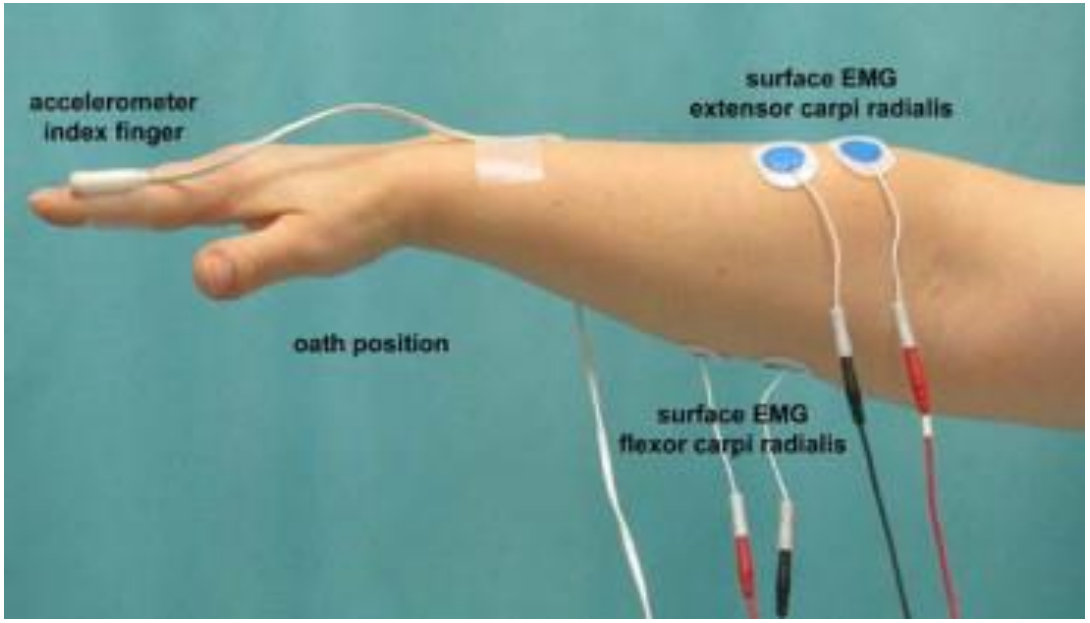


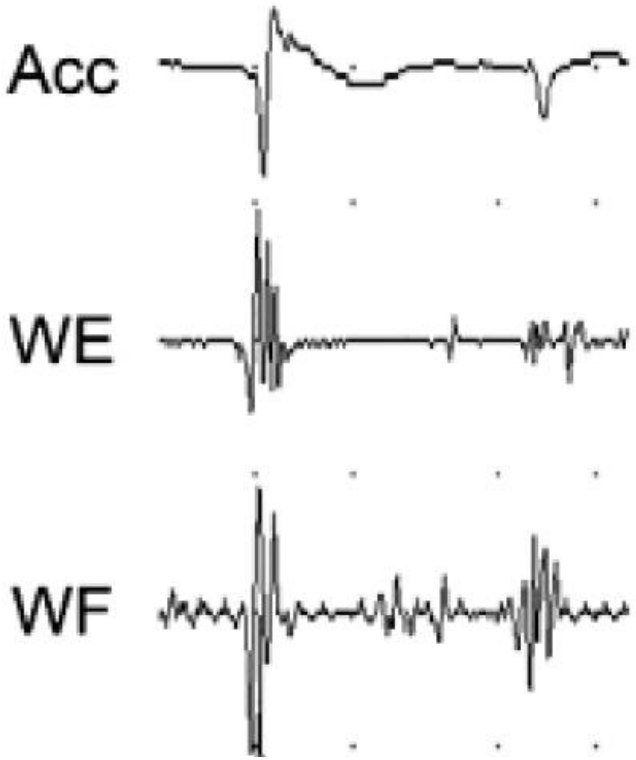
Diagnosis

- Clinical diagnosis
- Electrophysiology:
  - Distinguishing myoclonus from other involuntary movements in complex cases
  - Determining Myoclonus Generator

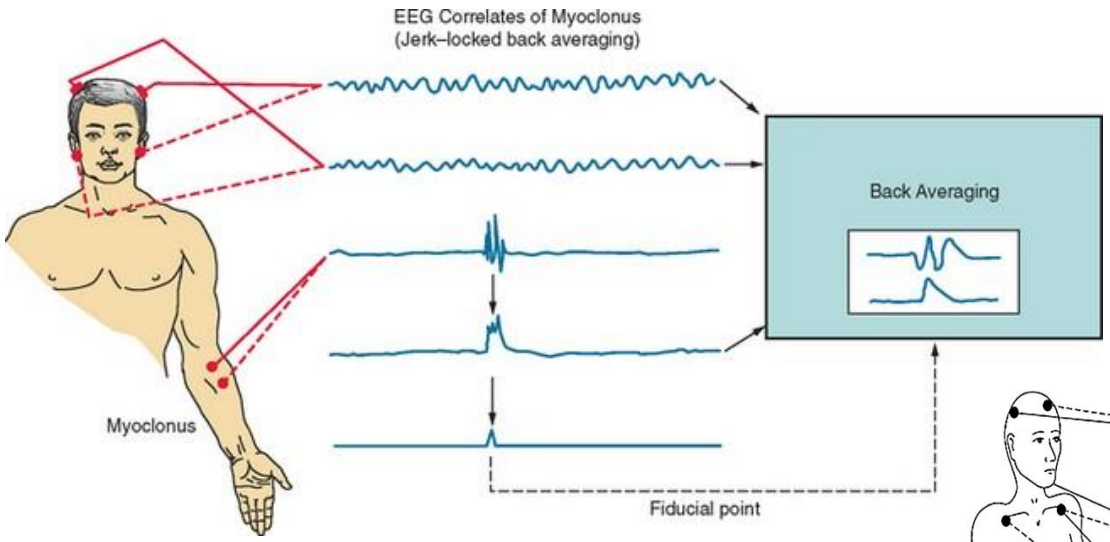
Neurophysiology

Polymyography and accelerometry

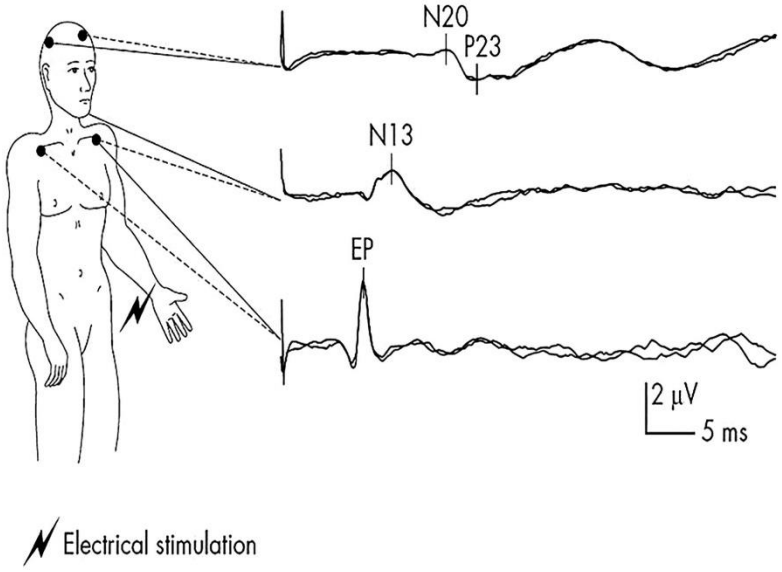




Neurophysiology



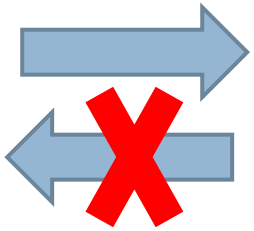
EEG-EMG Polygraphy



Somatosensory evoked potentials

Diagnosis

Myoclonus

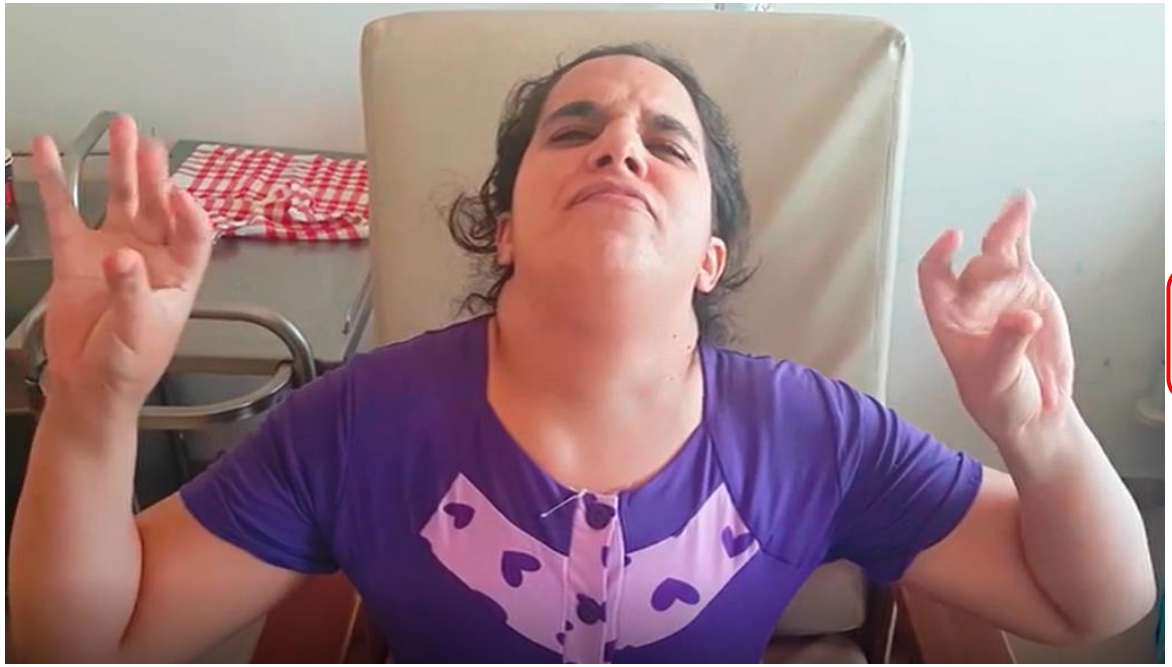


Jerk

Myoclonus or not myoclonus ?

Tics

Myoclonus or not myoclonus ?



Dystonia

Myoclonus or not myoclonus ?

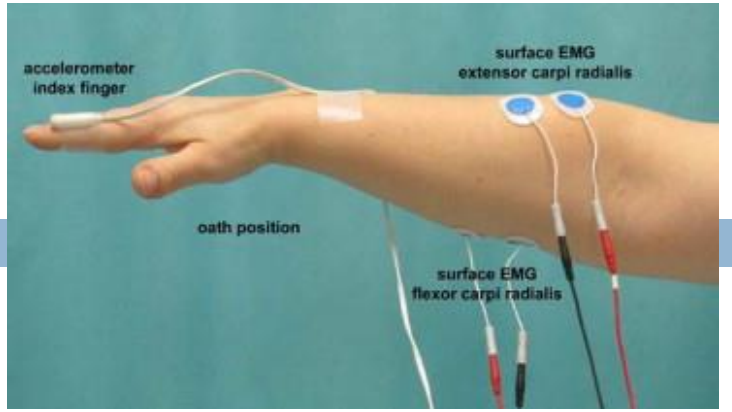
Chorea

Myoclonus or not myoclonus ?

Cotical
« tremor »
= Cortical
Myoclonus

Termsarasabet al, 2015

Polymyography



Myoclonus

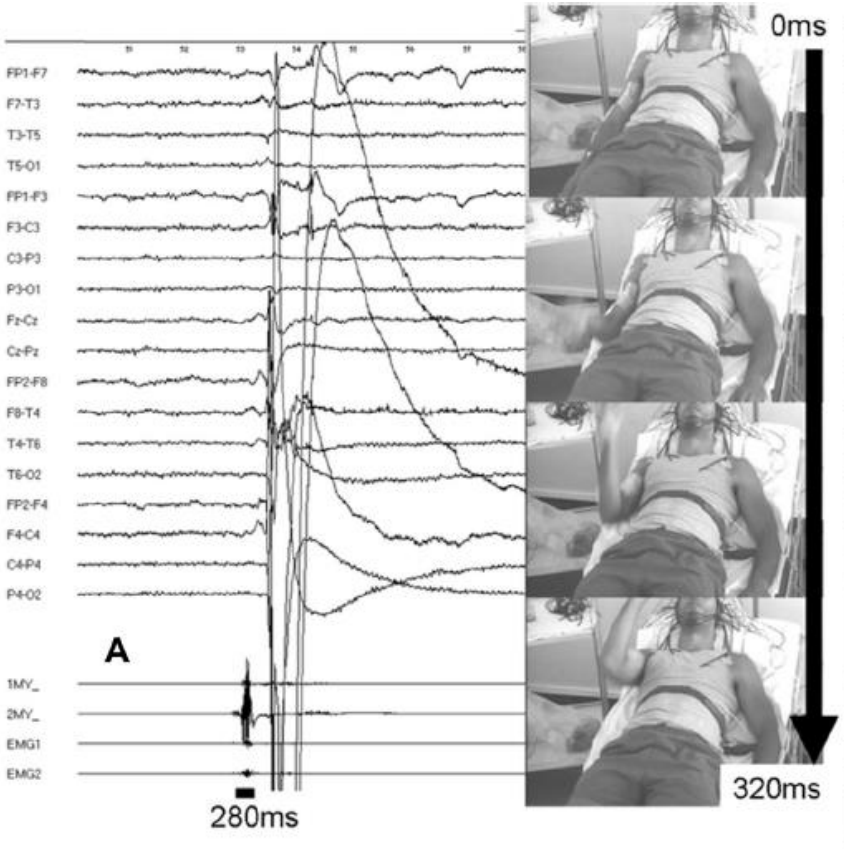
Tremor

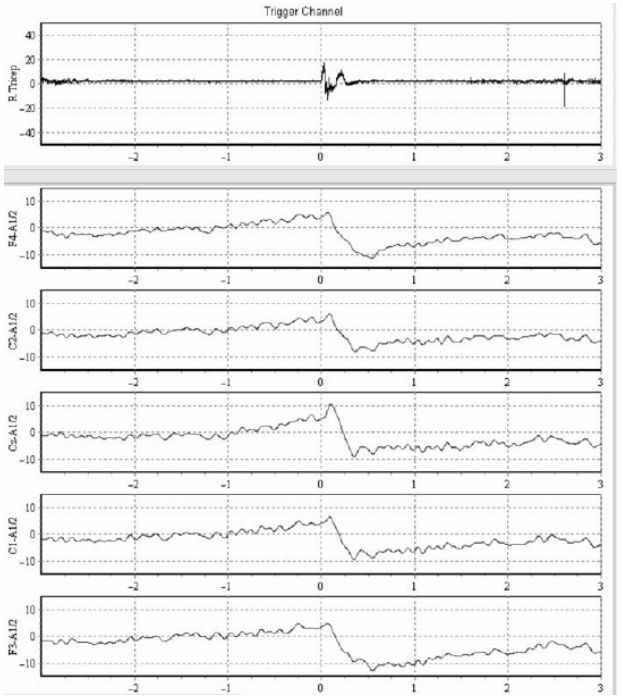
Apartis, 2013

Myoclonus or not myoclonus ?

