How clinical neurophysiology helps clinician in movement disorders

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Clinical Neurophysiology in Movement Disorders

- *Objective movements measurement*
  - Understand characteristic of movements
    - Application for differentiation phenomenology of movements
    - Application for differentiation etiology of movements
- Localization generator of movements
  - Implication for proper investigation and treatment

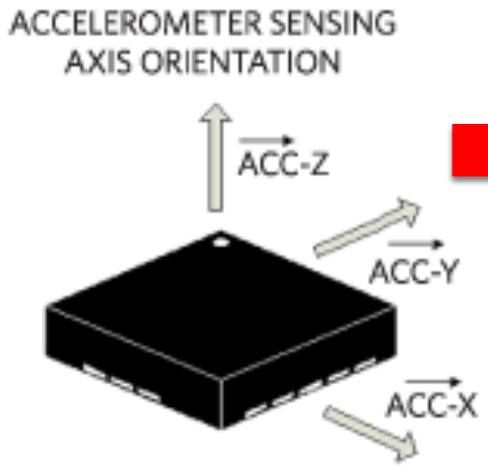
Hallett M, Aminoff's Electrodiagnosis in Clinical Neurology 2012
Apartis E. Handbook of Clinical Neurology 2013

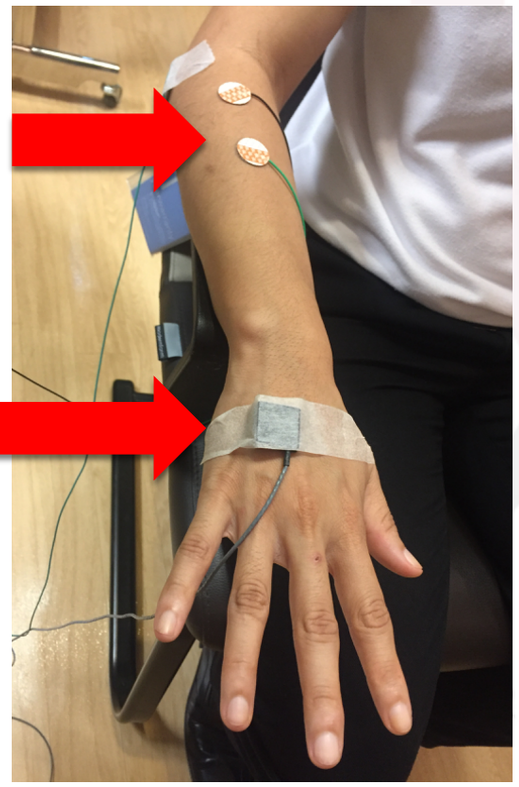
Measurement of movement
"Character of movement"

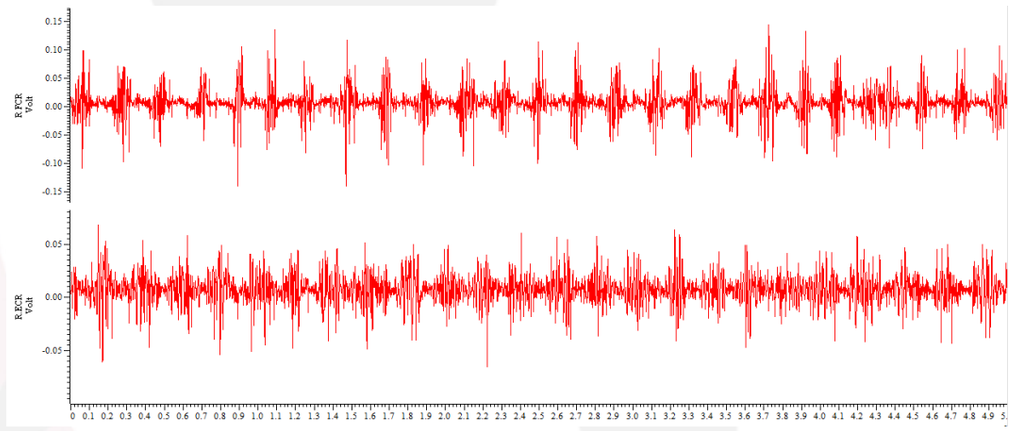
- Surface EMG : direct measure movement from muscle, record from at least 2 muscles with antagonist actions.

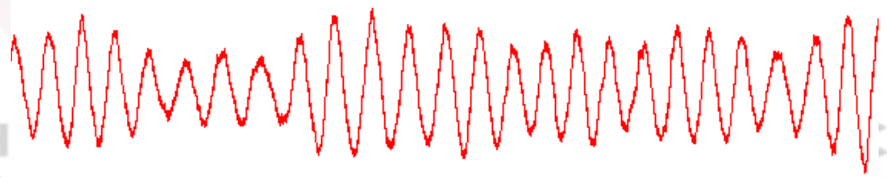
- Accelerometer : measure movement acceleration

Surface EMG (bipolar)





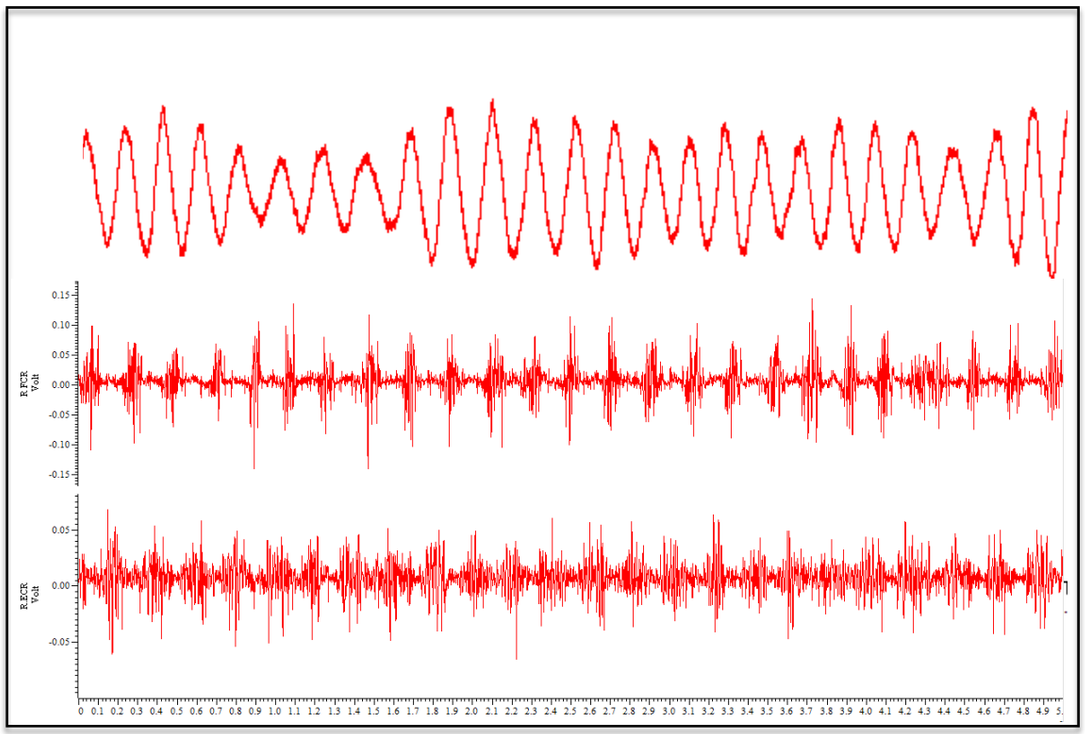




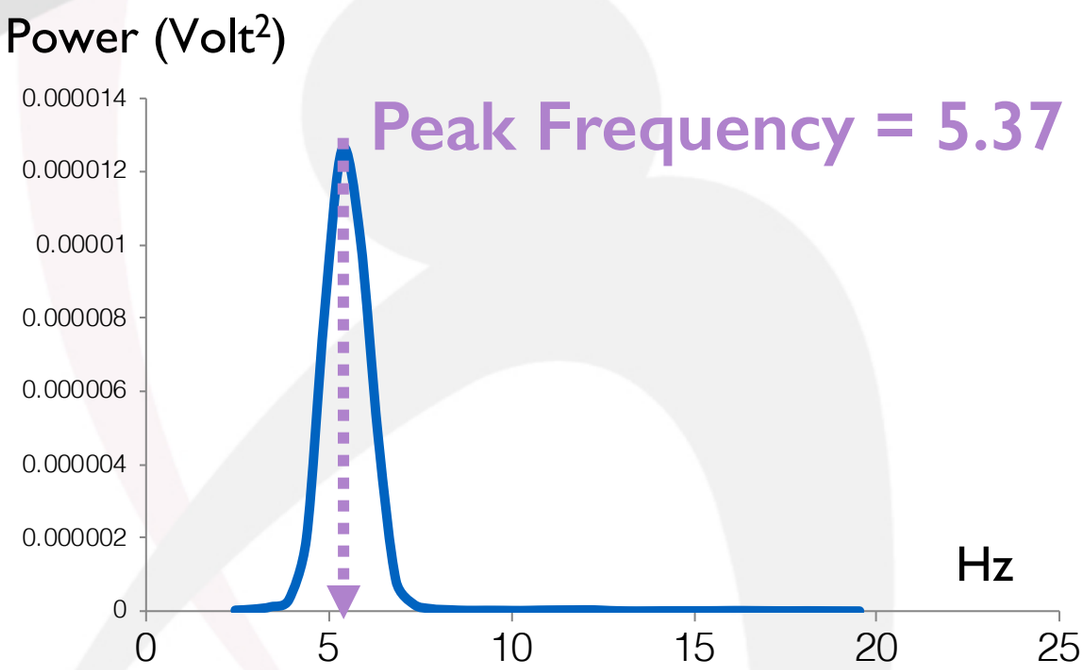
Phenomenology = tremor

Result from recording

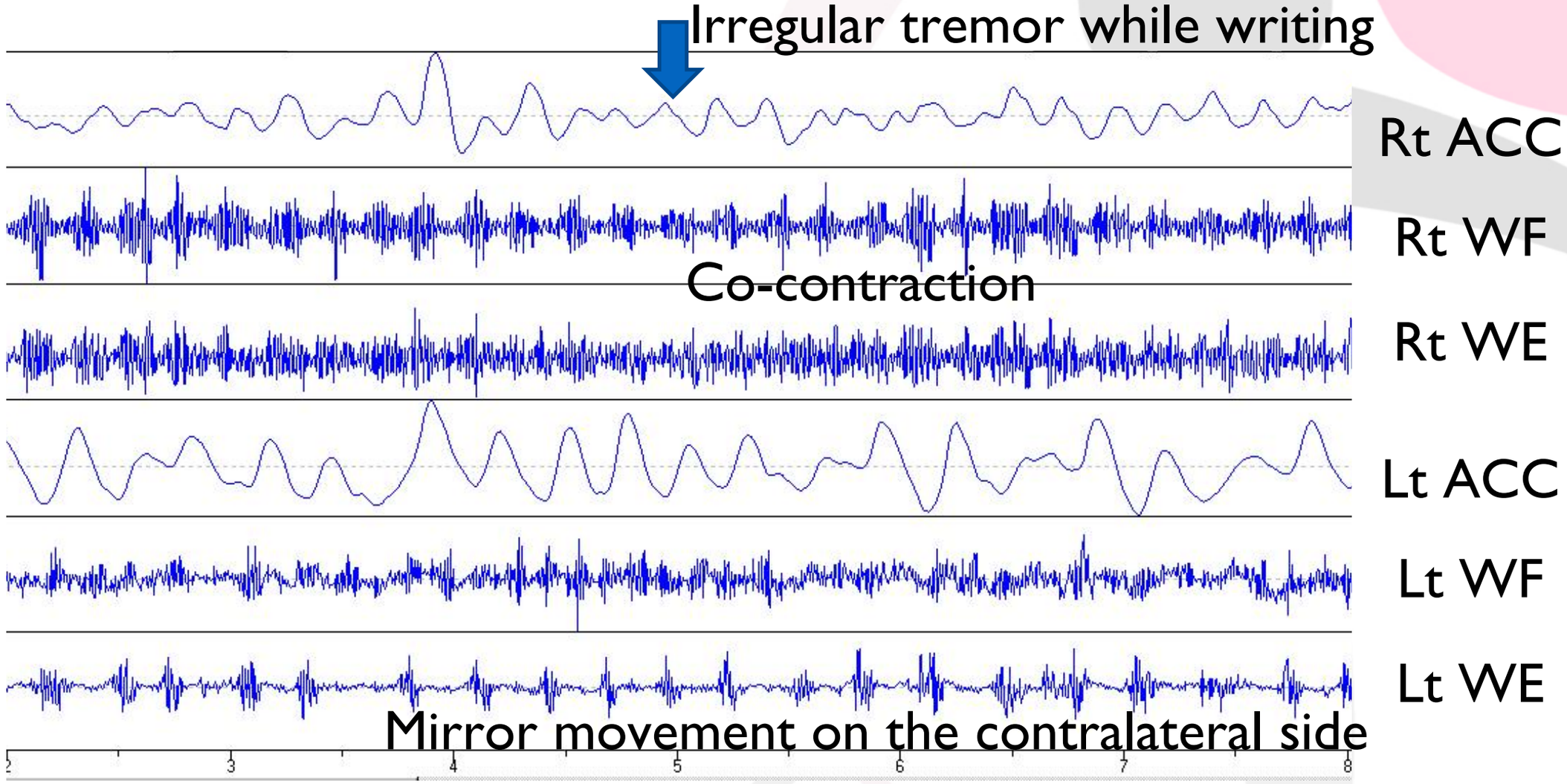
Direct signal



Frequency analysis (FFT)