Psychogenic

Psychogenic jerk





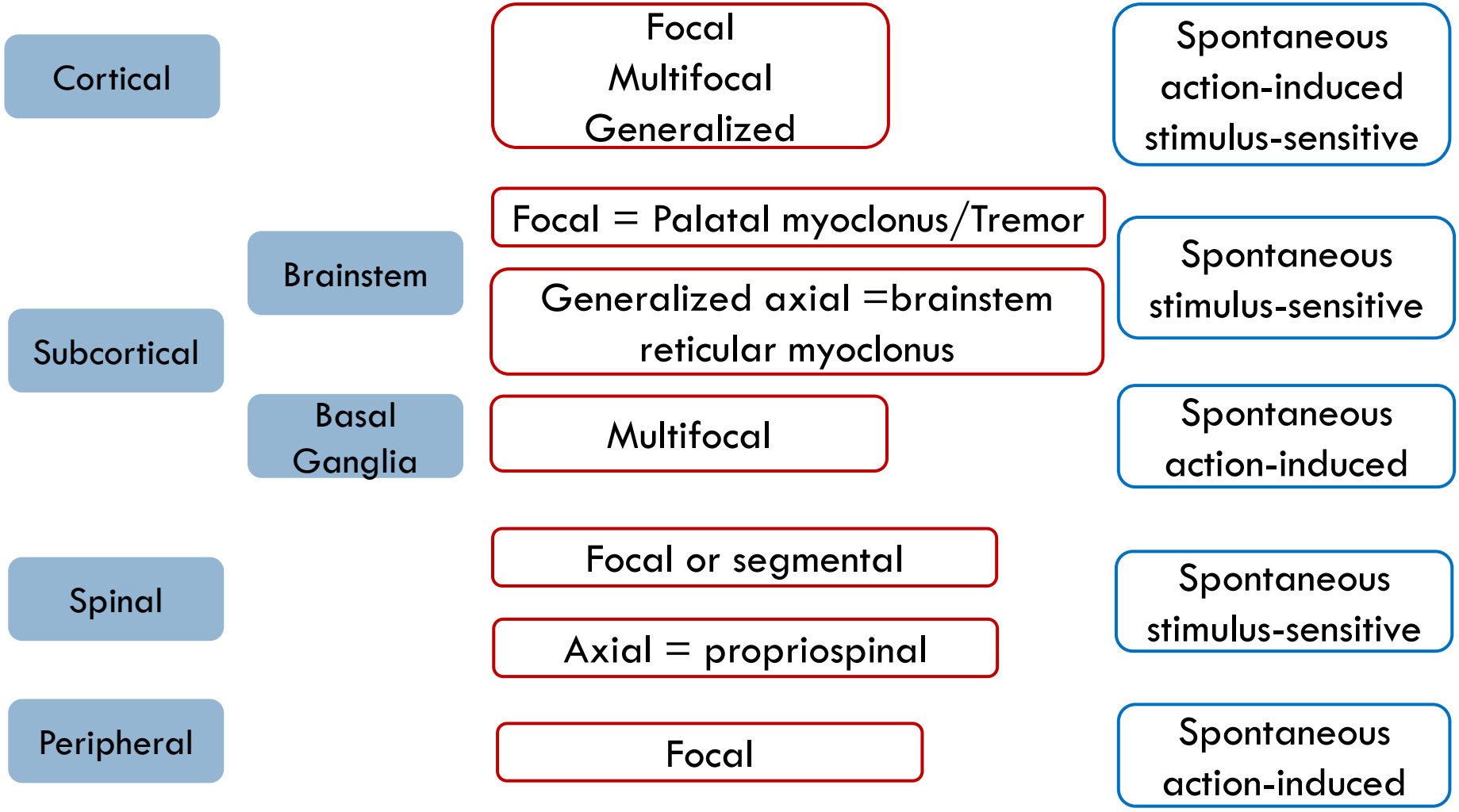
Bereitschafts potential

Apartis et al, 2016

Myoclonus

Distribution	Mode of presentation	Anatomical Source	Etiology
Focal	Rest	Cortical	Physiologic
Segmental	Posture	Subcortical	Essential
Multifocal	Action	Spinal	Epileptic
Generalized	Reflex	Peripheral	Symptomatic

Anatomical Source



Etiology

Physiologic

Hypnic jerks
Anxiety-induced
Exercise-induced
Hiccough
Benign infantile myoclonus with feeding

Essential

No known cause other than Genetic and no other gross neurologic deficit
Hereditary/Sporadic

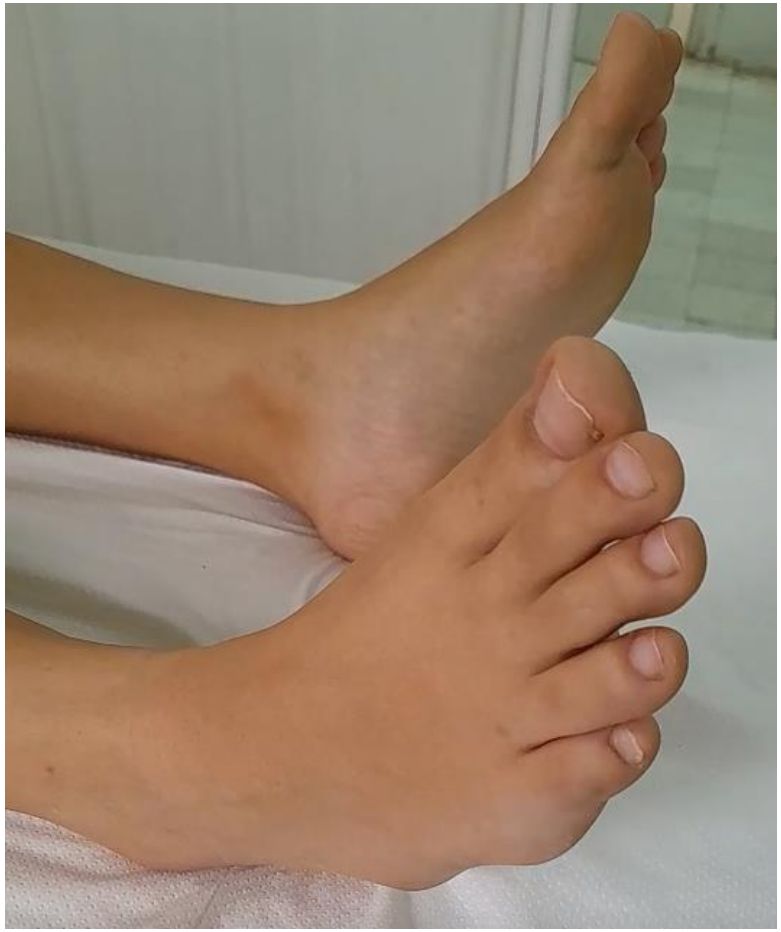
Epileptic

Seizures dominate and no encephalopathy, at least initially

Symptomatic

Progressive or static encephalopathy dominates

Myoclonus or not myoclonus ?



14-year old

Onset : 11-year old

Right focal tonic-clonic seizures

Rare grand-mal seizures

Normal neurological exam

Myoclonus

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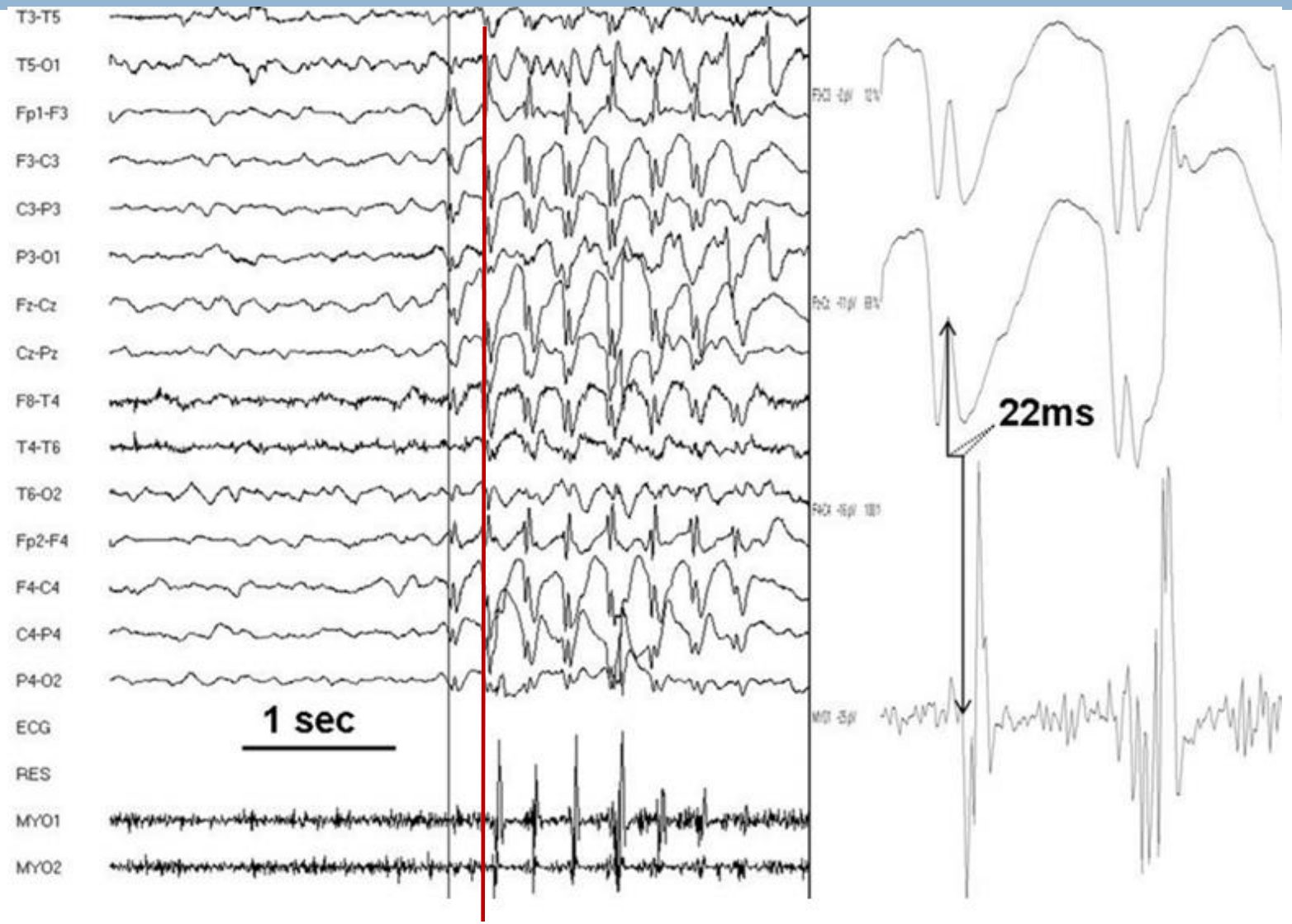
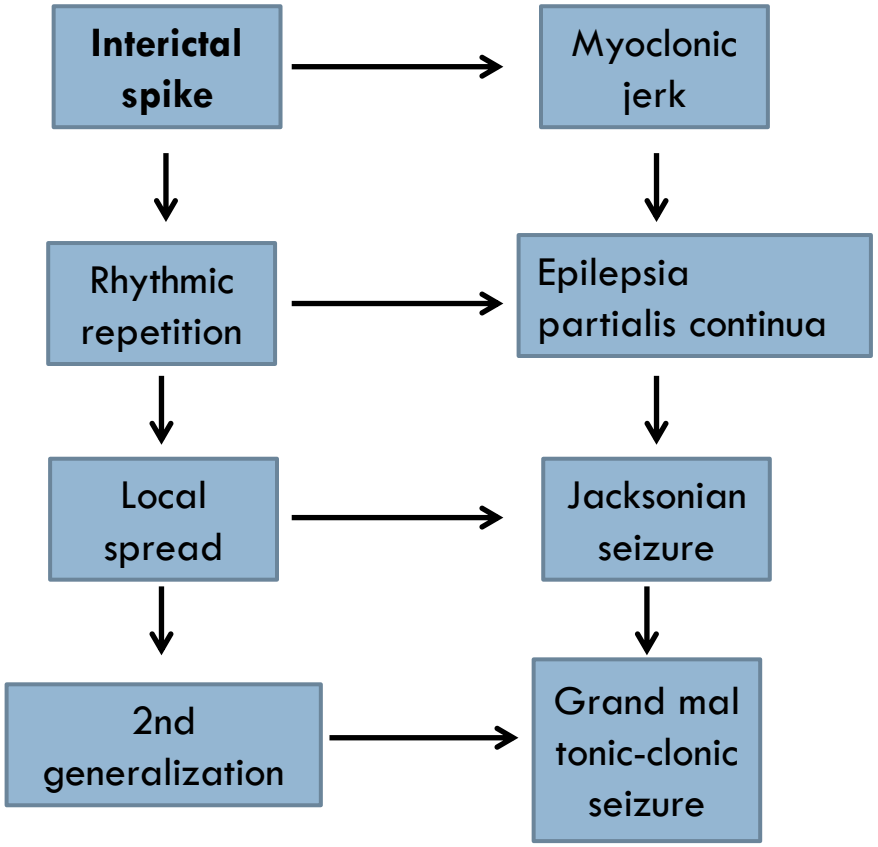
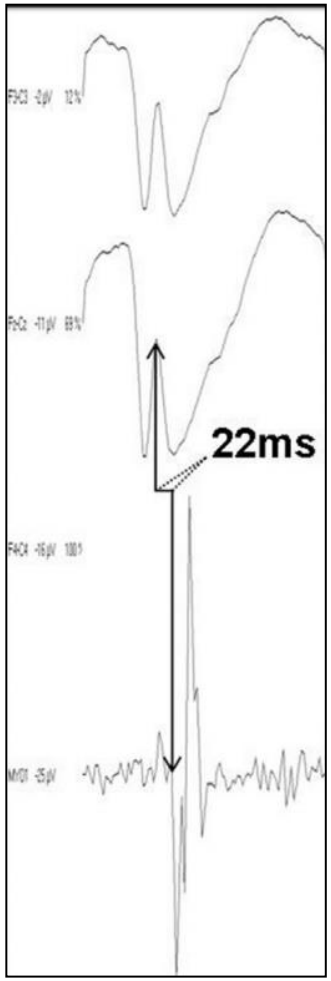
Epileptic Myoclonus