Measurement of movement
"Character of movement"

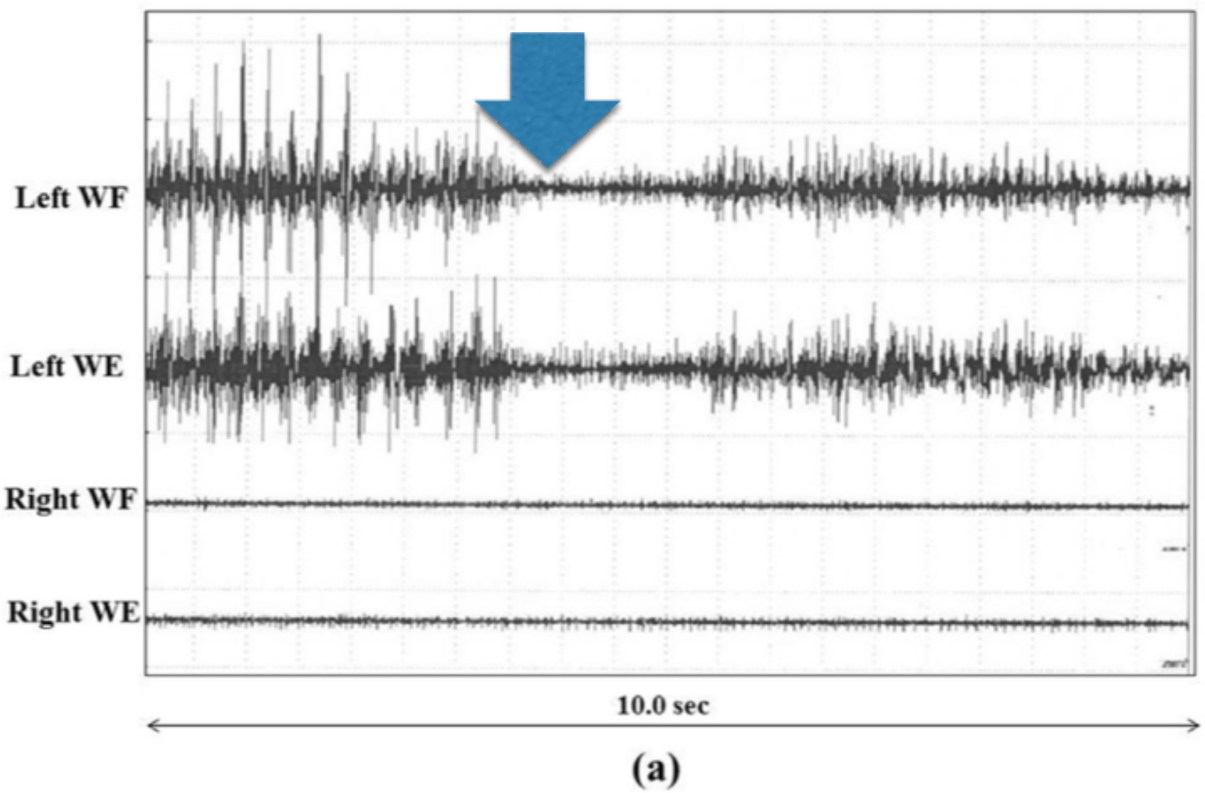


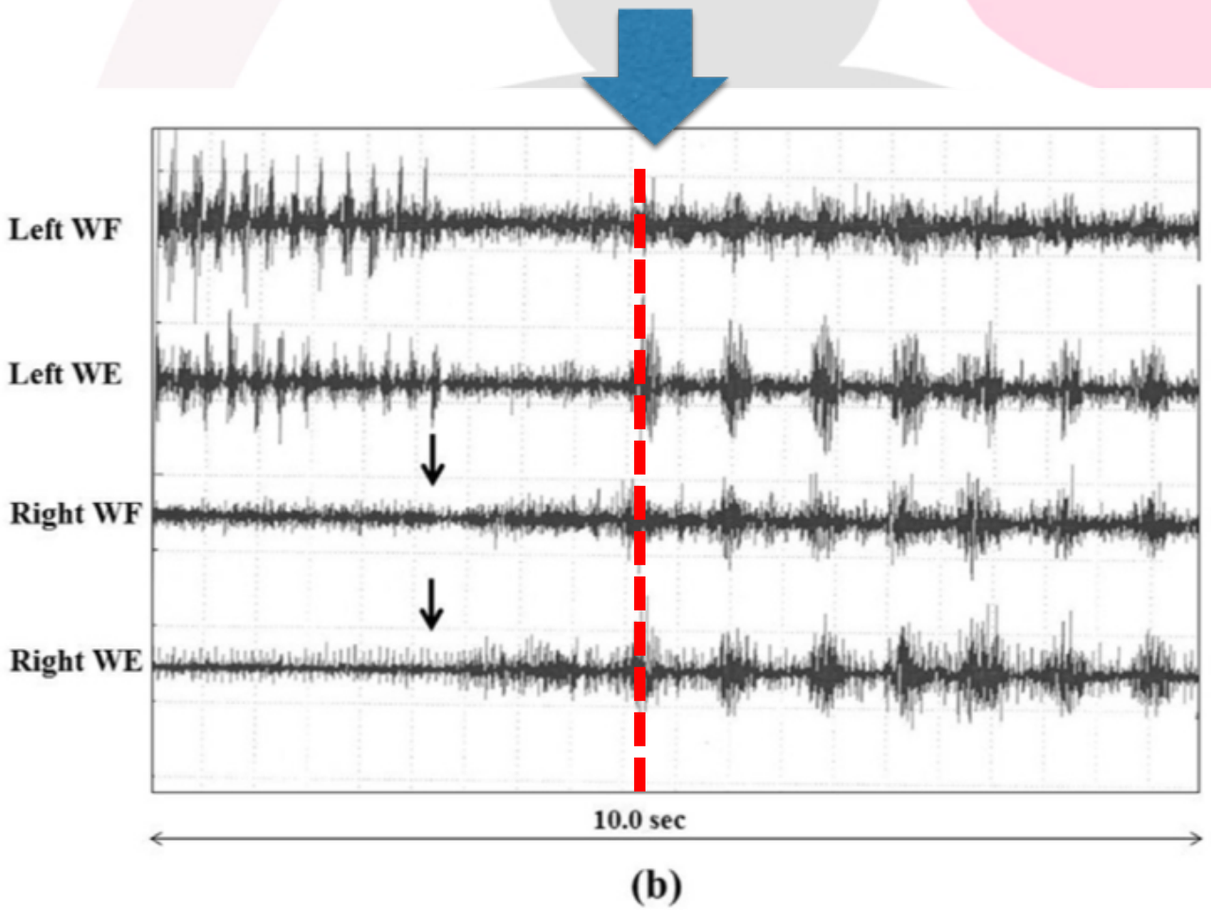
Phenomenology = tremor + dystonia

Demonstrate and locate area of movements involvement

Measurement of movement
"Character of movement"

Phenomenology = tremor





Distractibility with mental task

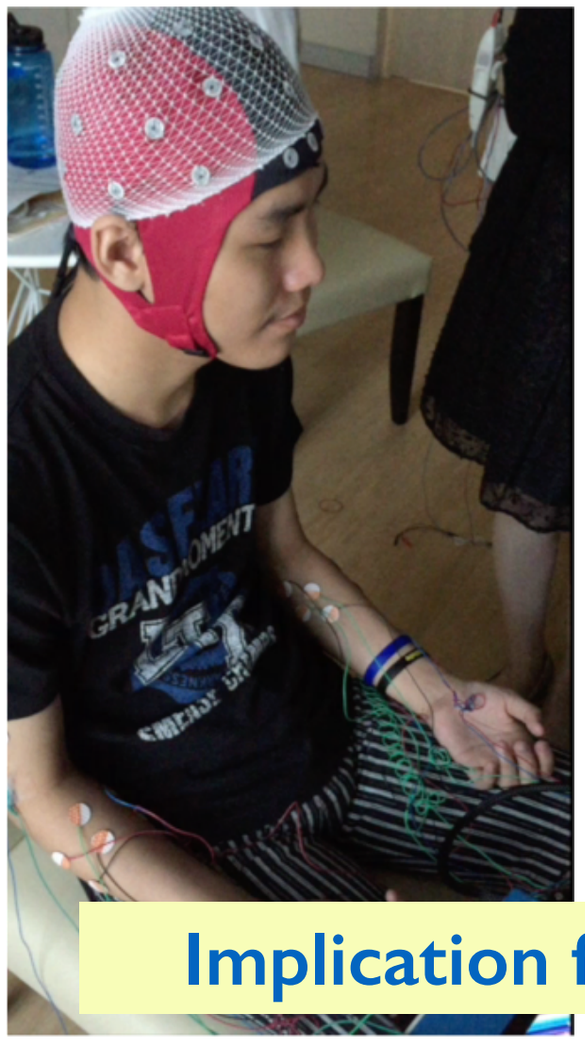
Entrainability with tapping Rt

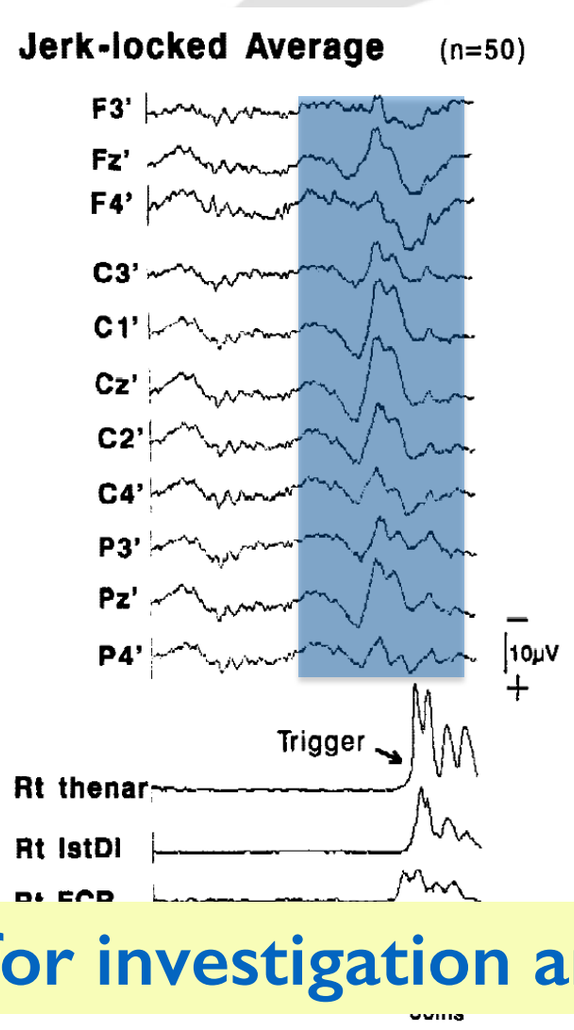
Etiology = psychogenic tremor

Kumble N.L and Pal P.K. PRD 2016

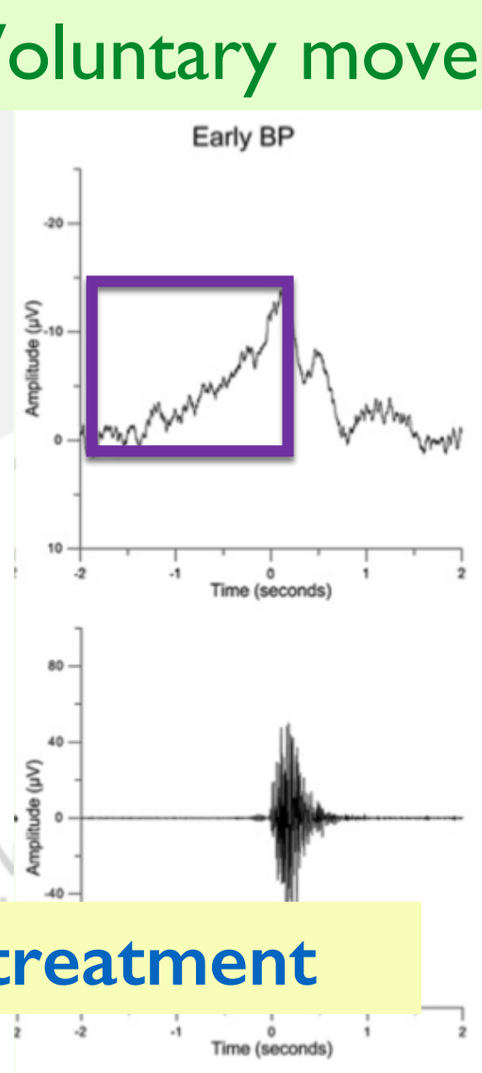
Measurement of movement "Where dose it come from?"

- EEG (simultaneous with EMG) : EEG wave before onset of movement – cortical in origins





Voluntary movement

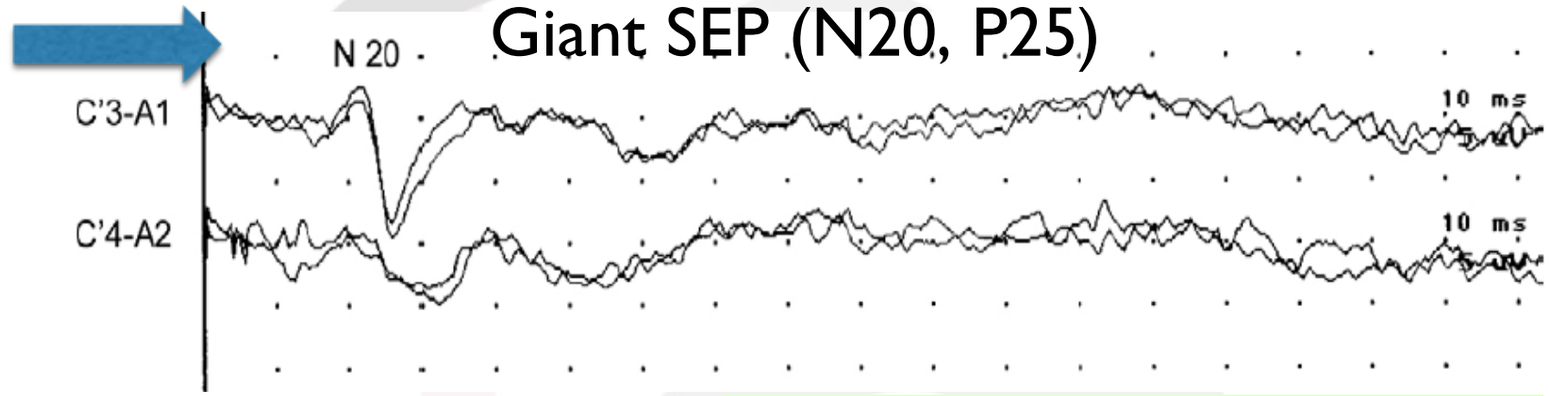


Implication for investigation and treatment

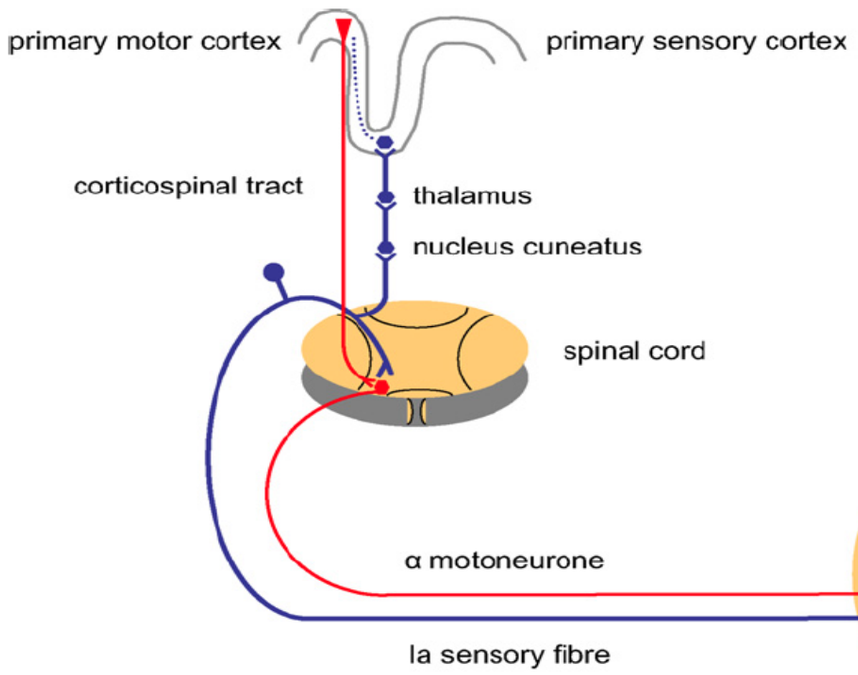
Measurement of movement "Where dose it come from?"

- Sensory evoked potential (SEP) : EEG (simultaneous with nerve stimulation without movement - cortical in origins

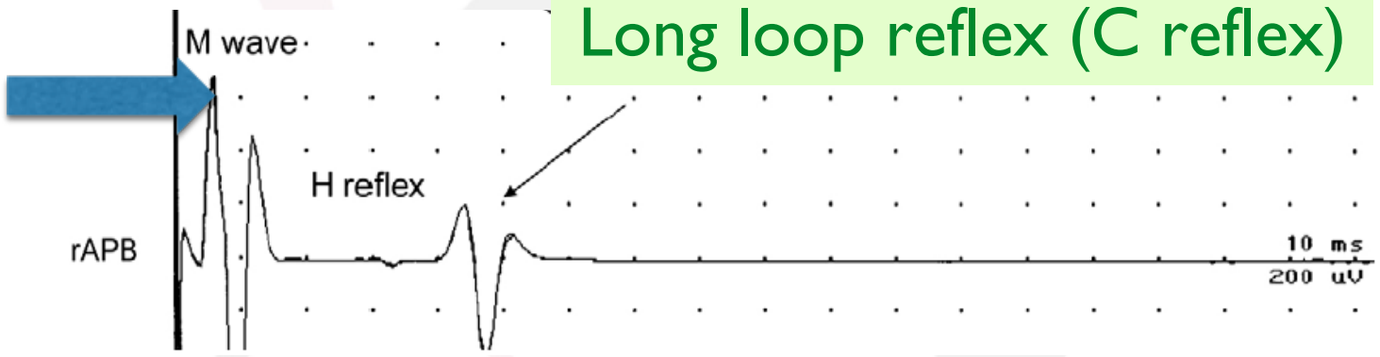
EEG - N20, P27, N33



Giant SEP (N20, P25)



EMG



Long loop reflex (C reflex)

Nerve stimulation

Implication for investigation and treatment

Applied Clinical Neurophysiology in movement Disorders

- *For diagnosis ; measure unclear movements*
  - *Useful for tremulous and jerky movements, not chorea/dystonia*
  - Differentiate phenomenology of abnormal movements
    - Jerky movement : tremor vs myoclonus (+/- vs motor tics)
    - Demonstrate and locate dystonia in jerky movement – overflow/mirror
- Localize generator of movements : Only for myoclonus – cortical ?
- Differentiate nature, etiology of abnormal movements
  - Enhanced physiologic tremor vs ET, OT, organic vs psychogenic

Hallett M, Aminoff's Electrodiagnosis in Clinical Neurology 2012
Hallett M & Rothwell J. Movement Disorders 2011

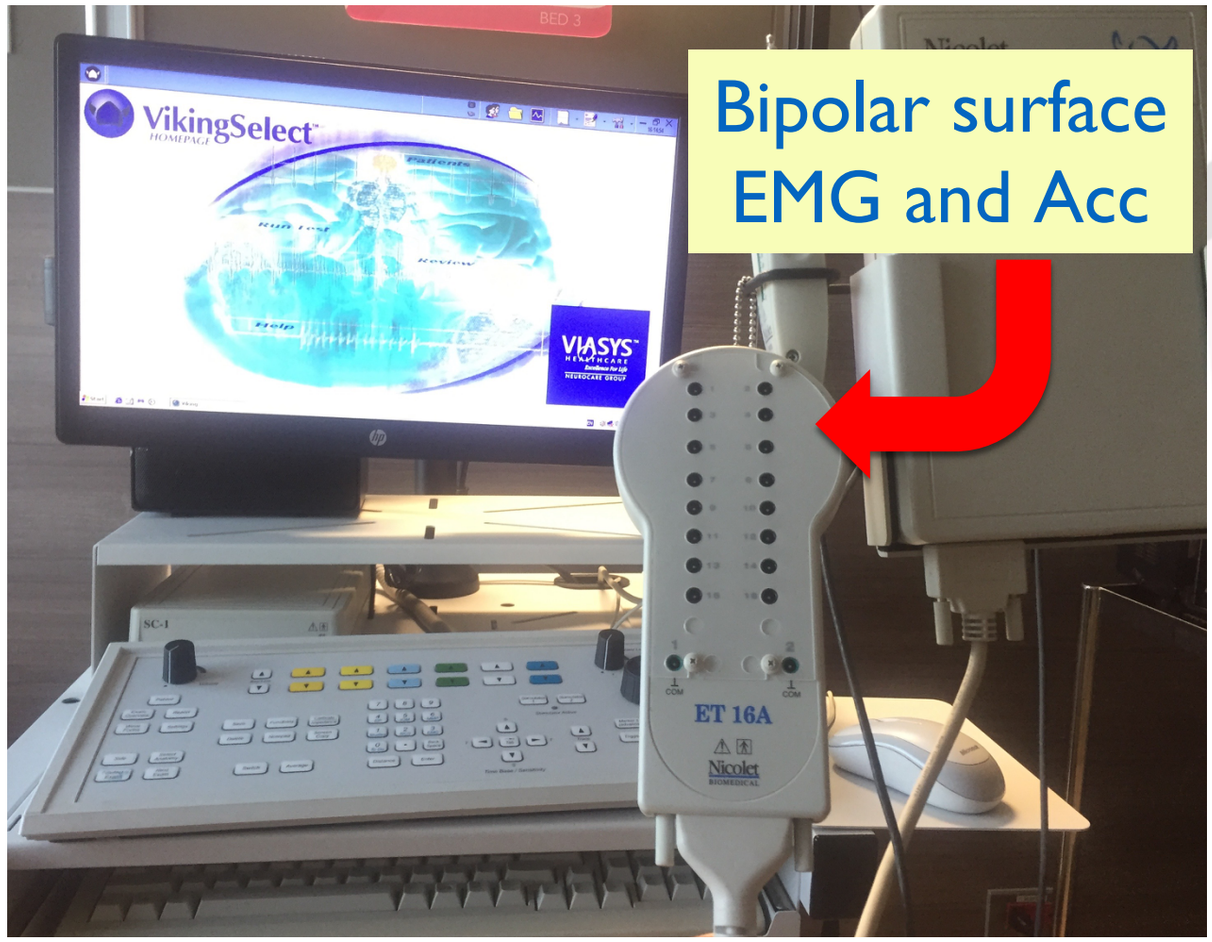
Applied Clinical Neurophysiology in movement Disorders