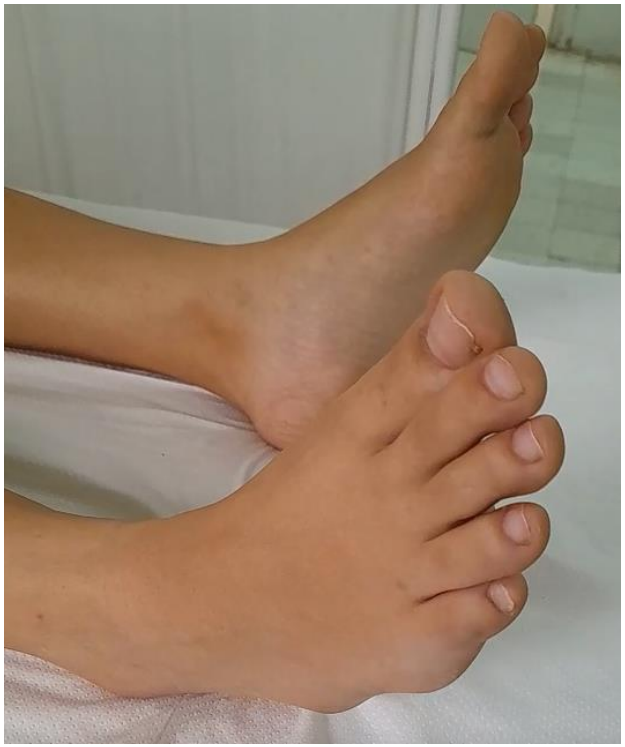


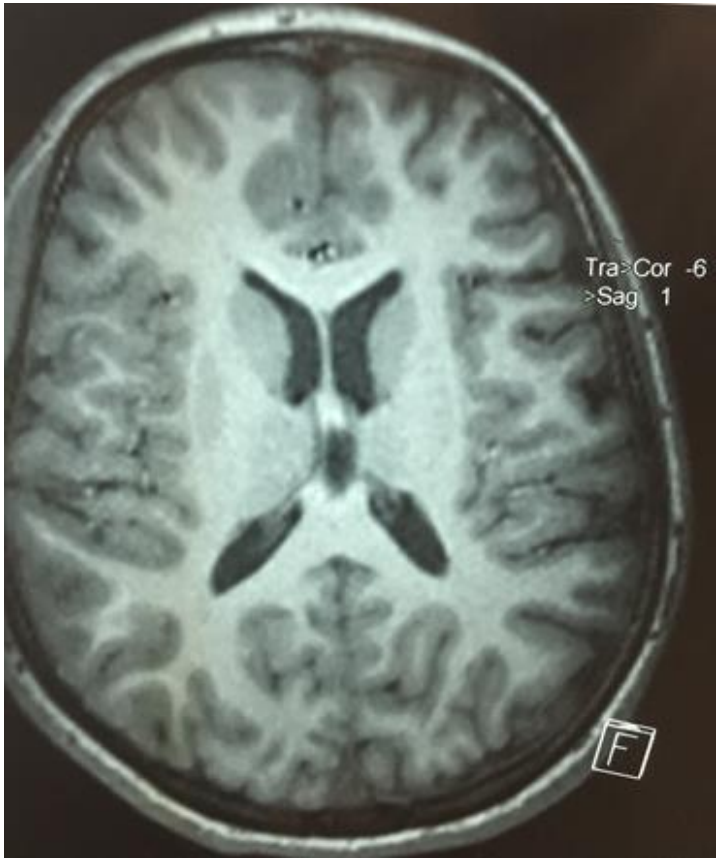
Epileptic myoclonus





Epileptia partialis continua





Rasmussen's encephalitis

Myoclonus or not myoclonus ?

Myoclonus

Rittweger et al, 2014

Myoclonus

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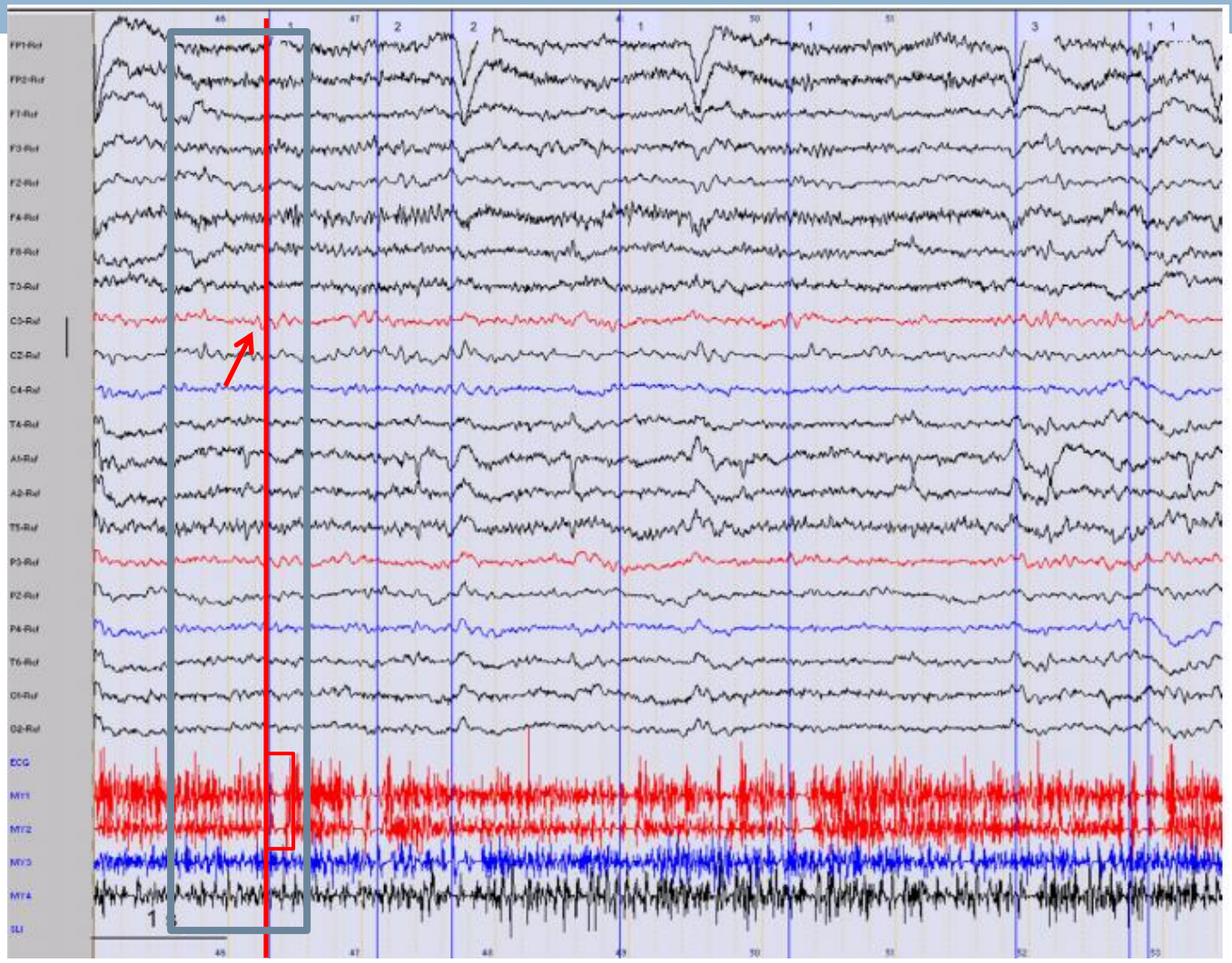
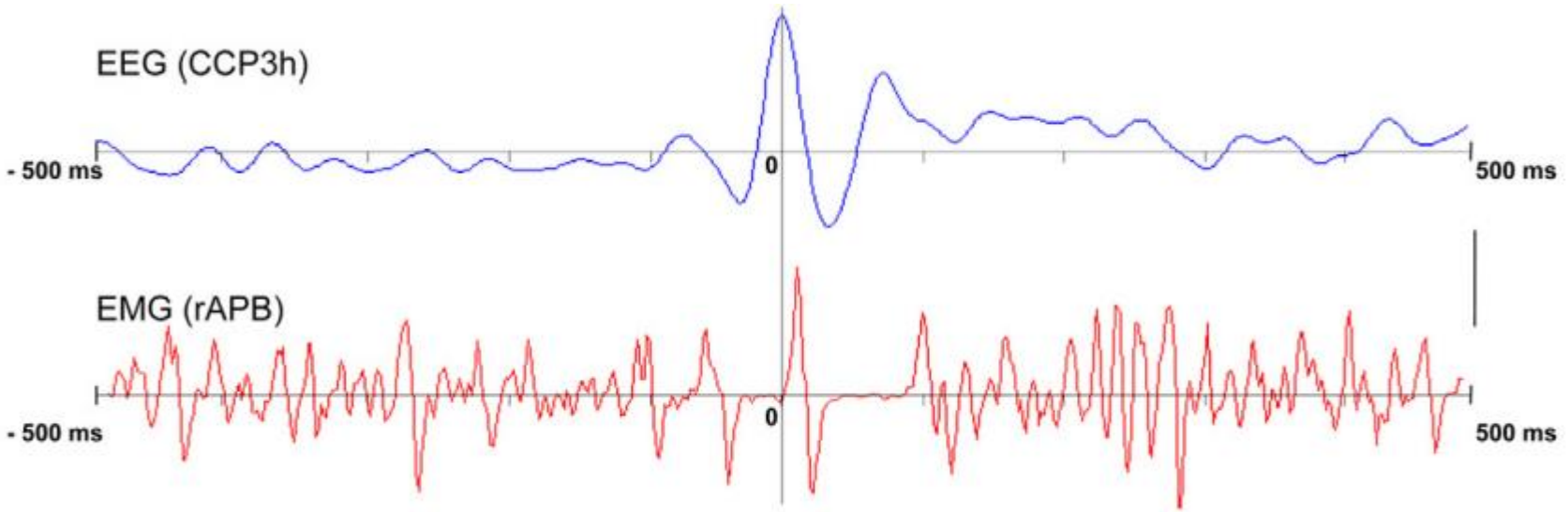
EEG-EMG polygraphy : Cortical myoclonus



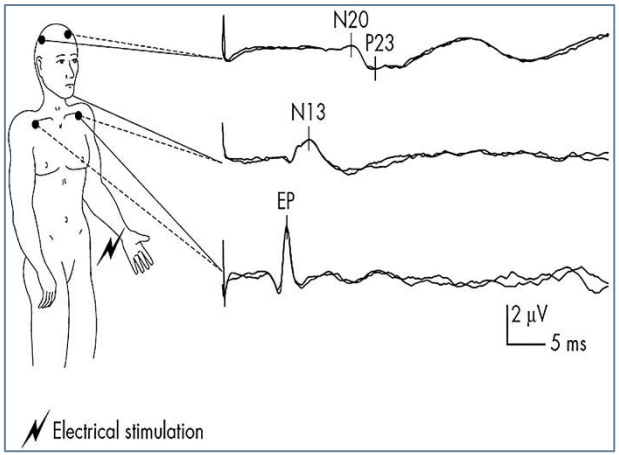
EEG-EMG polygraphy : **Cortical myoclonus**

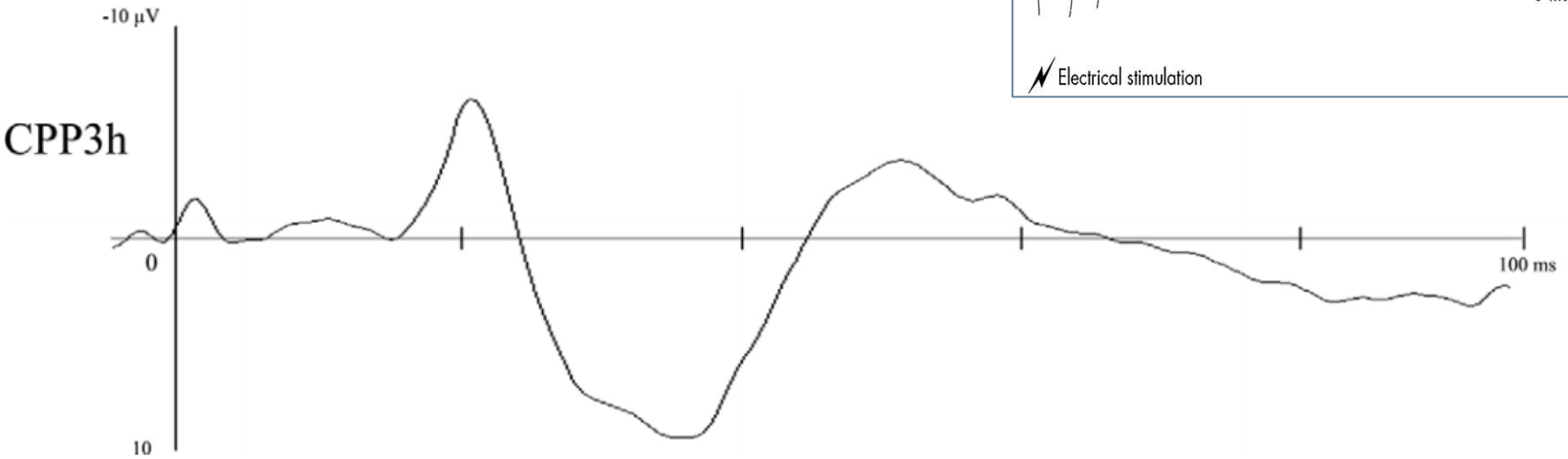
- jerk-locked back averaging (JLBA)



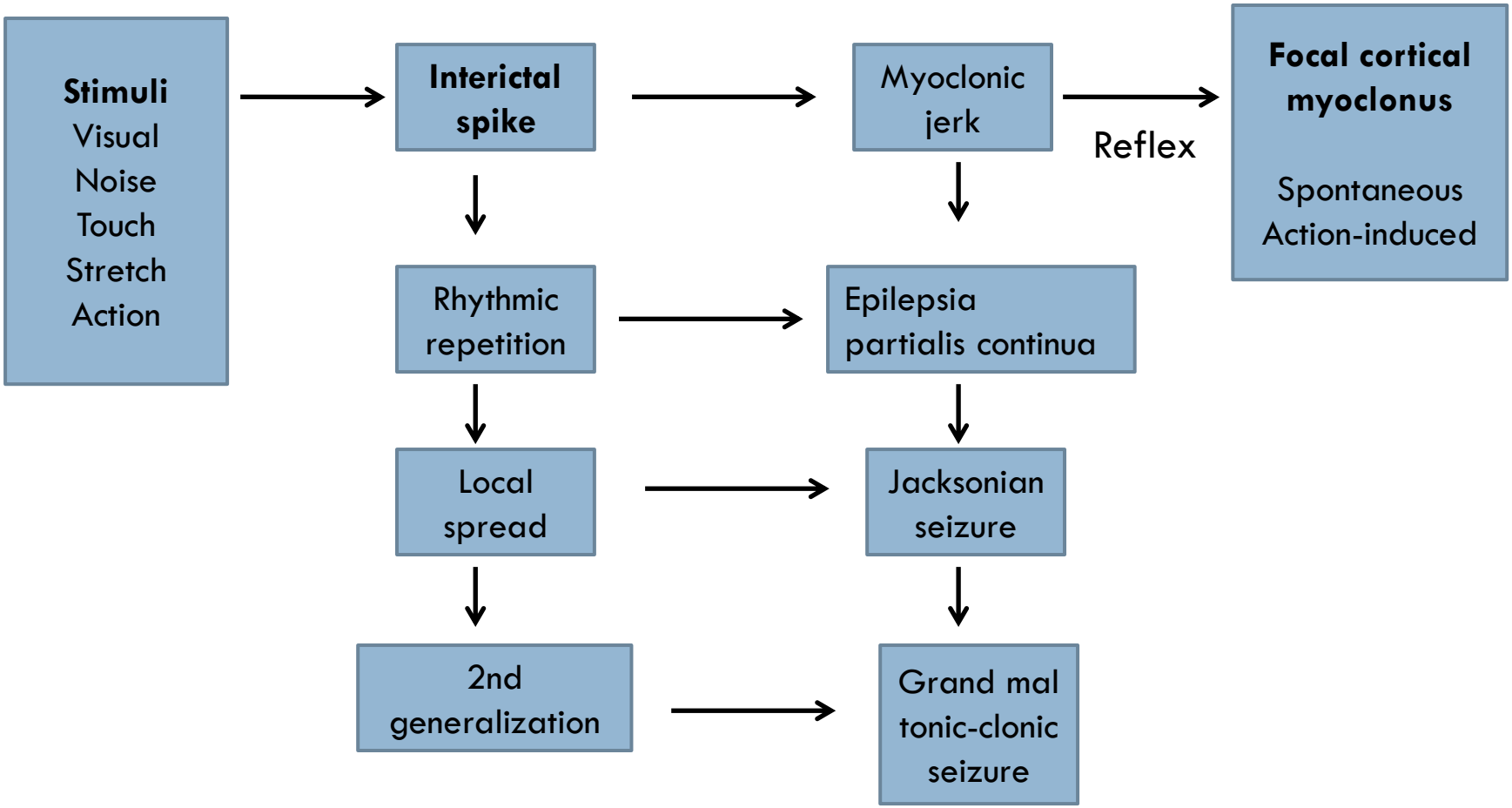
Cortical myoclonus

- Giant SEPs



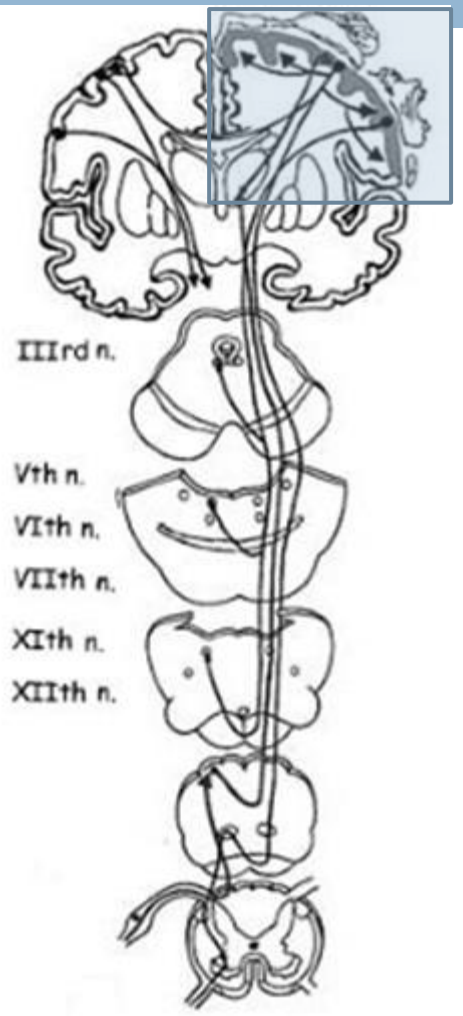


Focal cortical myoclonus

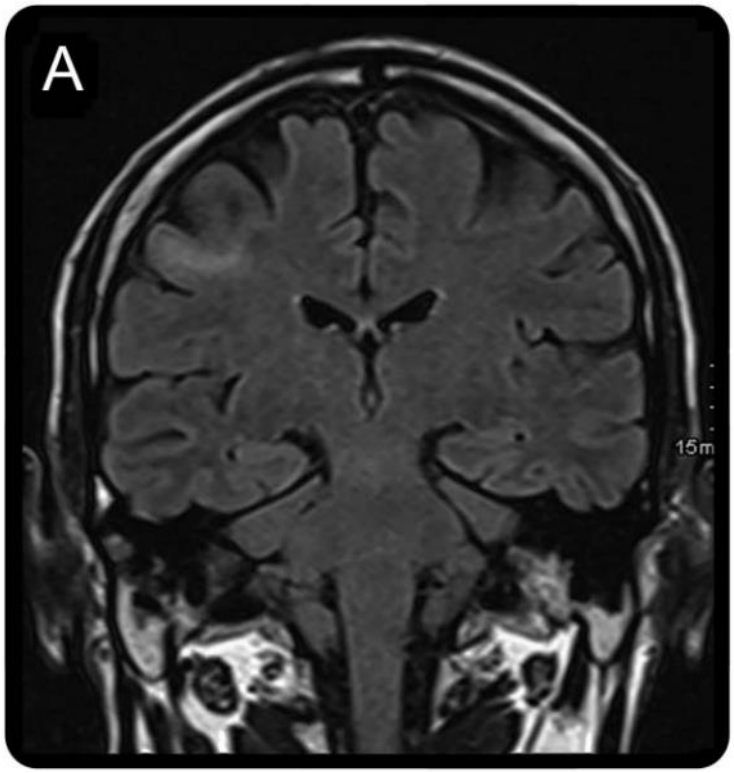


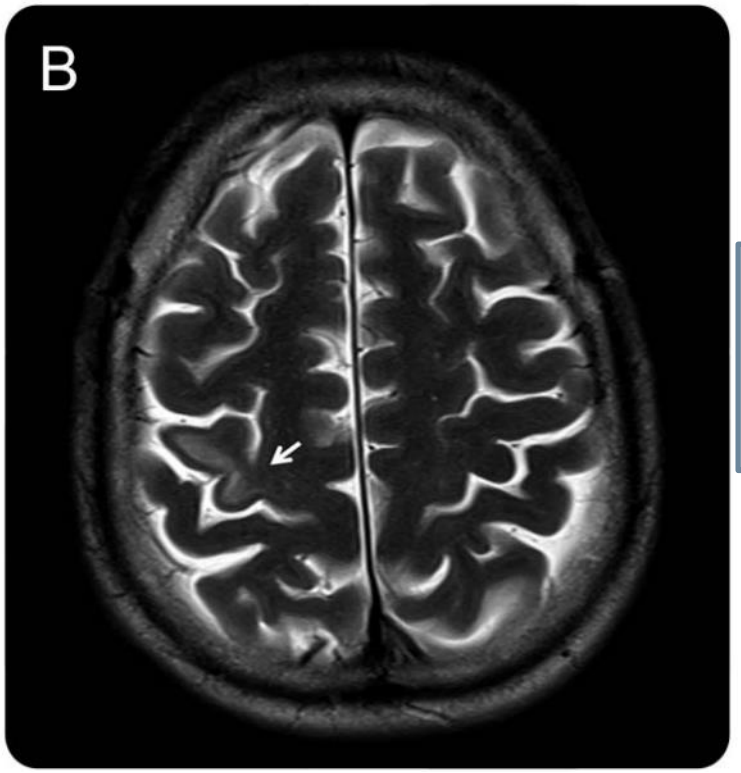
Focal Cortical Myoclonus

- Stroke
- Tumour
- Encephalitis
- Trauma
- Hepatic encephalopathy
- Subarachnoid hemorrhage
- Idiopathic



Cortical Myoclonus

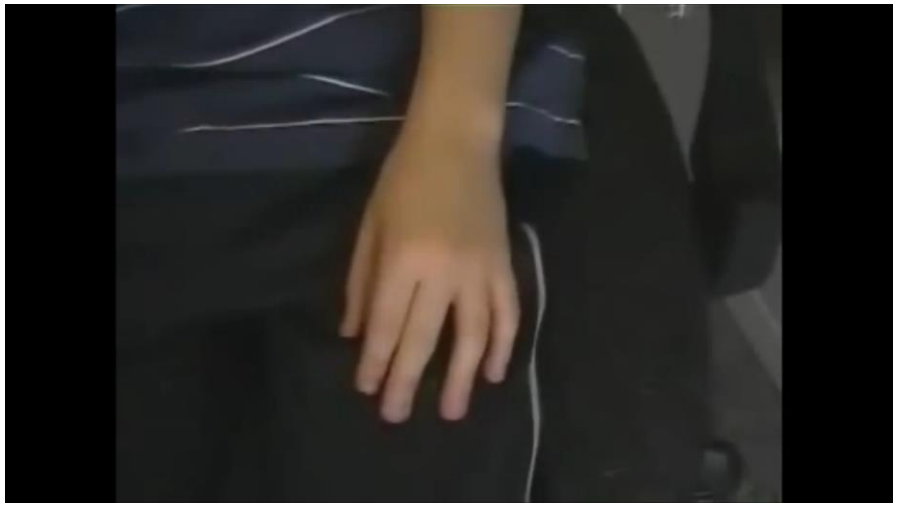




CSF PCR
JCV +

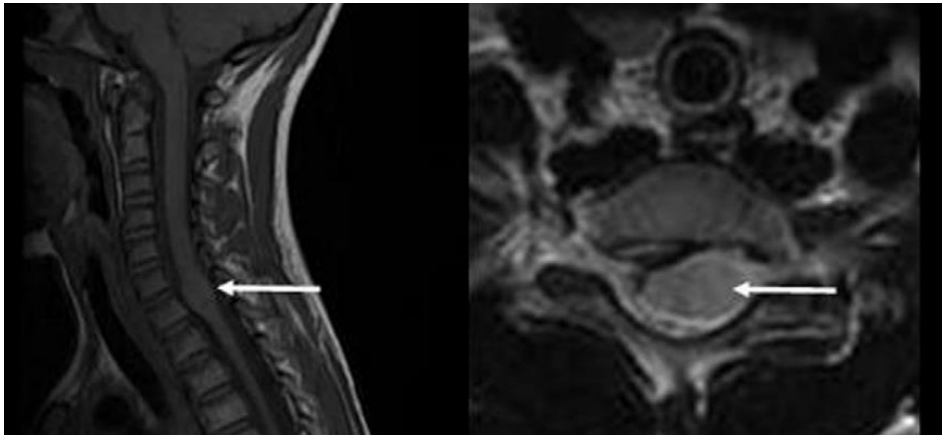
Progressive multifocal leukoencephalopathy