- *For treatment*
  - Demonstrate and locate dystonia in jerky movement – guided for BoNT injection
  - Localize generator myoclonus – select proper investigation and treatment
- *Understanding pathophysiology of movements and implication for tremor*

Hallett M, Aminoff's Electrodiagnosis in Clinical Neurology 2012
Hallett M & Rothwell J. Movement Disorders 2011

Machine

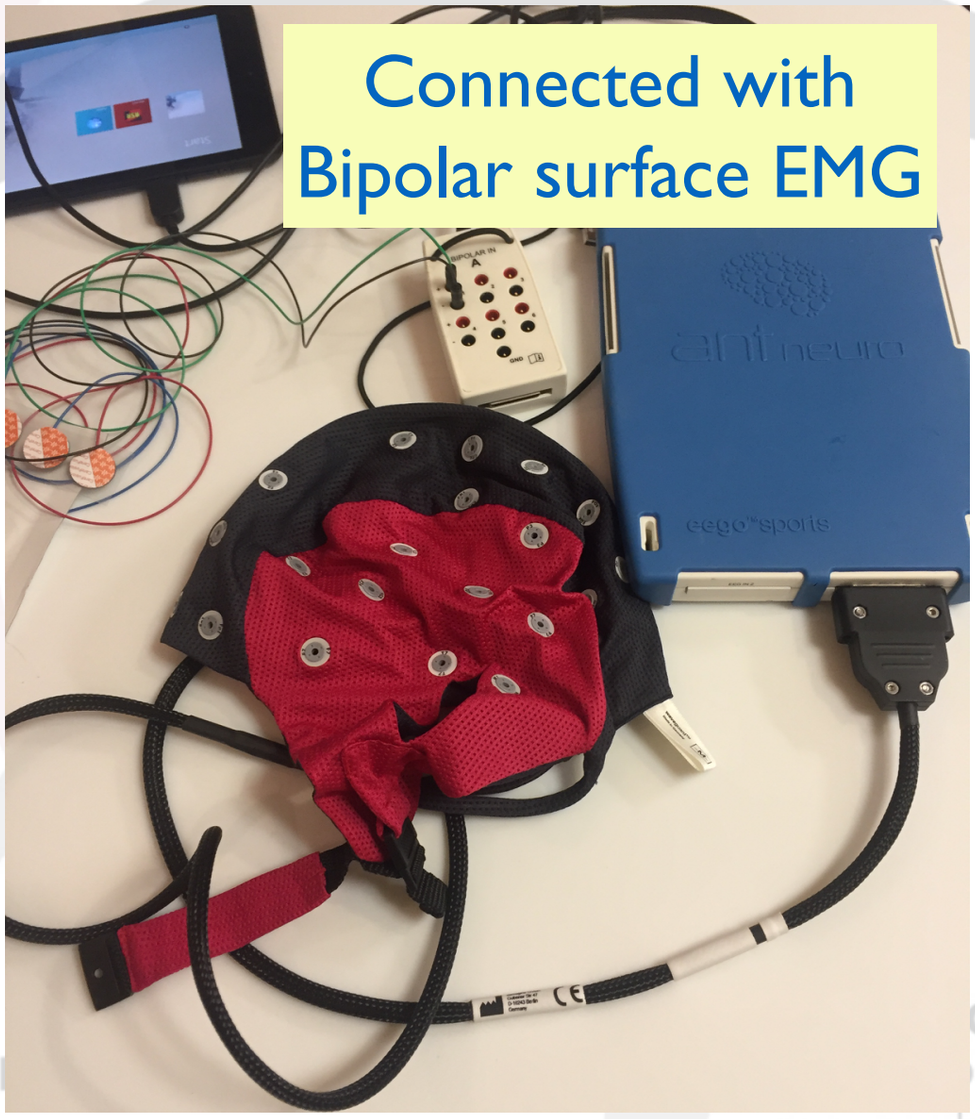
Conventional EMG machine



Bipolar surface EMG and Acc

Multi-channels EMG (at least 4)

Conventional EEG machine



Connected with Bipolar surface EMG

Band-pass filter at 20-500 Hz for EMG, 0.5-100 for ACC

Machine

Conventional EMG machine

- Tremor study
  - Define phenomenology
  - Define etiology of tremor
- Myoclonus study
  - Define phenomenology
  - Sensory Evoked Potential
  - Long loop reflex
- Locate dystonia for BoNT
- Double sensory stimulation

Conventional EEG machine

- Myoclonus study
  - Localization of myoclonus
  - Define etiology of myoclonus
- Psychogenic Movement Disorders

Diagnosis of movements

Indication for neurophysiological assessment in clinical practice

- Unclear phenomenology of movement by clinical evaluation
  - Useful for tremulous or jerky movements : confirmation of tremor, tremor vs myoclonus (+/- vs motor tics)
- Unclear etiology of movement
  - Physiologic vs essential tremor
  - Psychogenic vs organic tremor, jerks (NOT dystonia)
- Localize generator of myoclonus
- Confirmation of orthostatic tremor

Apartis E. Handbook of Clinical Neurology 2013

Clinical Evaluation
"The 2018 MDS tremor classification"

Axis 1: Clinical Features

- Historical Features
  - Age at onset
  - Temporal onset and evolution
  - PMH
  - FH
  - Alcohol and drug sensitivity
- Tremor Character
  - Distribution
  - Activation
  - Tremor frequency
- Associated signs
  - Systemic illness
  - Neurological signs
  - Soft signs
- Additional lab tests
  - Electrophysiological tests
  - Structural imaging
  - Receptor imaging
  - Serum and tissue biomarker

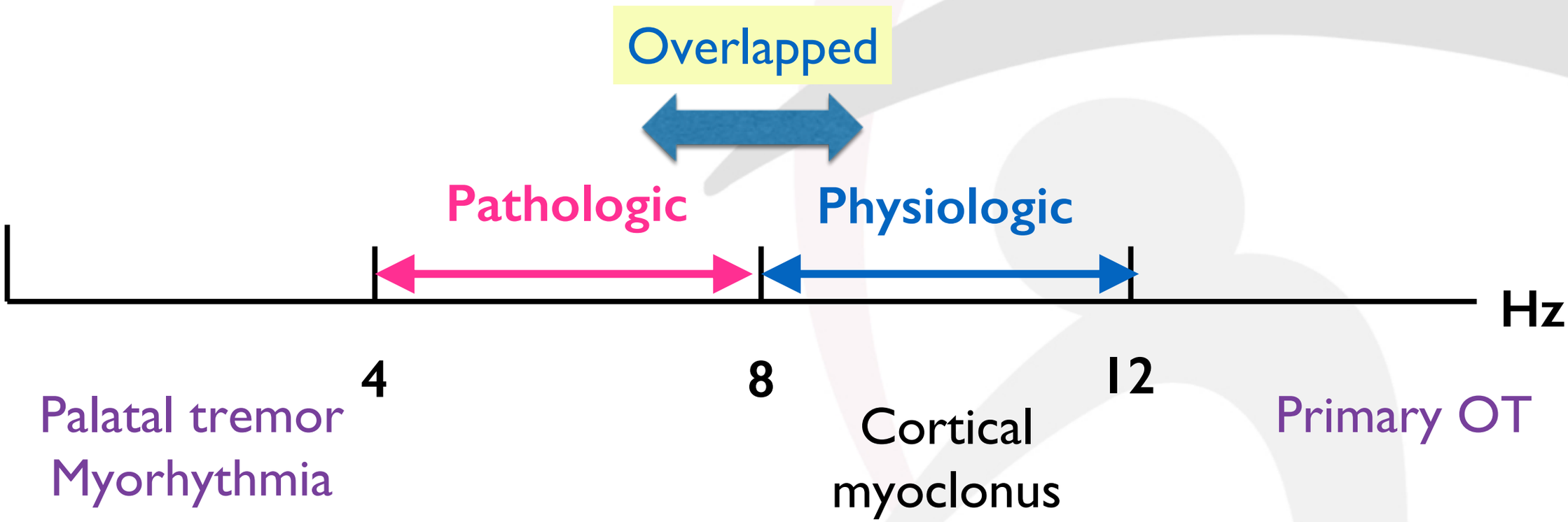
Axis 2 : Etiology

- Acquired
- Genetic
- Idiopathic
  - Familial
  - Sporadic

Bhatia K, et al. Mov Disord. 2018 Jan;33(1):75-87

Frequency of tremor

NEED neurophysiological test



Bhatia K, et al. Mov Disord. 2018 Jan;33(1):75-87

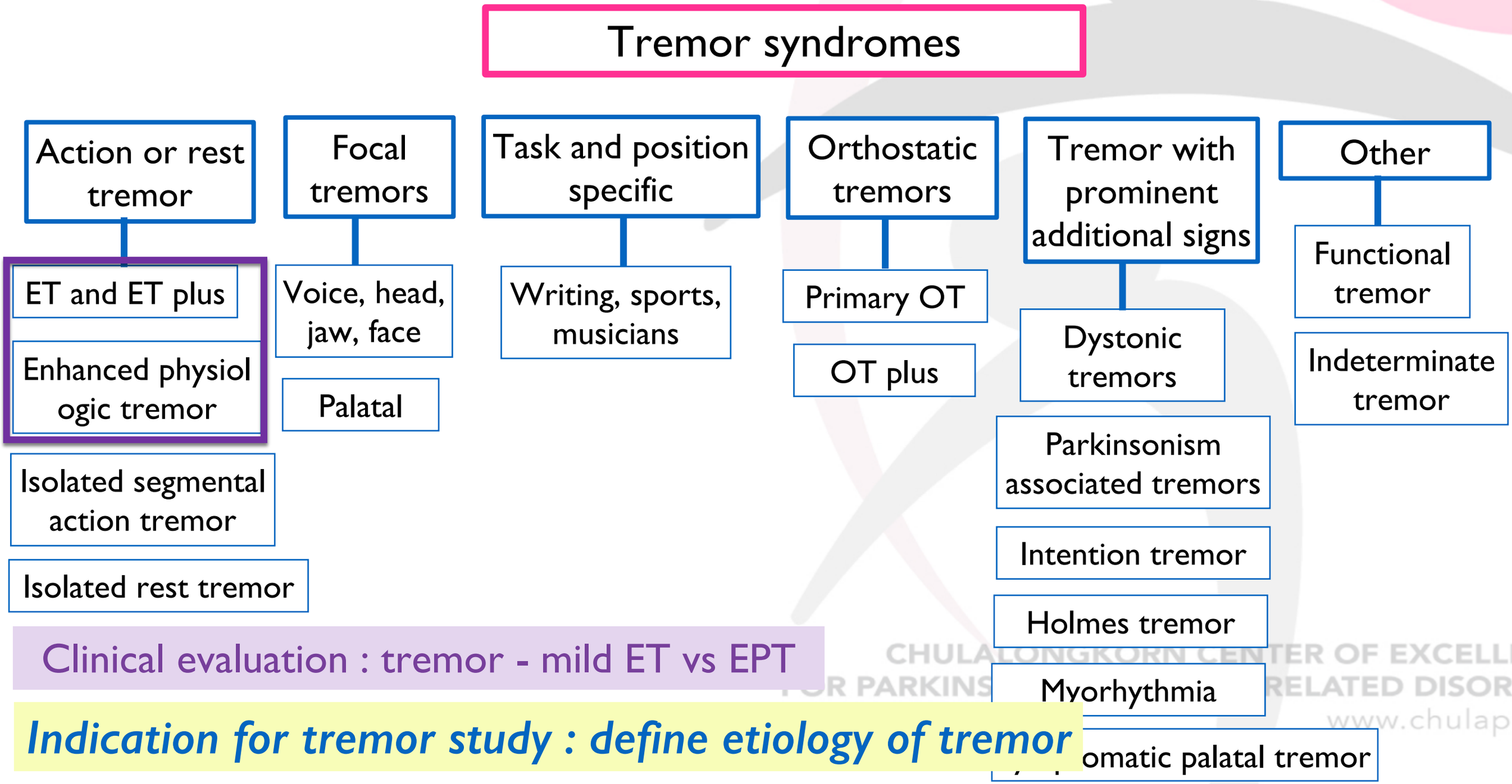
Classification of tremor : Axis I
"Additional lab tests"

TABLE 1. Tests that are useful for delineating Axis 1 syndromes (1, 2, and 3) and for elucidating Axis 2 etiologies (2, 3, and 4)

1. Electrophysiological tests	Surface EMG to document the presence of tremor, measure tremor frequency, and evaluate EMG burst morphology and rhythmicity (e.g., to identify myoclonus and asterixis)
	Fourier analysis of accelerometric and EMG recordings with and without loading the hand with a weight to identify mechanical-reflex and central neurogenic tremors
	Fourier and coherence analysis of EMG recordings from multiple limbs to diagnose primary orthostatic tremor
2. Structural imaging	MRI, CT for detection of lesions, metabolic disorders, etc.
3. Receptor imaging	Dopamine and serotonin transporter imaging for disturbances or deficiency syndromes
4. Serum and tissue markers	Metabolic blood tests, tests for infections, genetic tests, etc.