Spinal focal myoclonus



EEG was normal

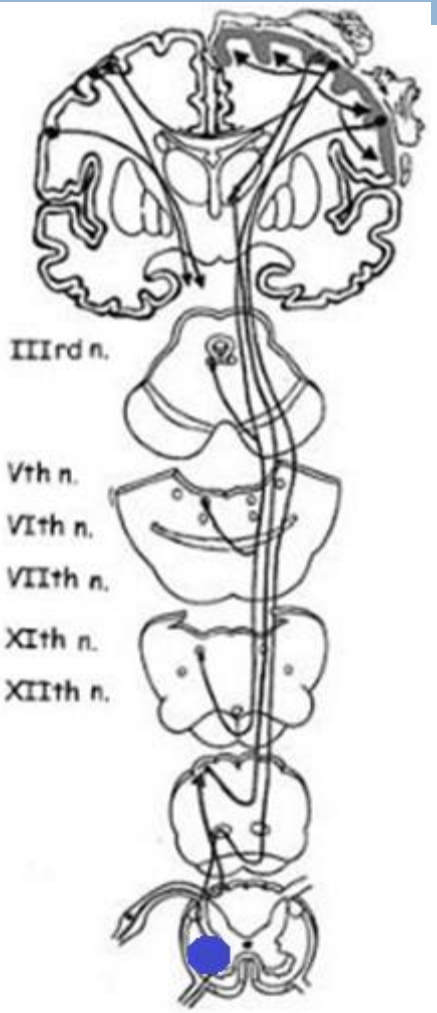
Brain MRI was normal



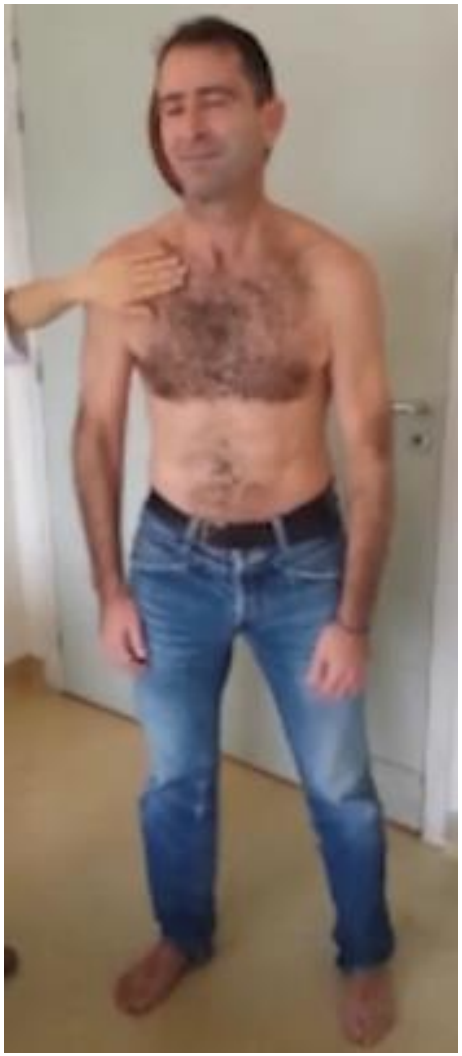
Allen et al, 2013

Spinal focal and segmental myoclonus

- Trauma
- Inflammation
- Infection
- Demyelination
- Tumor
- A-V malformation
- Surgery
- Spondylitic myelopathy
- Spinal-anaesthesia



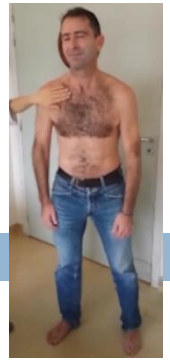
Myoclonus or not myoclonus ?



Myoclonus

Mariani et al, 2017

Myoclonus



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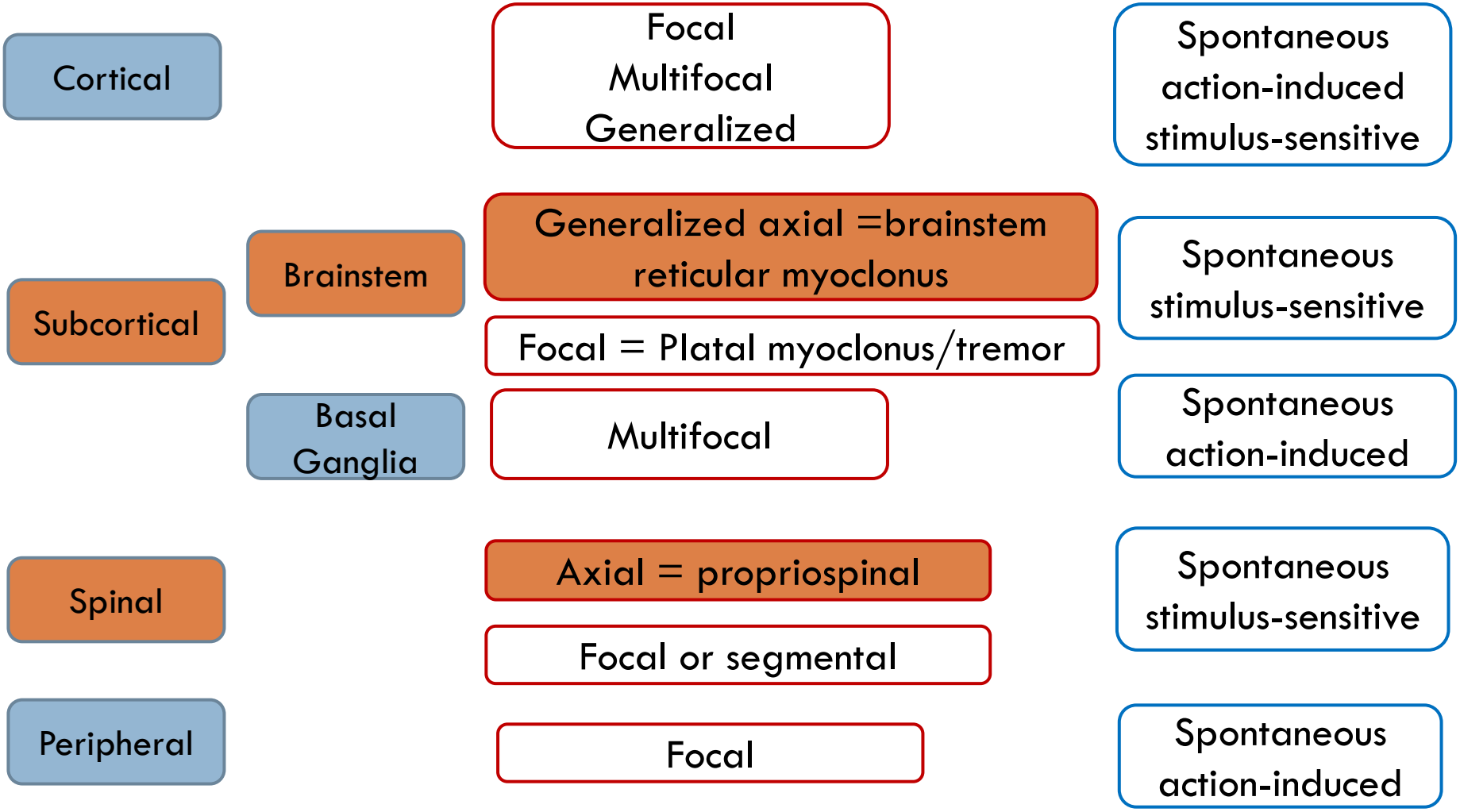
Axial myoclonus Anatomical Source



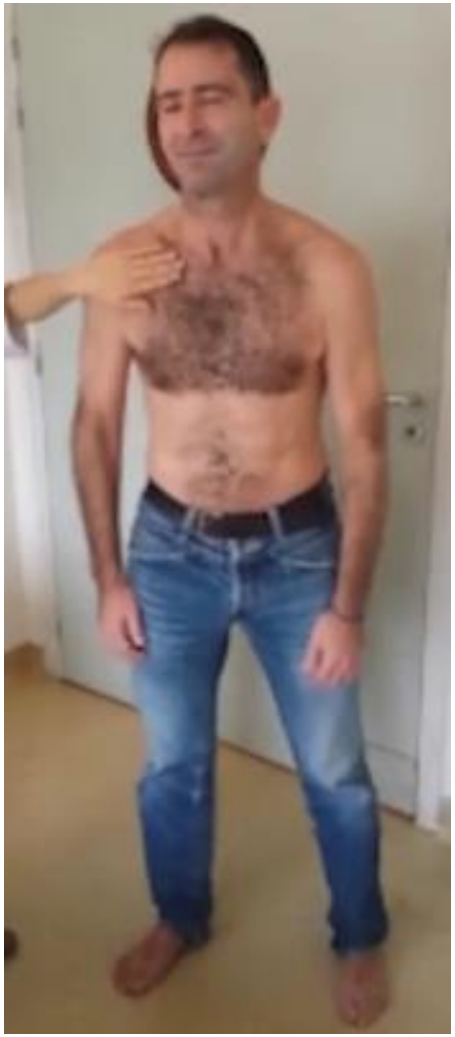
Brainstem Reticular myoclonus

- Sensistivity to auditory stimuli

- Two types :

Exaggerated Startle/Hyperekplexia:
Evoked by noise, light or sensory stimuli to the mantle area
Spontaneous jerks not prominent

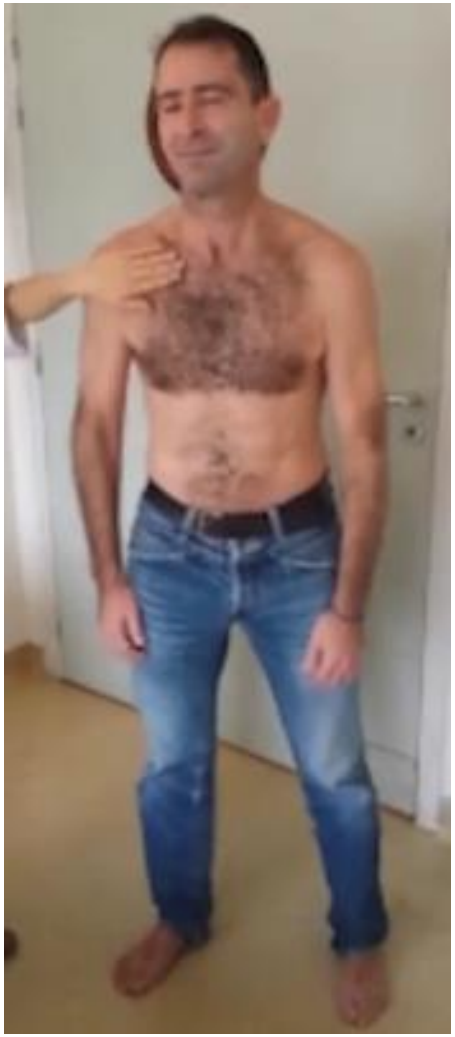
Reticular reflex myoclonus
Sensitivity is greater over the limbs
Spontaneous jerks are common



Brainstem Reticular myoclonus

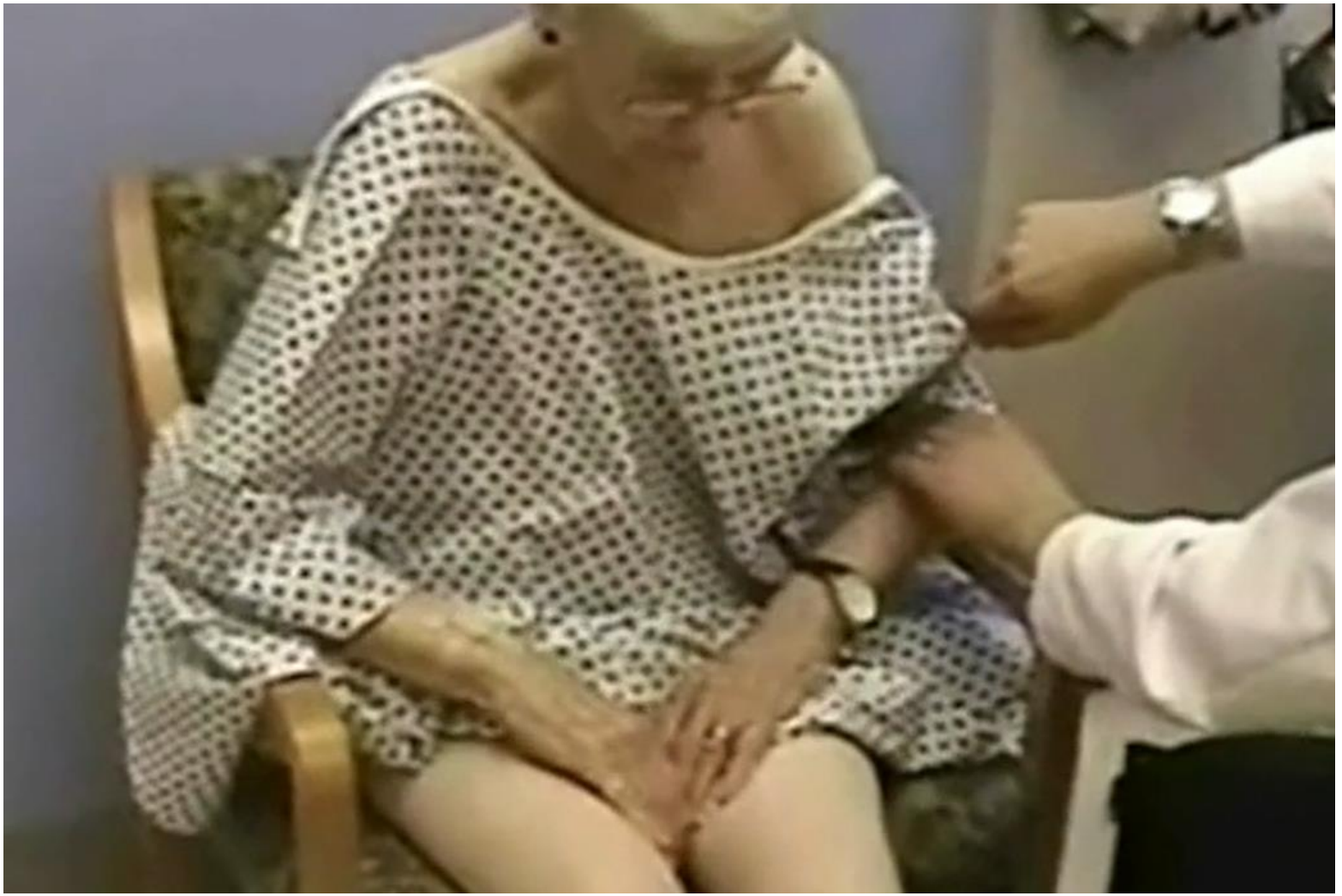
Exaggerated Startle/Hyperekplexia

c896 G > A mutation *in GLRA1*

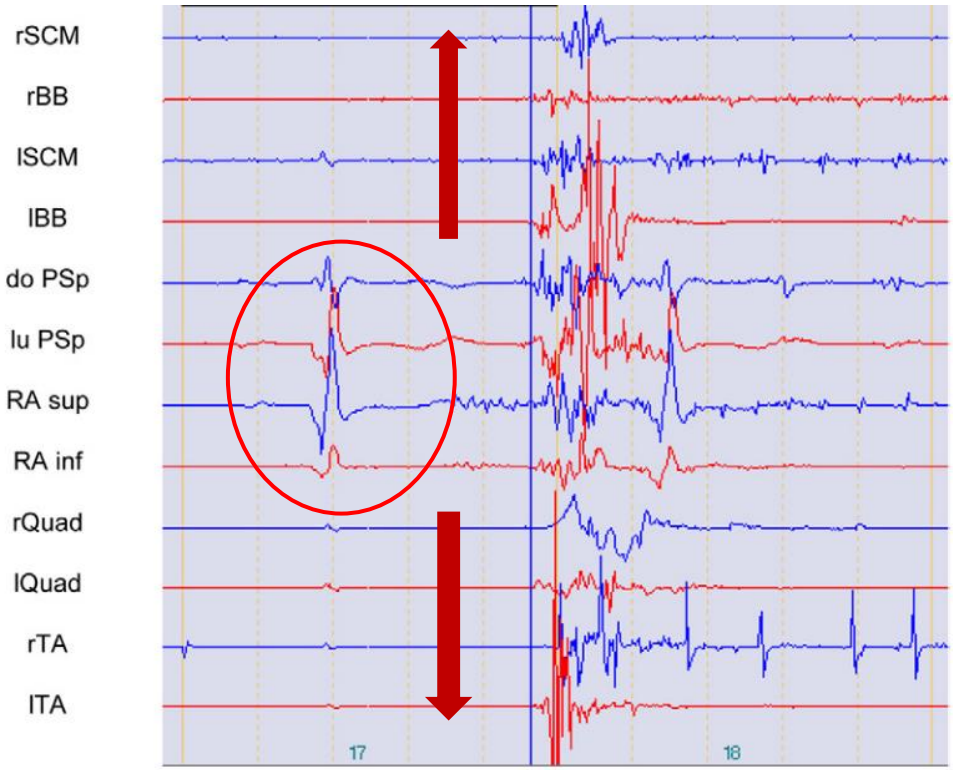


Mariani et al, 2017

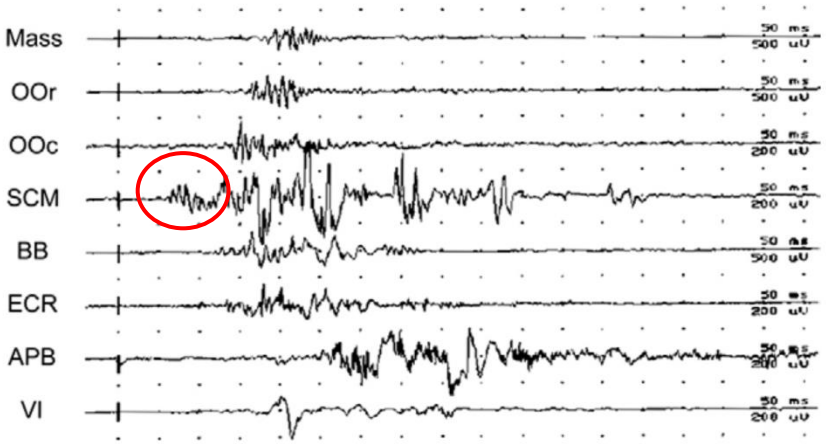
Propriospinal myoclonus



Polymyograph recordings



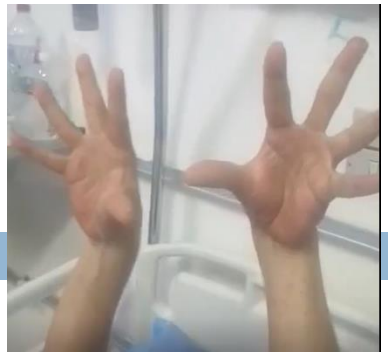
Propriospinal myoclonus



Brainstem reticular myoclonus

47-year-old, Chronic alcoholism

Myoclonus



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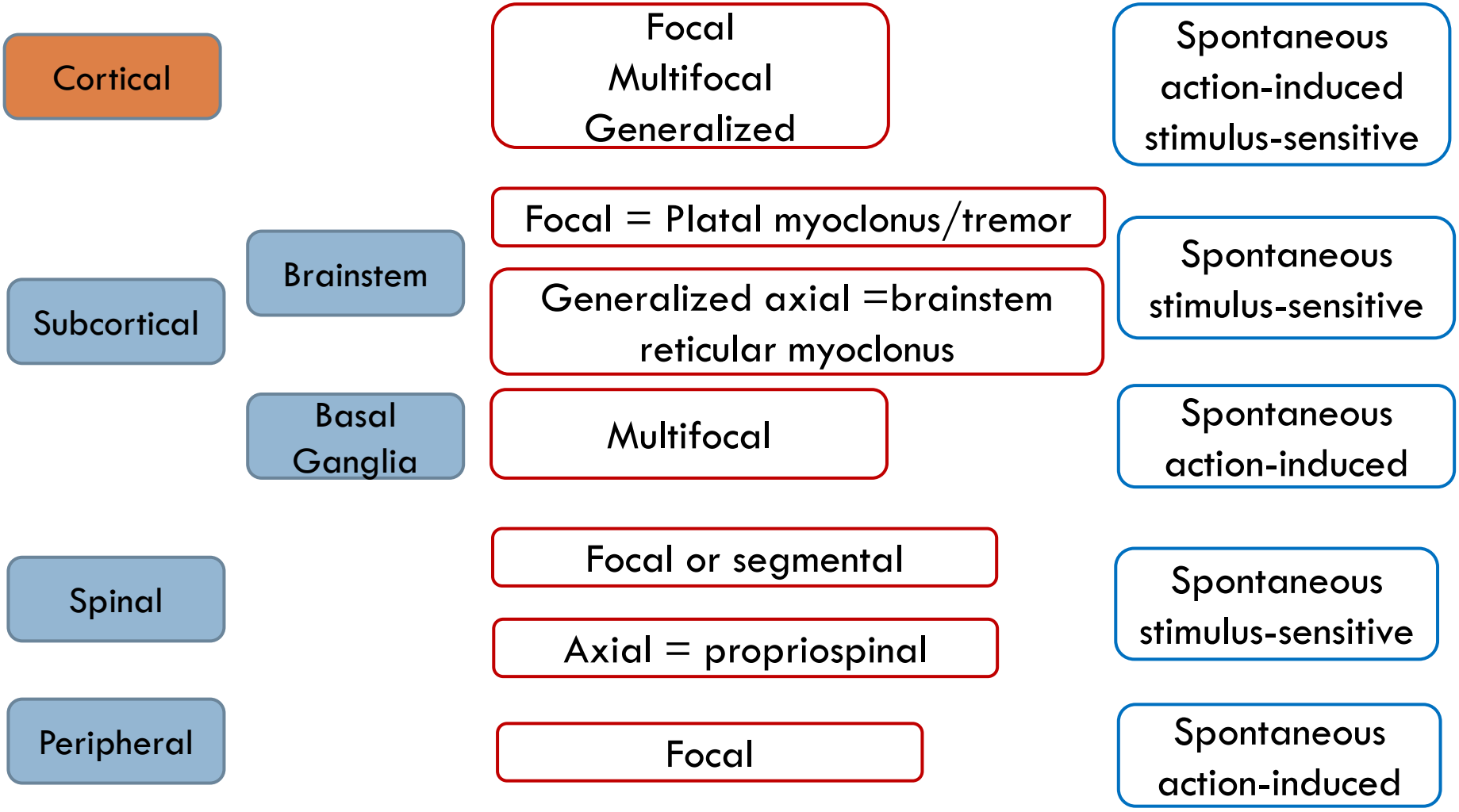
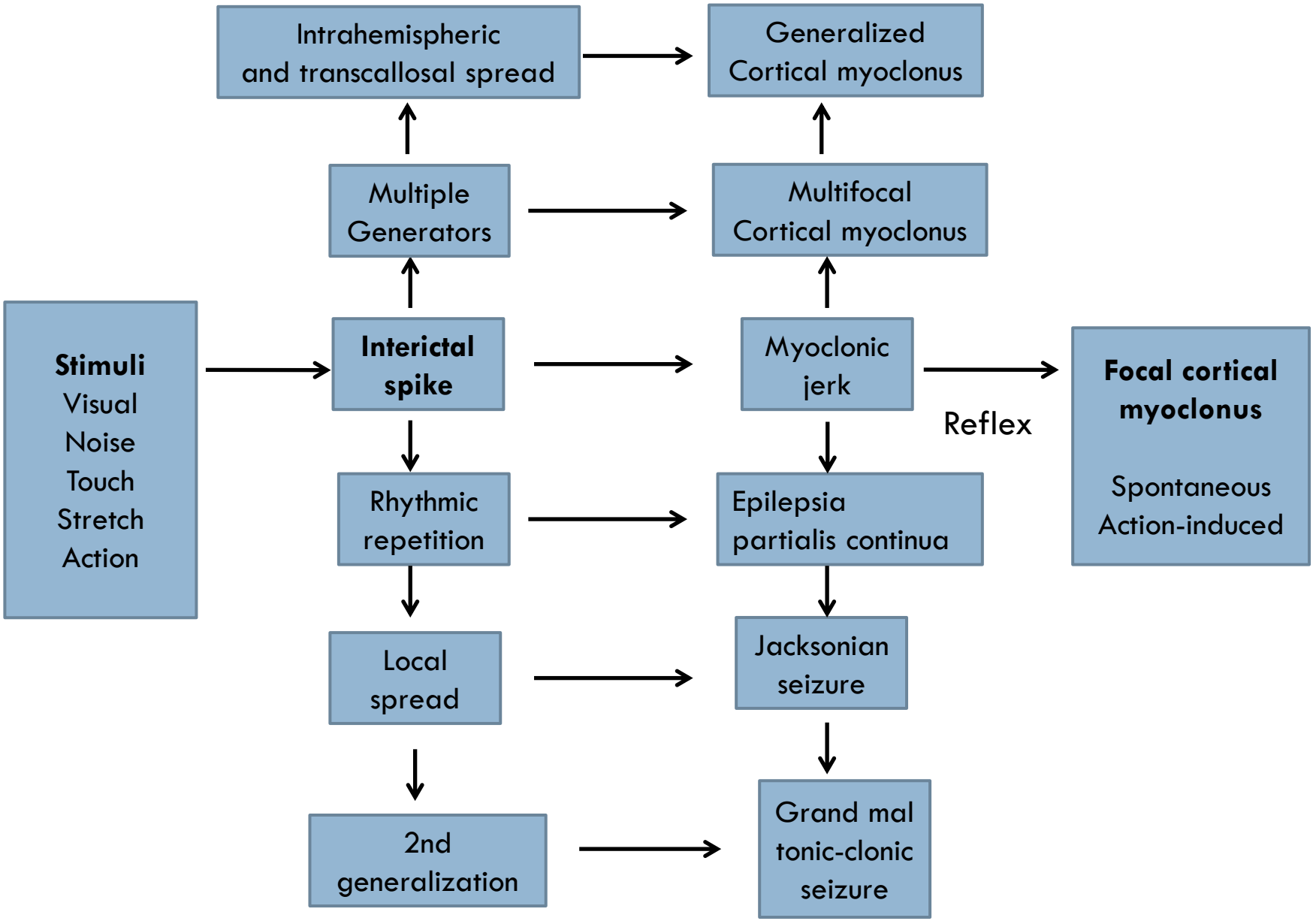
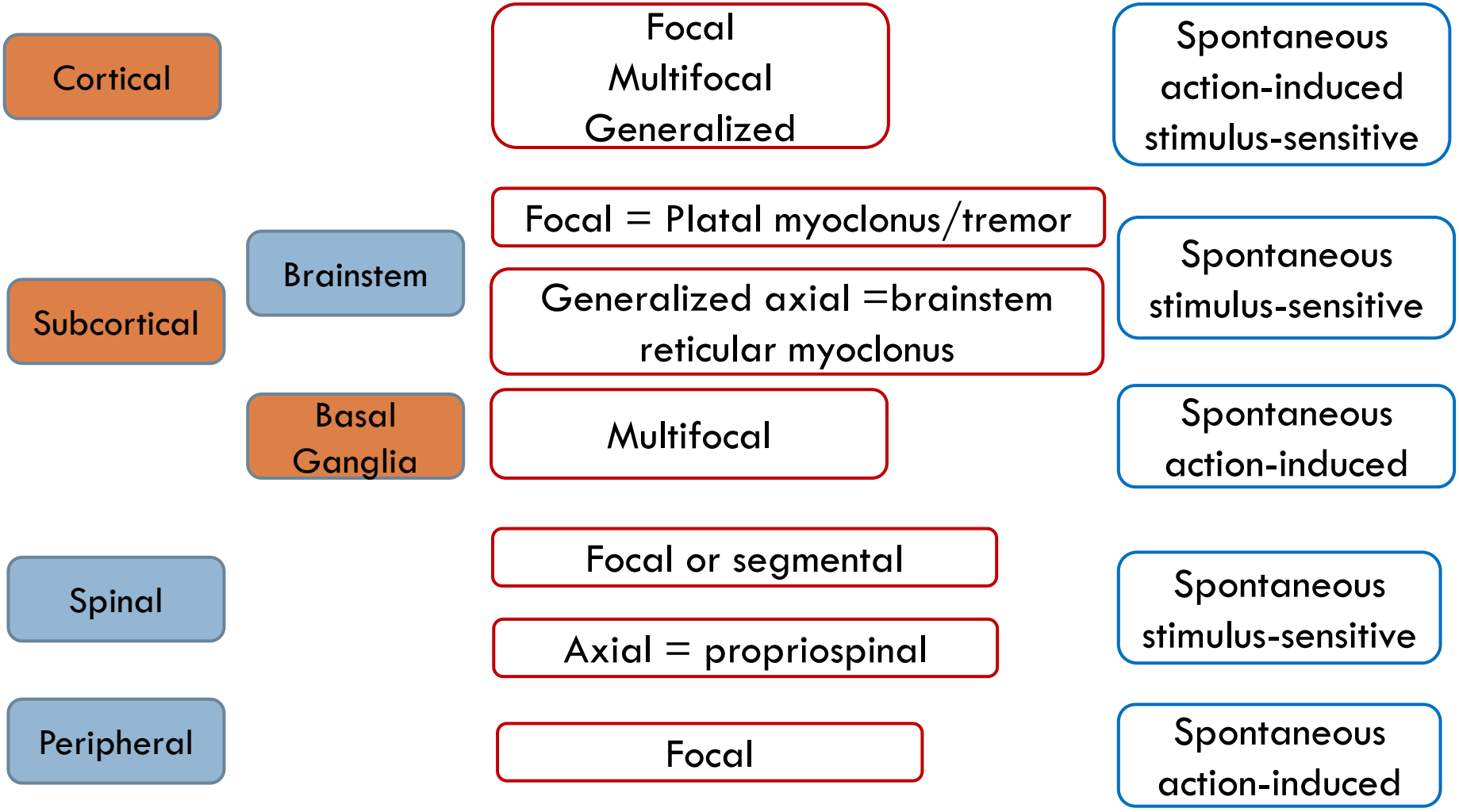
Multifocal Myoclonus