Bhatia K, et al. Mov Disord. 2018 Jan;33(1):75-87

Classification of tremor : Axis I
"The tremor syndrome"



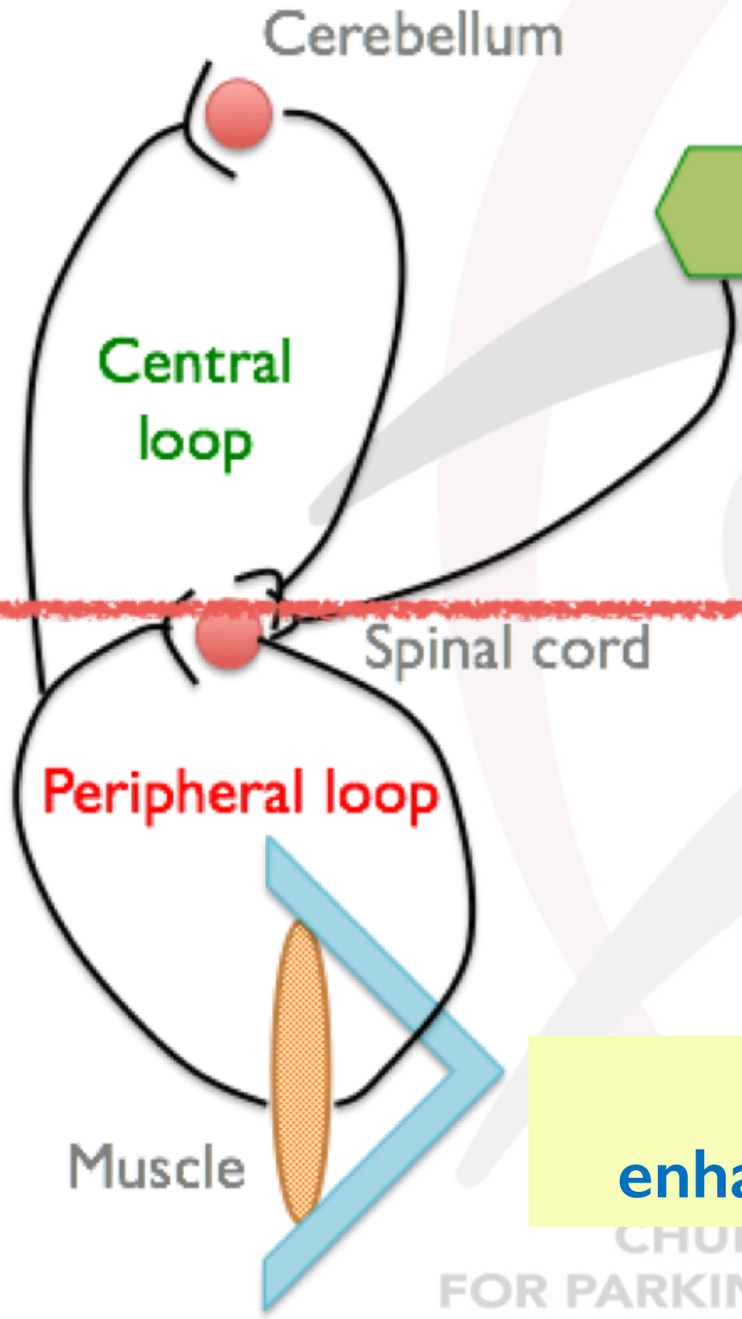
Clinical evaluation : tremor - mild ET vs EPT

Indication for tremor study : define etiology of tremor

Principle of tremor genesis

No Frequency changes with weighting

central



ET, PD, cerebellar/ rubral tremor

Frequency changes with weighting

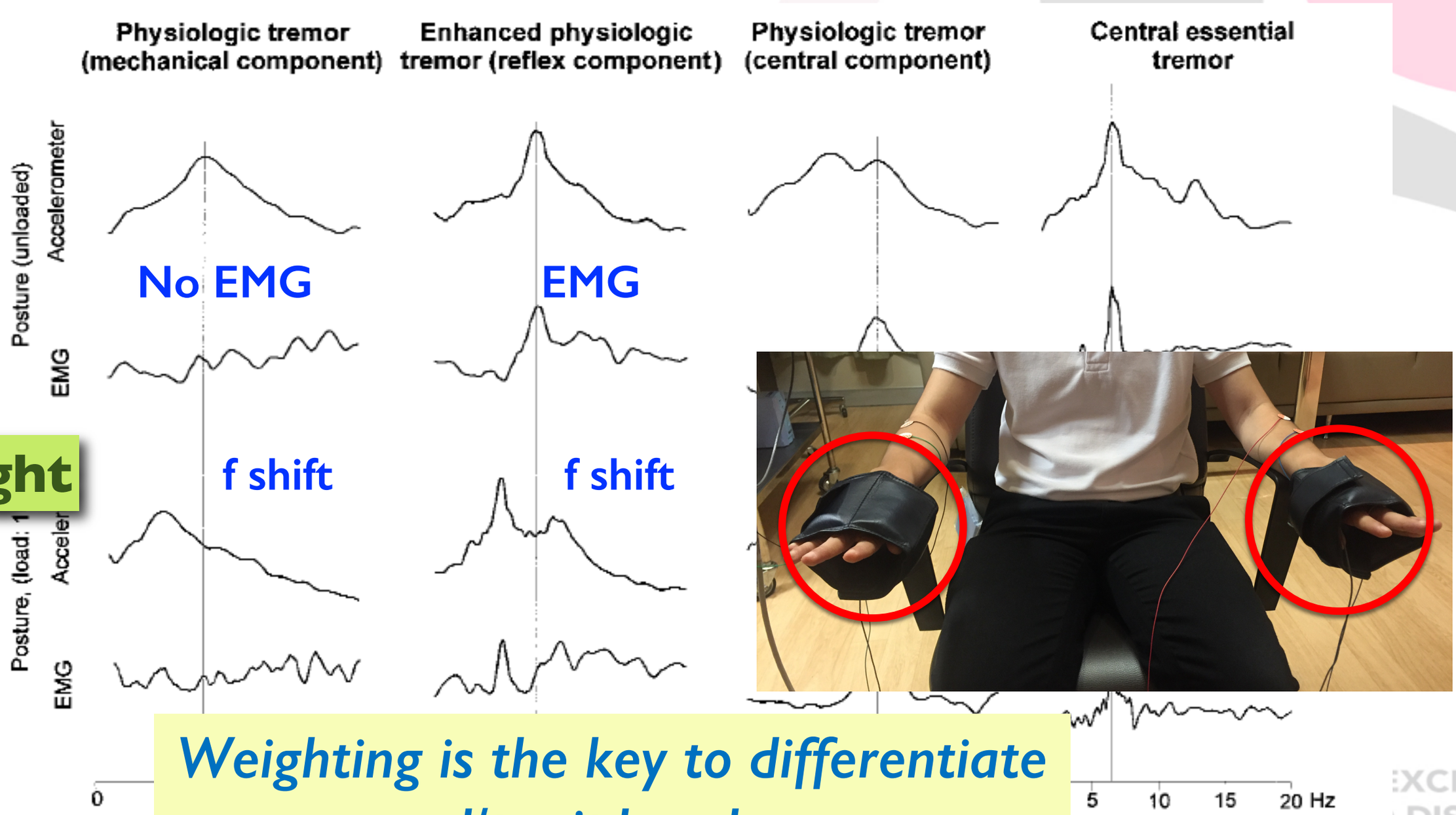
Peripheral

Physiologic tremor
enhanced physiologic tremor

Tremor depends on mass and stiffness

Hallett 1998, 2014, Deuschl, et al. 2001

Applied physiology of tremor to tremor study



Weighting is the key to differentiate central/peripheral tremor

Deuschl, et al. 2001

"Tremor analysis using conventional EMG is able to define phenomenology and etiology"

Neurophysiological criteria for ET *all criteria must be present*

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1. Rhythmic burst of postural tremor on EMG
2. Tremor frequency ≥4 Hz
3. Absence of rest tremor, or, if present, frequency 1.5 Hz lower than the postural tremor
4. Absence of tremor latency from rest to postural position (>2 s)
5. Changes of the dominant frequency peak ≤1 Hz after the weight load test
6. No changes in tremor amplitude after mental concentration

Sensitivity = 97.7, specificity = 82.3, PPV = 95.1, NPP = 91.1%

Gironell et al. 2004

Table 3
Sensitivity and specificity of five typical tremor characteristics.

	Sensitivity	Specificity
Freq. decrease upon loading in EPT	42%	95%
≥2 positive for EPT: • Frequency decrease upon loading • Frequency >6 Hz • Frequency variability >1.75 Hz	84%	94%
Amp. increase upon loading in FT	22%	92%
Entrainment in FT	91%	91%
Distractibility in FT	94%	92%
≥2 positive for FT: • Entrainment • Distractibility • Frequency variability >1.75 Hz	100%	93%
Intention tremor in ET	42%	85%

Freq. = frequency, amp. = amplitude. EPT: enhanced physiological tremor, FT: functional tremor, ET: essential tremor.

A.M.M. van der Stouwe et al. PRD 2016

The new definition of essential tremor and ET plus

Essential tremor	Essential tremor plus
• Isolated tremor syndrome of bilateral upper limb action tremor.	• Tremor with the characteristics of ET *and*
• At least 3 years duration	• Additional neurological signs of uncertain significance such as *impaired tandem gait, questionable dystonia, memory impairment* or other mild neurologic signs of unknown significance.
• With or without tremor in other locations (head, voice, lower limbs)	
• Absence of other neurologic signs, such as *dystonia, ataxia, parkinsonism*	

Electrophysiological tests with presence of central oscillation – ET, ET plus

- Isolated focal tremors (voice, head)
- Orthostatic tremor with a frequency > 12 Hz
- Task- and position-specific tremors
- Sudden onset and stepwise deterioration

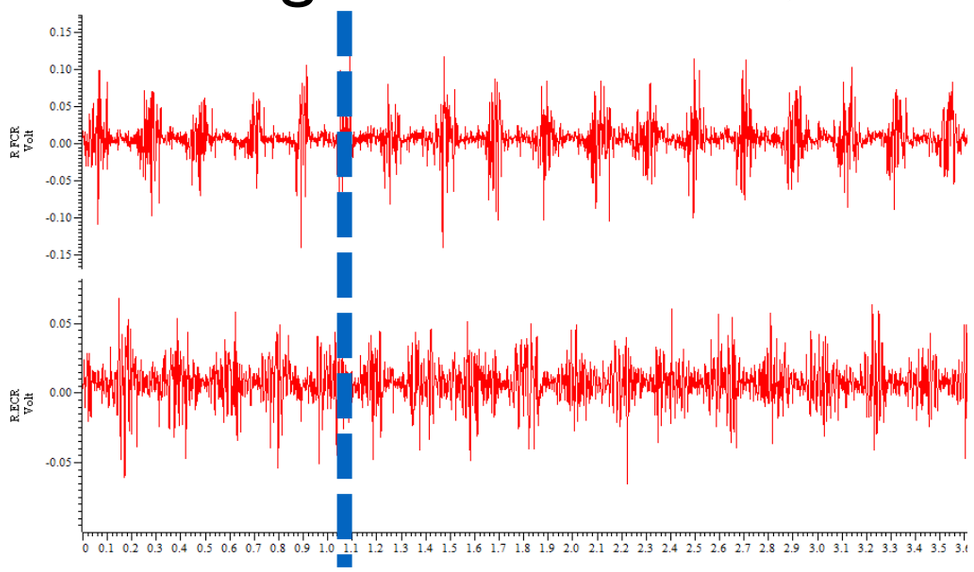
Bhatia K, et al. Mov Disord. 2018

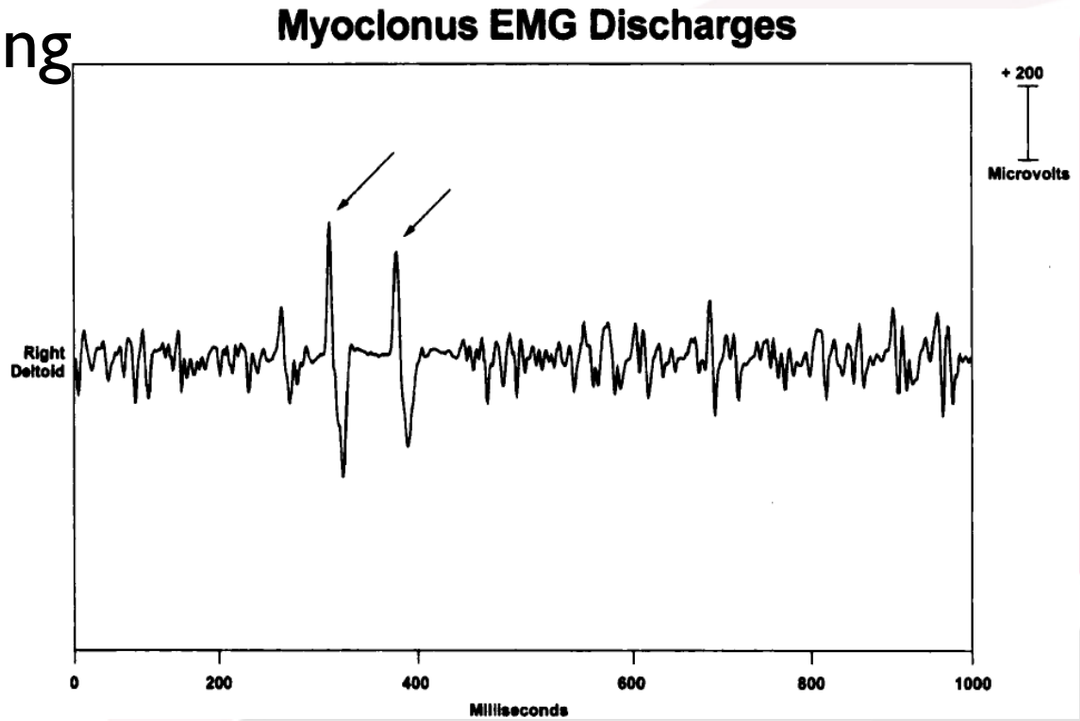
Neurophysiological test

- Define movement ; myoclonus or tremor
  - Measure movement by surface EMG +/- Accelerometer at the relevant muscles (> 2 muscles : progression)
  - Outcome - EMG burst duration, rhythmicity, pattern
- Localization if myoclonus

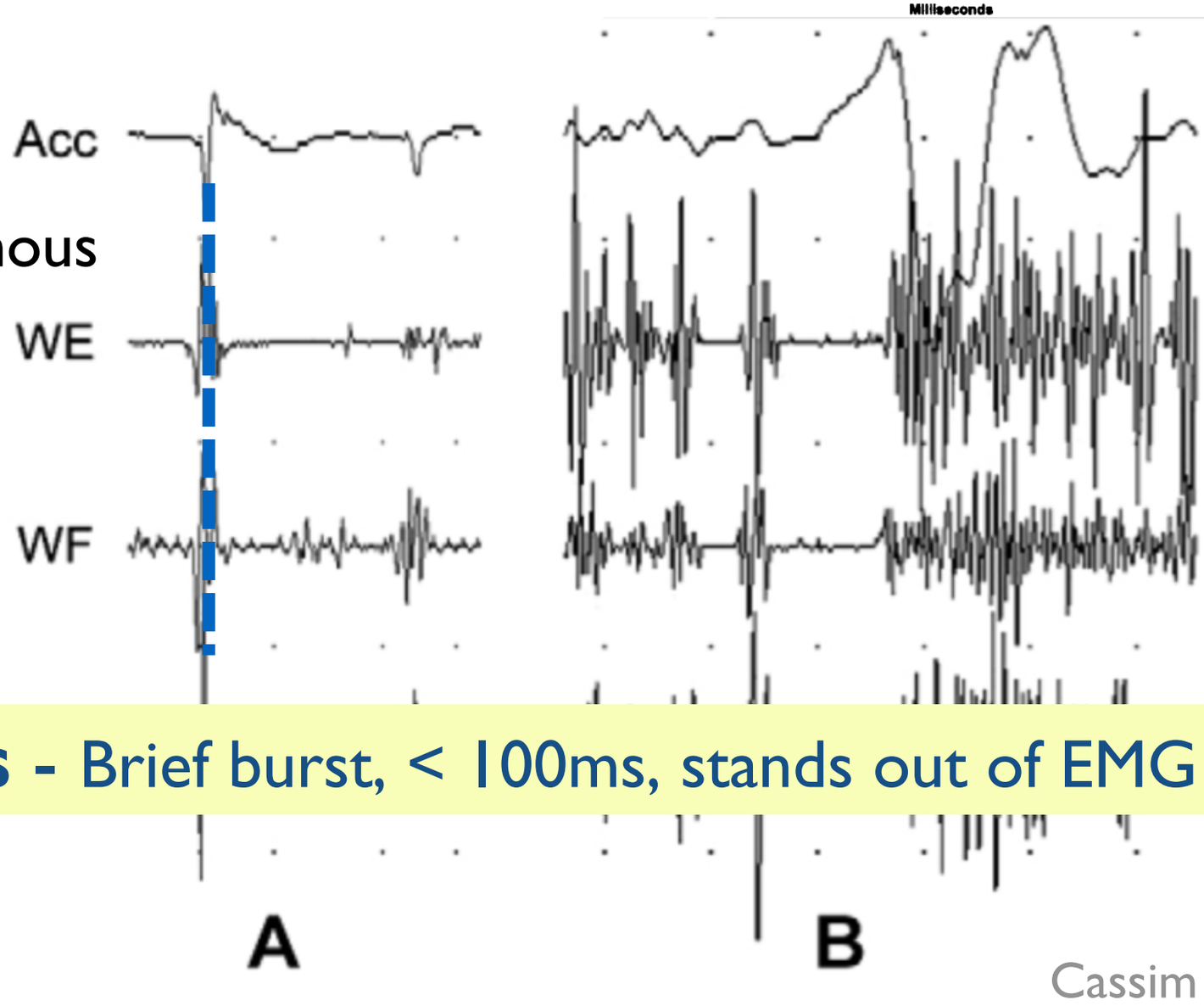
Apartis 2013
Cassim and Houdayer 2006

Tremor – regular EMG burst, alternating





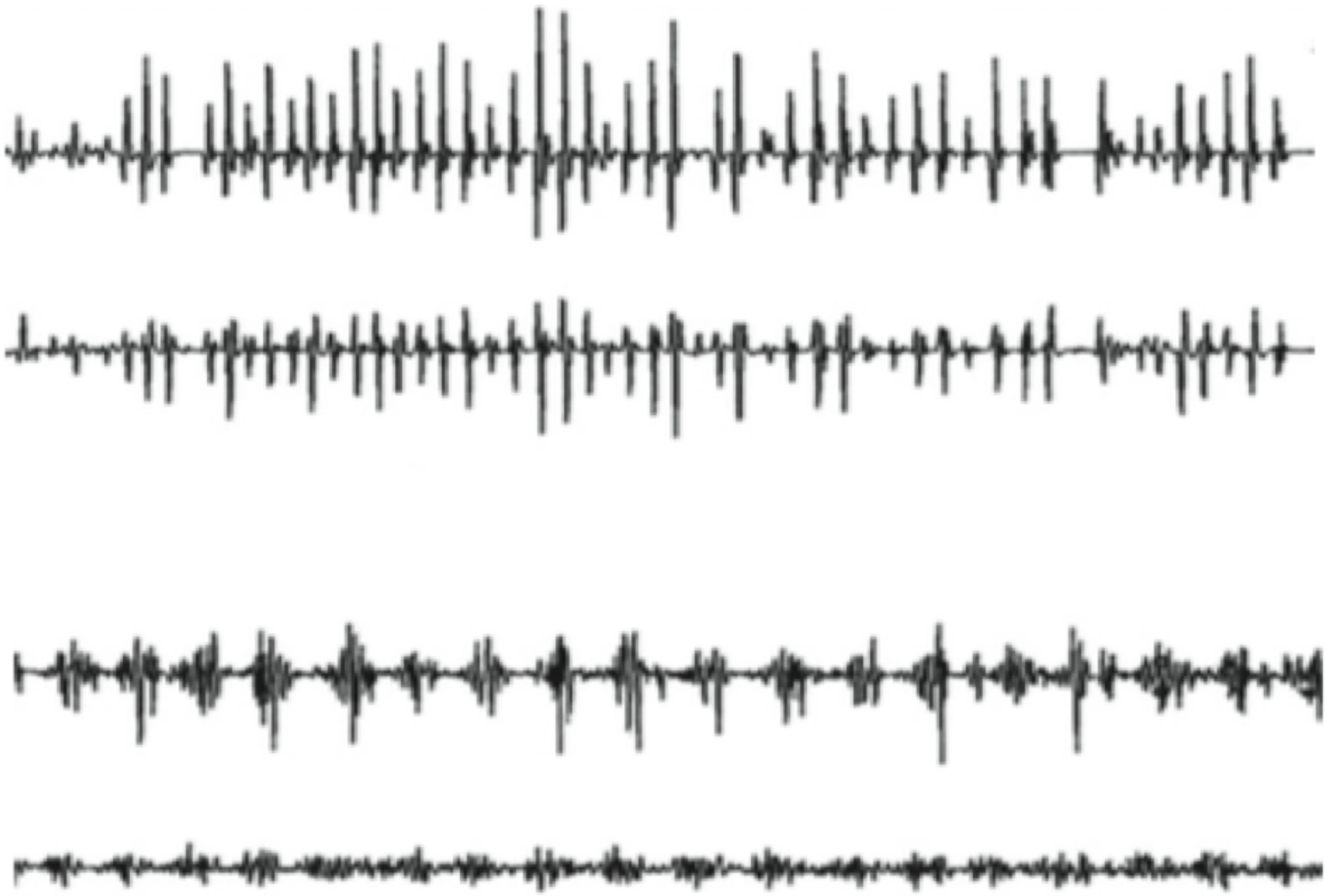
Caviness 2003



Myoclonus - Brief burst, < 100ms, stands out of EMG background

Cassim and Houdayer 2006

Myoclonus or tremor?