Multifocal and generalized cortical myoclonus



Multifocal Myoclonus



Multifocal and generalized myoclonus

Anatomical substrate	Etiology	
Cortical	Degenerative cortical disorders	Creutzfeldt-Jacob disease
		Dementia with Lewy bodies
		Corticobasal degeneration
		Alzheimer's disease
		Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)
	Infectious	Subacute sclerosing panencephalitis
		Herpes simplex encephalitis
		Whipple disease
		Postinfectious encephalitis
	Epileptic syndromes	Familial cortical myoclonic tremor with epilepsy
		Epilepsia partialis continua
	Focal CNS damage	Post-stroke
		Neoplasia
		Post-traumatic
Cortical-Subcortical	Degenerative basal ganglia disorders	Progressive supranuclear palsy
		Parkinson's disease
		Huntington's disease
		Neurodegeneration with brain iron accumulation type 1
		Corticobasal degeneration
		Multiple system atrophy
		SCA 2, SCA14, SCA19, SCA24
		Wilson's disease
		Dentatorubro-pallidoluysian atrophy
	Epileptic syndromes	Juvenile myoclonic epilepsies
		Childhood absence epilepsy
		Progressive myoclonic encephalopathies
		Angelman syndrome
		Myoclonic epilepsy with ragged-red fibers (MERRF)
	Metabolic	Post-hypoxic myoclonus (Lance-Adams syndrome)
		Hepatic/renal failure
		Dialysis syndrome
		Hyponatremia
		Hypoglycemia
		Biotin deficiency
		Celiac disease
		Hashimoto encephalopathy
Subcortical	Basal ganglia disorders	Myoclonus-dystonia syndrome
	Toxic	Bismuth
		Heavy metal poisons
		Methyl bromide
		Dichlorodiphenyltrichoroethane (DDT)
	Medication induced	See Table 2
	Autoimmune	Opsoclonus-myoclonus-ataxia syndrome

Levy et al, 2016

Multifocal and generalized myoclonus
Metabolic causes

Routine laboratory tests
Electrolytes, glucose, renal and hepatic function tests, thyroid function, vitamin E, infection parameters

Metabolic

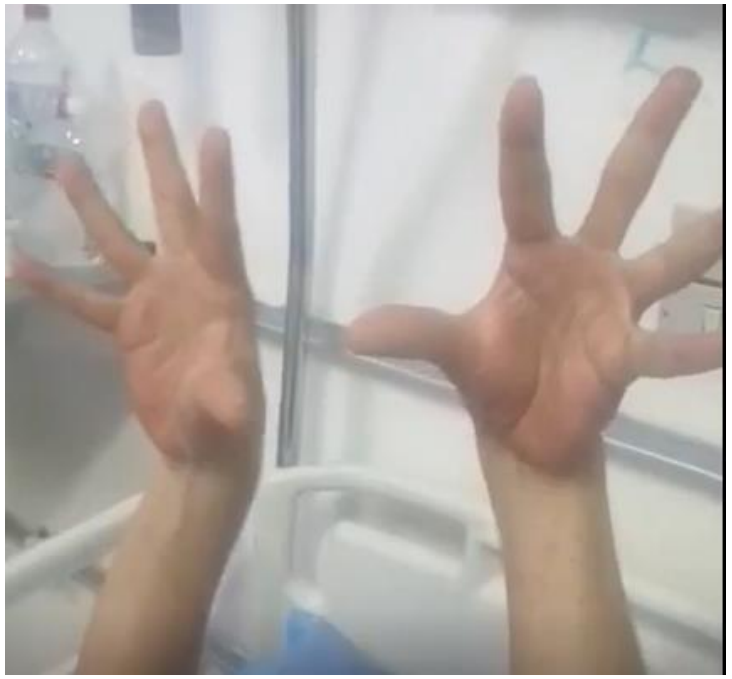
Hyperthyroidism
Hepatic failure
Renal failure
Dialysis syndrome
Hyponatraemia
Hypocalcaemia
Hypomagnesaemia
Hypoglycemia
Non-ketotic hyperglycemia
Biotin deficiency
Mitochondrial dysfunction
Hypoxia
Metabolic alkalosis
Vitamin E deficiency

47-year-old, Chronic alcoholism

Biological tests

- Blood count: platelets: 84*10^3 /UI (thrombocytopenia),
- TCA:29/27, prothrombin : 53%
- C Reactive Protein: 1mg/l
- ASAT/ALAT: 28/20
- Cholesterol:4.2 mmol/l
- Total bilirubin : 18
- Blood glucose: 7.58 mmol/l
- Ammonia: 270

(nl: 10 à 60 micromol/l)



Abdominal ultrasound

Hepato-splenomegaly

Hepatic Encephalopathy

Myoclonus Induced by Ciprofloxacin

Van Samkar et al, 2017

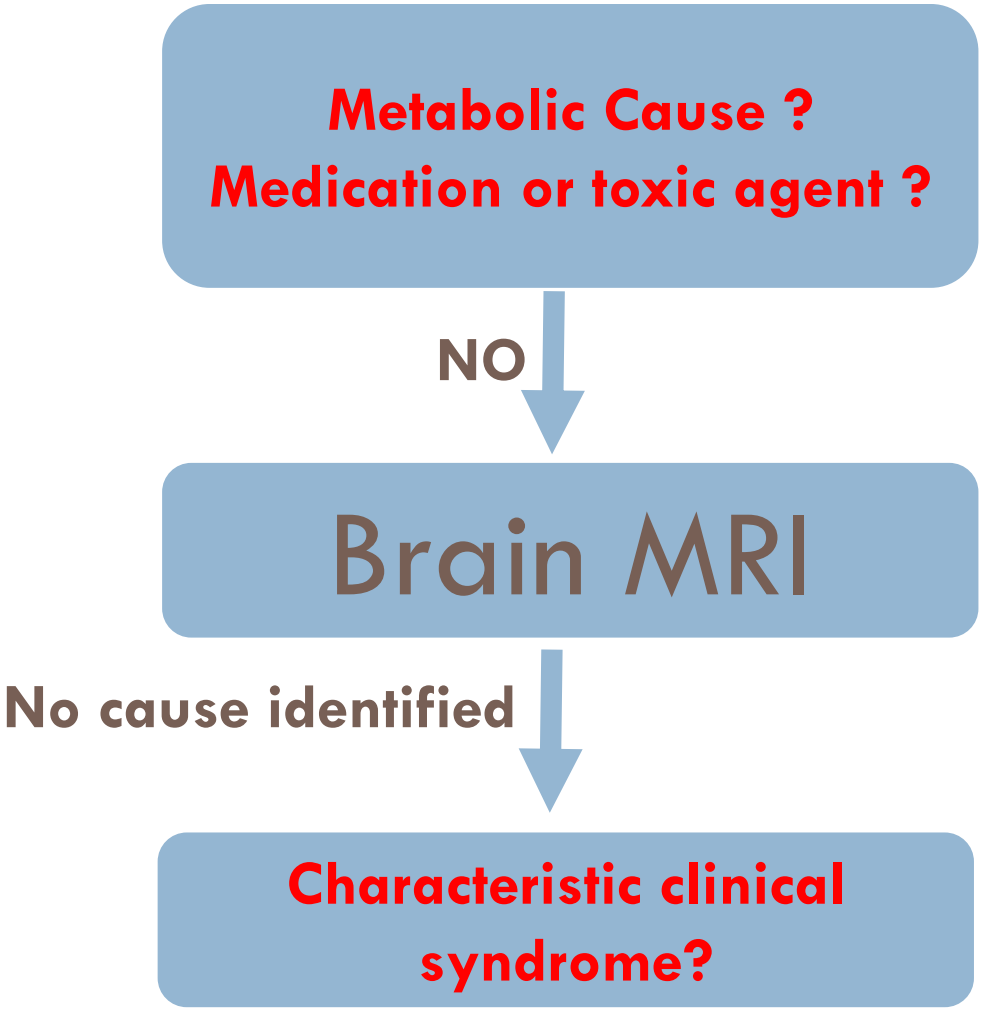
Medication and Toxin-induced Myoclonus

Medication and Toxin-Induced Myoclonus

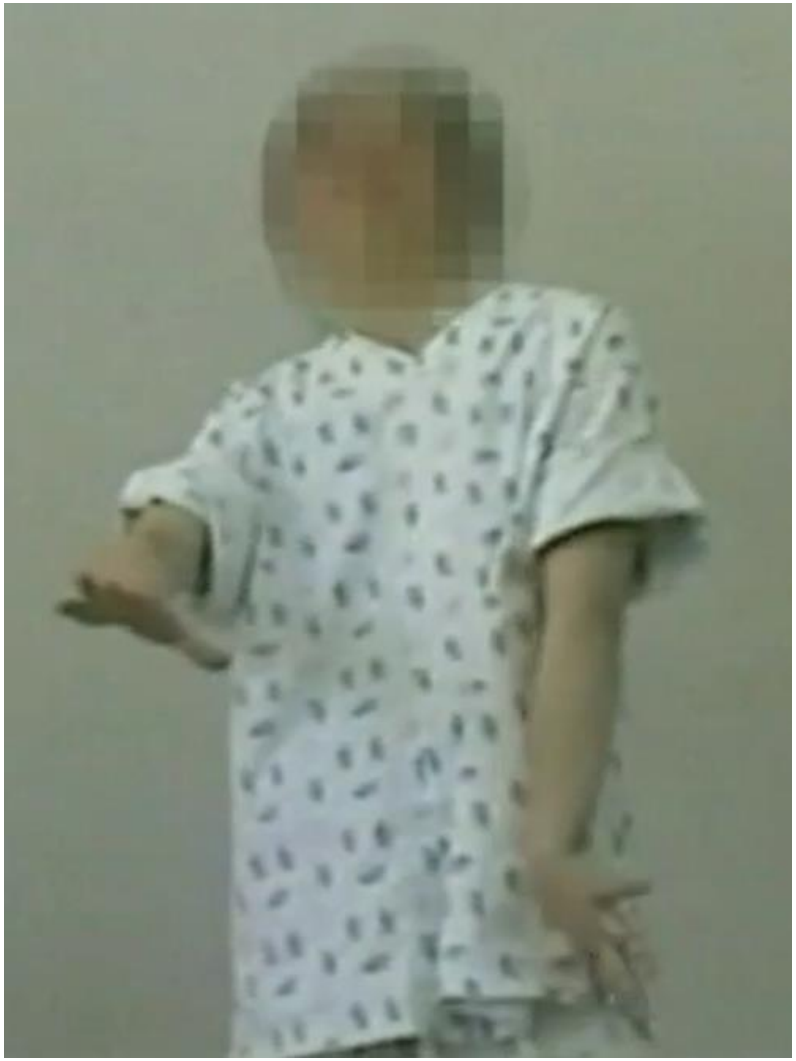
- **Medications**
  - Psychiatric
    - Tricyclic antidepressants
    - Selective serotonin reuptake inhibitors
    - Monoamine oxidase inhibitors
    - Lithium
  - Antibiotics
    - Penicillins
    - Cephalosporins
    - Quinolones
  - Narcotics
  - Antiepileptics
  - Anesthetics
  - Antiarrythmics
- **Toxins**
  - Bismuth
  - Heavy metals
    - Lead
    - Mercury
  - Methyl bromide
  - Dichlorodiphenyltrichloroethane

Frucht et al, 2015

Multifocal and generalized Myoclonus



Myoclonus-dystonia (SGCE mutation)