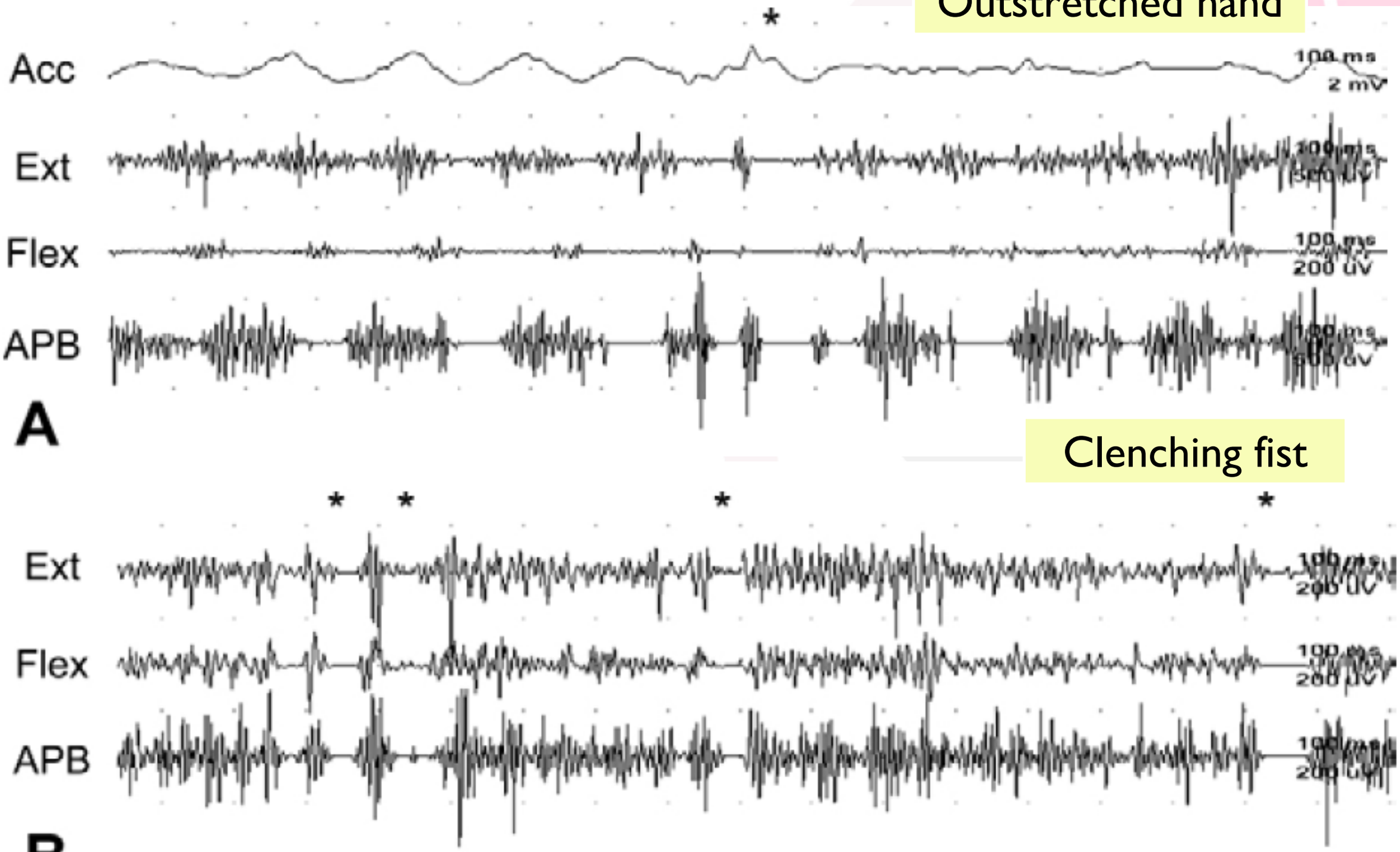
Myoclonus

Tremor

Apartis E. and Vercueil L. Revue Neurologique 2016

Myoclonus or tremor?

Outstretched hand



Cassim 2006

Clinical approach to myoclonus

Myoclonus

Exclude myoclonus mimic

Tremor, motor tics, jerky dystonia, FMD

Neurophysiological study

Anatomical localization

Neurophysiological study

Cortical or subcortical

- **Cortical : spontaneous, cortical reflex**
- **Subcortical**
- **Brainstem reticular myoclonus**
- **Startle/hyperekplexia**
- **Segmental : palatal, opsoclonus**

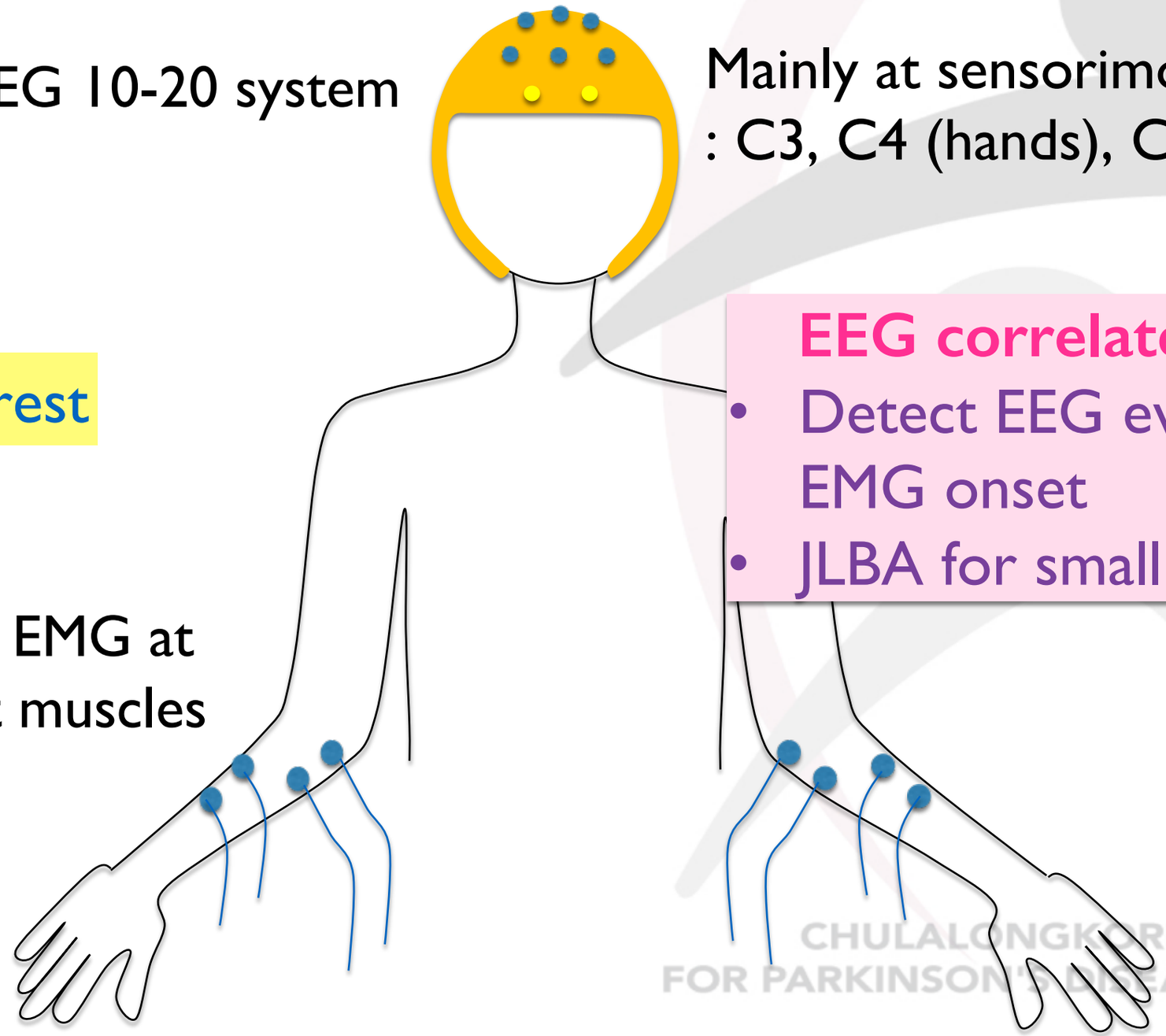
Spinal or segmental

- **Segmental**
- **Propriospinal**
- **peripheral**

Zutt R, et al, 2015.

Localization of myoclonus “Simultaneous EEG + EMG”

EEG 10-20 system



Mainly at sensorimotor area
: C3, C4 (hands), Cz (legs, trunk)

At rest

Surface EMG at relevant muscles

EEG correlate with EMG

- Detect EEG event, related to EMG onset
- JLBA for small EEG events

EEG/EMG correlate

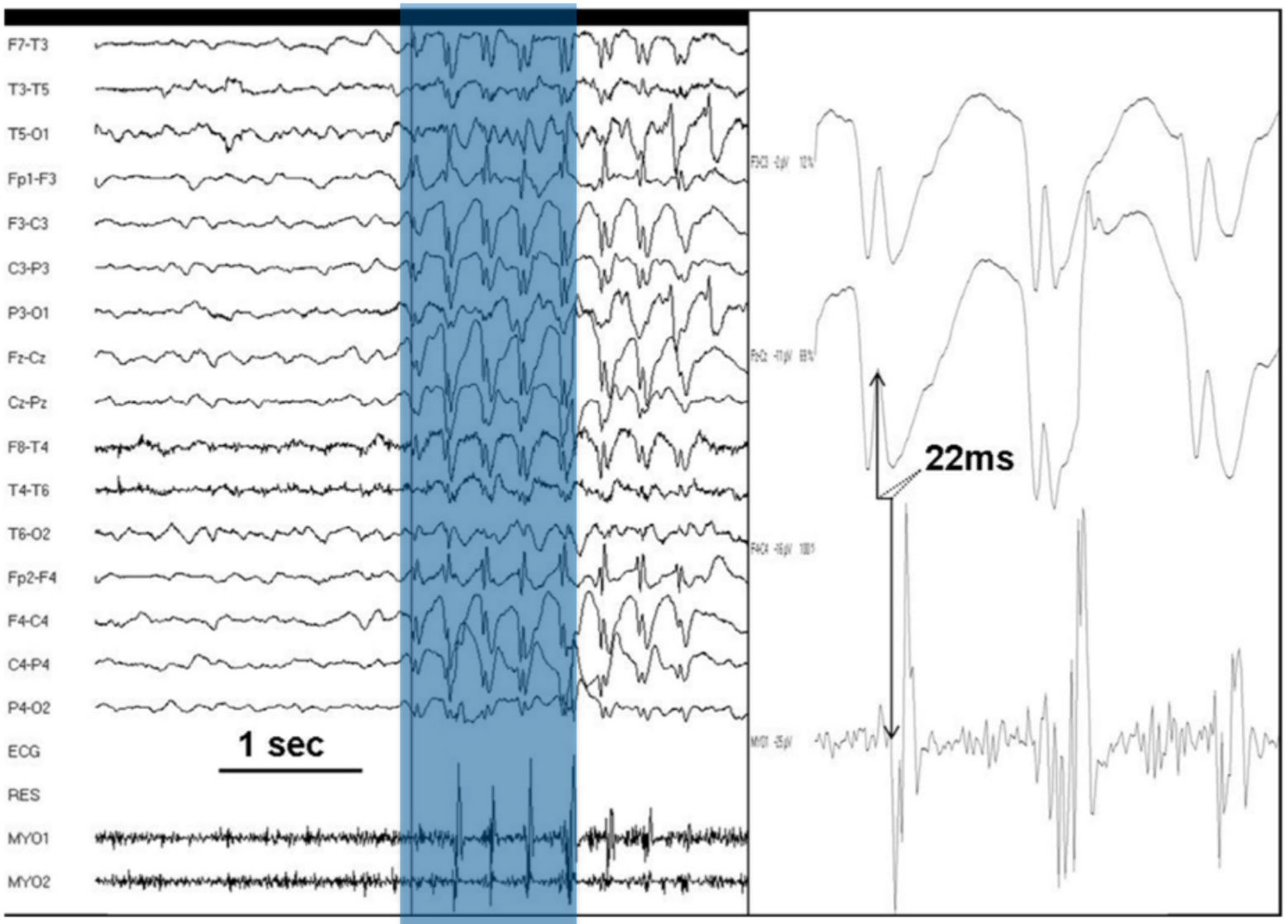
Localization of myoclonus by EEG/EMG correlate