19-year old

Father affected

Onset : 5-year old

Porgessive Disorder

Normal cognition

MRI : Normal

Lee et al, 2011

22-year-old man

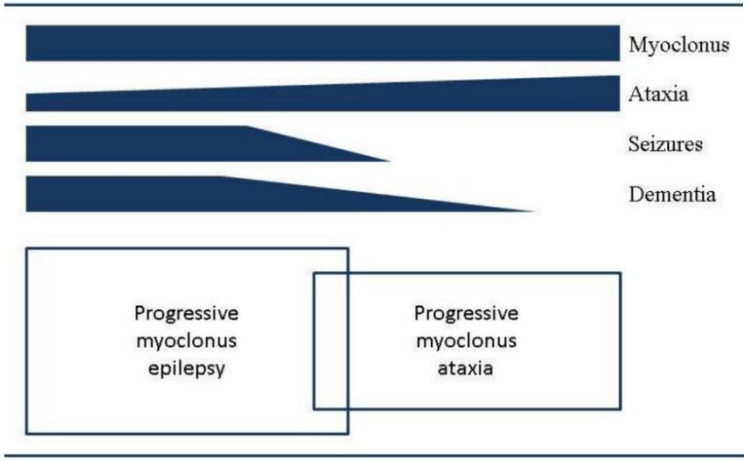
Onset : 5 years

Generalized tonic-clonic seizures
Progressive ataxia and cognitive impairement

Brain MRI: Brainstem atrophy

Barsottini et al, 2018

Progressive Myoclonic Epilepsy Type 8 Due to CERS1 Deficiency

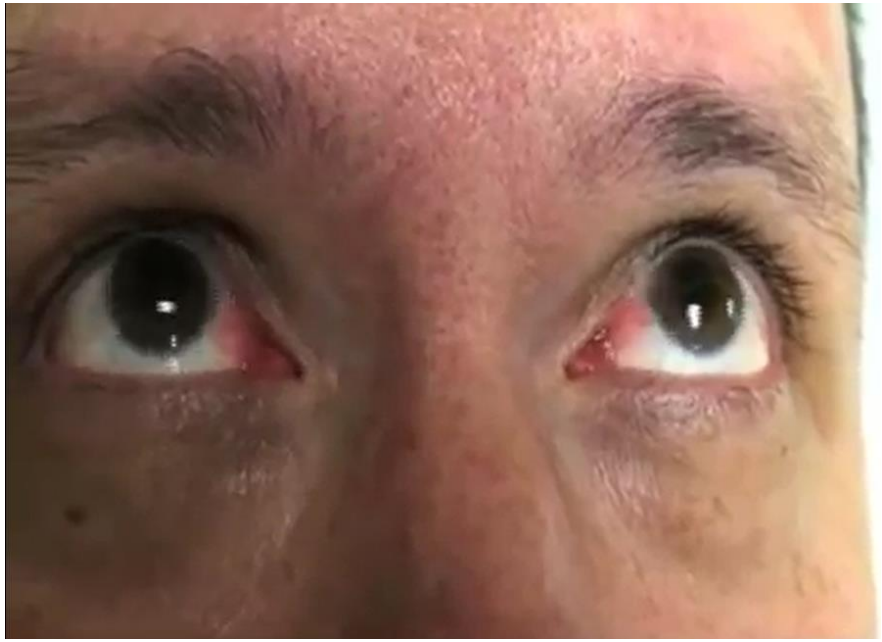


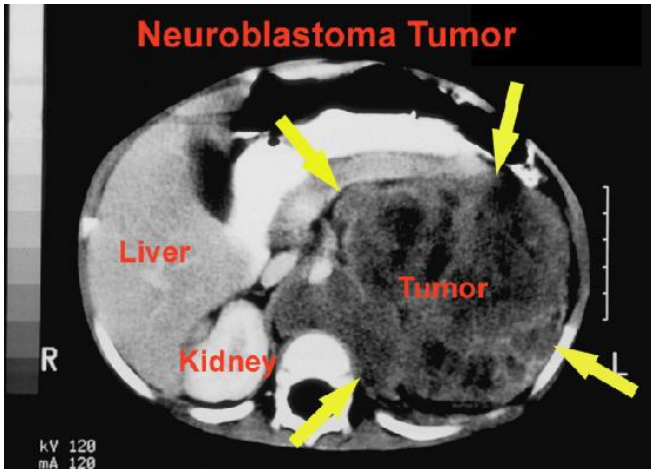
Progressive myoclonus epilepsies.

Entity	MIM	Phenotype	Gene	Inheritance
Myoclonic Epilepsy of Unverricht and Lundborg	254800	PME type 1A	CSTB	AR
Myoclonic Epilepsy of Lafora	254780	PME type 2A	EPM2A	AR
		PME type 2B	NHLRC1	AR
Action Myoclonus-Renal Failure Syndrome (AMRF)	254900	PME type 4	SCARB2	AR
North Sea PME	614018	PME type 6	GOSR2	AR
Myoclonus epilepsy and ataxia due to potassium channel mutation (MEAK)	616187	PME type 7	KCNC1	AR
PME type 8	616230	PME type 8	CERS1	AR
PME type 10	616640	PME type 10	PRDM8	AR
Neuronal Ceroid-Lipofuscinoses (NCL)	256730	NCL type 1	PPT1	AR
	204500	NCL type 2	TPP1	AR
	204200	NCL type 3	CLN3	AR
	256731	NCL type 5	CLN5	AR
	601780	NCL type 6	CLN6	AR
	610951	NCL type 7	MFSD8	AR
	600143	NCL type 8	CLN8	AR
	610127	NCL type 10	CTSD	AR
	162350	NCL type 4B	DNAJC5	AD
	611726	PME type 3	KCTD7	AR
Neuraminidase Deficiency	256550	Sialidosis, type I & II	NEU1	AR
Myoclonic Epilepsy Associated With Ragged-Red Fibers (MERRF)	545000	MERRF	MT-TK	Maternal
Spinal Muscular Atrophy With Progressive Myoclonic Epilepsy (SMAPME)	159950	SMAPME	ASAH1	AR
PME type 1B	612437	PME type 1B	PRICKLE1	AR/AD
Gaucher disease	230800	–	GBA	AR
PME type 9	616540	PME type 9	LMNB2	AR
Juvenile Huntington disease	143100	Juvenile Huntington disease	HTT	AD
Newly identified PME-associated diseases/genes				
Gerstmann-Straussler-Scheinker disease	137440	–	PRNP	AD
–	–	Childhood-onset progressive myoclonic epilepsy	SERPINI1	AD
Lipodystrophy, Congenital Generalized, Type 2 (CGL2)	269,700	–	BSCL2	AR

Barsottini et al, 2018

Opsoclonus myoclonus





Klass et al, 2012

Post-hypoxic myoclonus = Lance Adams

Ramdhani et al, 2017

Myclonus Treatment

- Etiopathogenic
- Symptomatic

Cortical myoclonus treatment

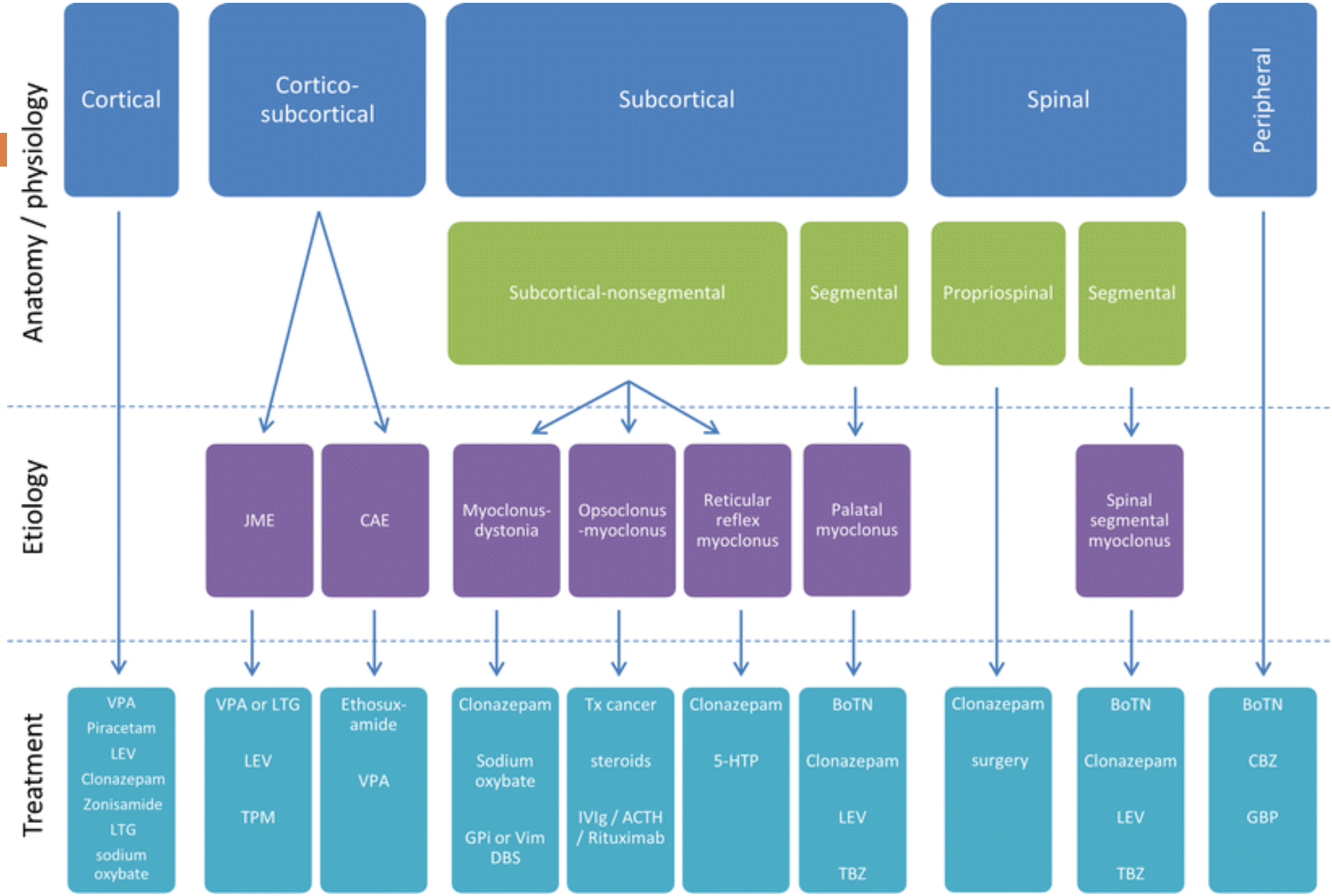
- Aim to enhance deficient GABAergic inhibitory neurotransmission
- Polytherapy often needed/ initial low dosages with a slow increase advised

- Sodium valproate (max 2000 mg/d)

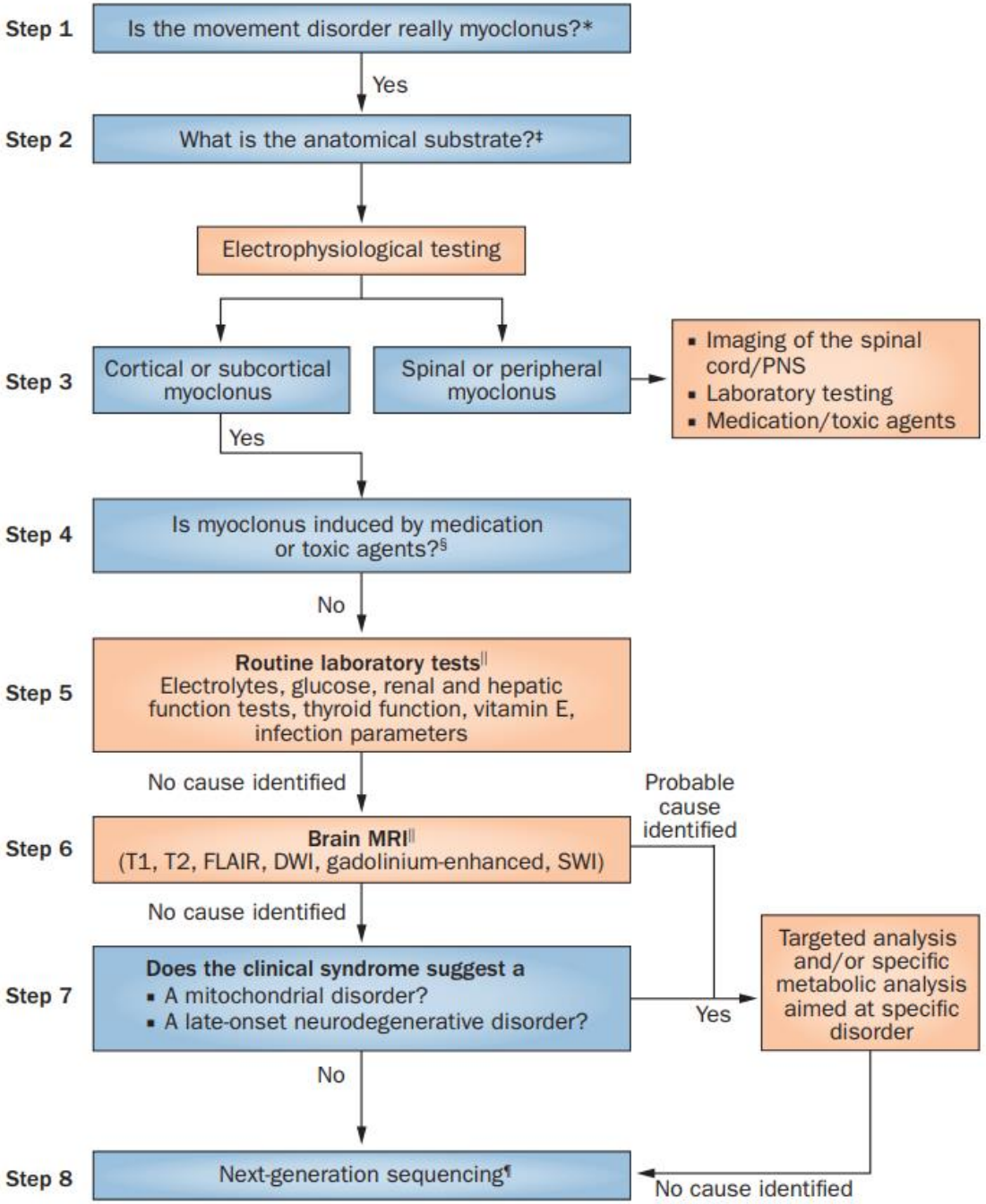
  Piracetam (max 24g/d)/ levetiracetam (max 3000mg/d)

  Clonazepam (max 15 mg/d)
- PME : Zonisamide

- Phenytoin, carbamazepine and vigabatrin should be avoided



Mills et al, 2015



Zutt et al, 2015

Thank you