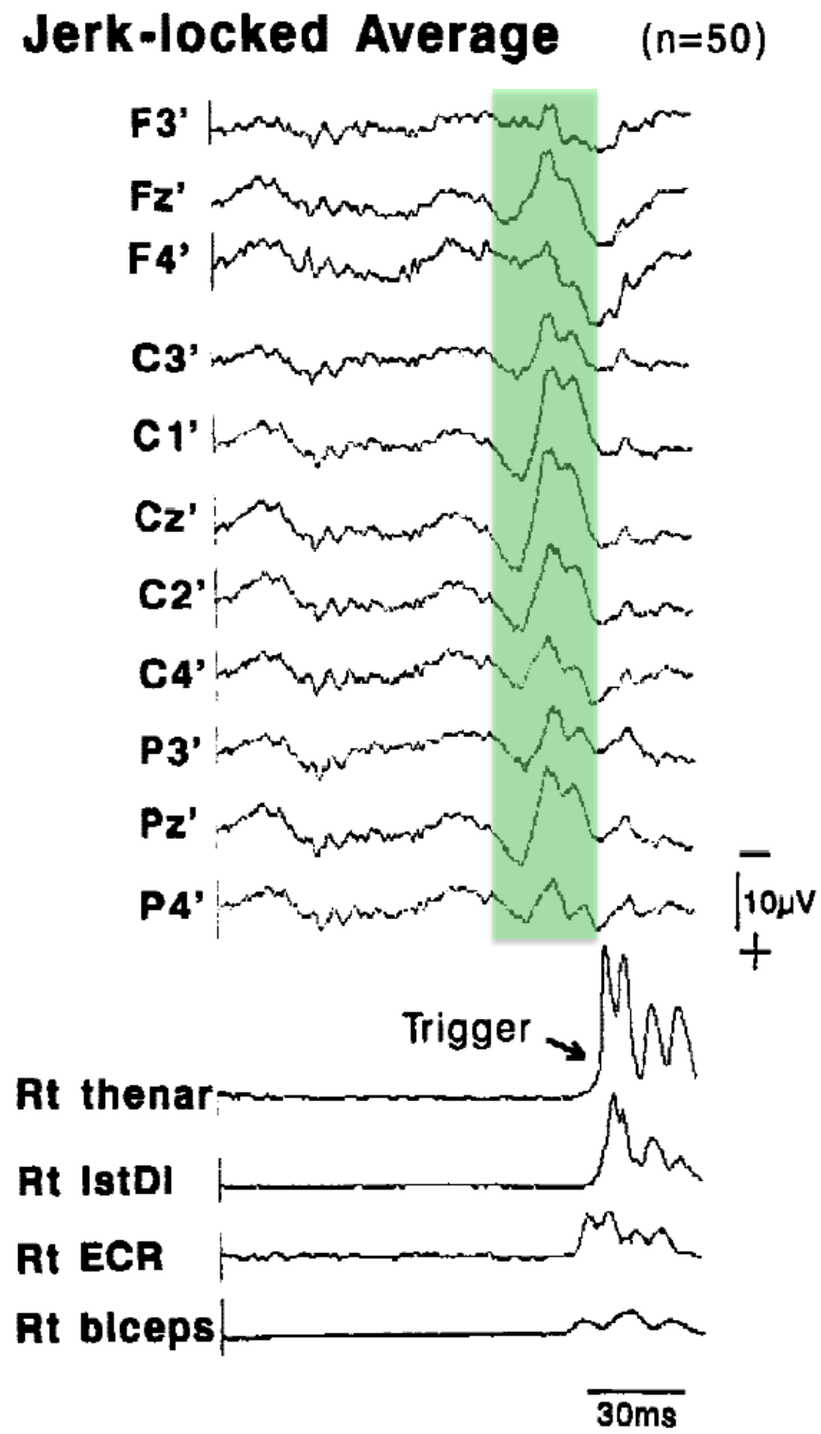
- Eplieptic : cortical
- Non-epileptic : subcortical/brainstem, spinal, peripheral

Criteria	epileptic	non epileptic
EMG burst duration	25-50 ms	50-300 ms
EMG antagonist muscle relationship	Always synchronous	Synchronous or alternating
EEG correlate	Typically present	Always absent

Hallett M, Aminoff's Electrodiagnosis in Clinical Neurology 2012

EEG-EMG correlate





Cortical myoclonus

Unknown sensitivity

Shibasaski 2000

Sensitivity of EEG-EMG back averaging

	JLBA	
	Studied	Positive
MSA (8 patients)	5	20%
CBS (10 patients)	10	30%
ADCME (4 patients)	3	0%
PME (9 patients)	7	29%
Coeliac disease (3 patients)	3	0%
Mitochondrial disease (6 patients)	6	33%
Postanoxic (4 patients)	3	0%
Total (44 patients):	37	22%
Negative/not giant/absent	22%	
Not possible to interpret (because of high frequency of myoclonic jerks, major EEG artefacts, neuropathy)	57%	

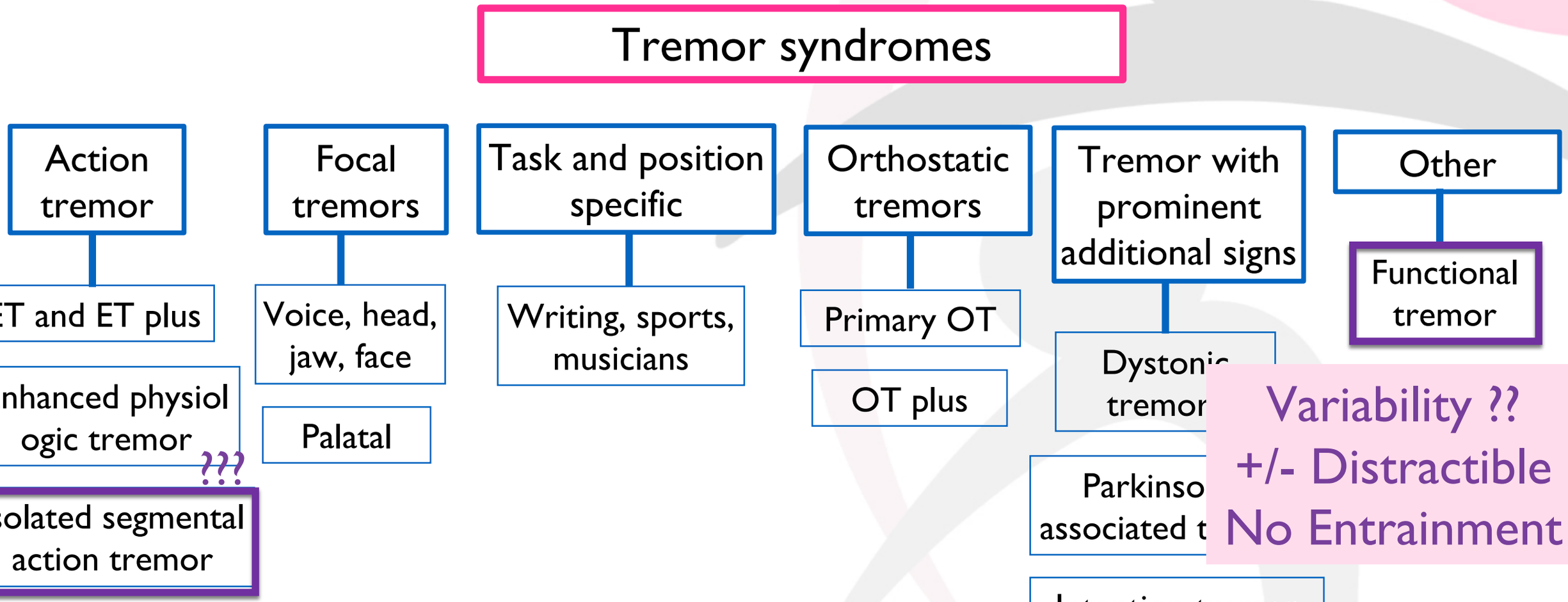
Limitation of EEG-EMG

- Need absence of EMG for >100 ms prior each EMG burst → not suitable for high frequency myoclonus
- Need average of > 40 trials → not for too infrequency jerks

Apartis E. and Vercueil L. Revue Neurologique 2016
Latorre A, et al. Mov Disord 2018

Clinical Evaluation

"The new tremor syndrome"



Most likely clinical Dx of functional > DT

NEED neurophysiological test

tremors, from the Task Force on Tremor of the
International Parkinson and Movement Disorder Society Movement Disorders 2017, submitted.

- **Neurophysiological test has proven to be very useful in psychogenic or functional movement disorders, particularly with tremor and myoclonus.[1]**

- Tremor – special battery test ; validated, high sensitivity (90%) and high specificity (95%)[2]

- Tapping performance (3 different frequency) with metronome
  - distraction and entrainment

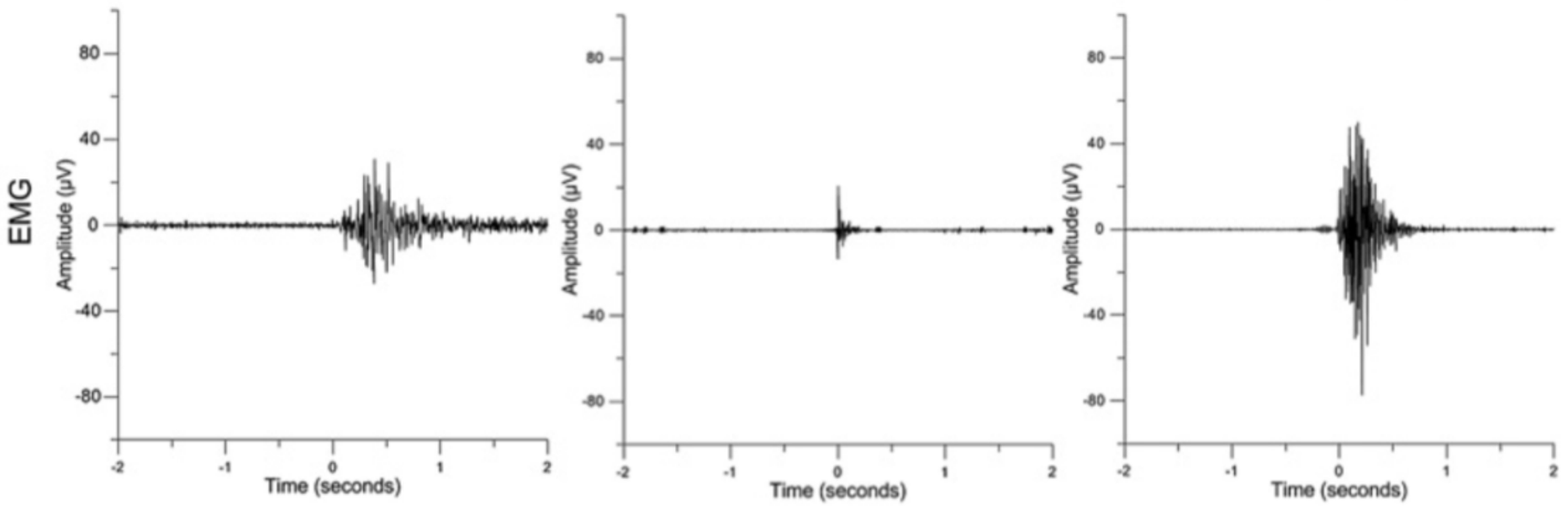
- Ballistic movement of less affected limb – transient stop of tremor

- Postural holding with loading – increase tremor amplitude

[1]Hallett M & Rothwell J. Movement Disorders 2011
[2]Schwingenschuh P. et al, Movement Disorders 2011, 2016

Psychogenic movement disorders

- Myoclonus – EMG, simultaneous EEG with EMG[1,2]
  - EMG - Prolonged EMG burst, inconsistent pattern, prolonged latency in reflex myoclonus



Psychogenic | Organic myoclonus | Voluntary

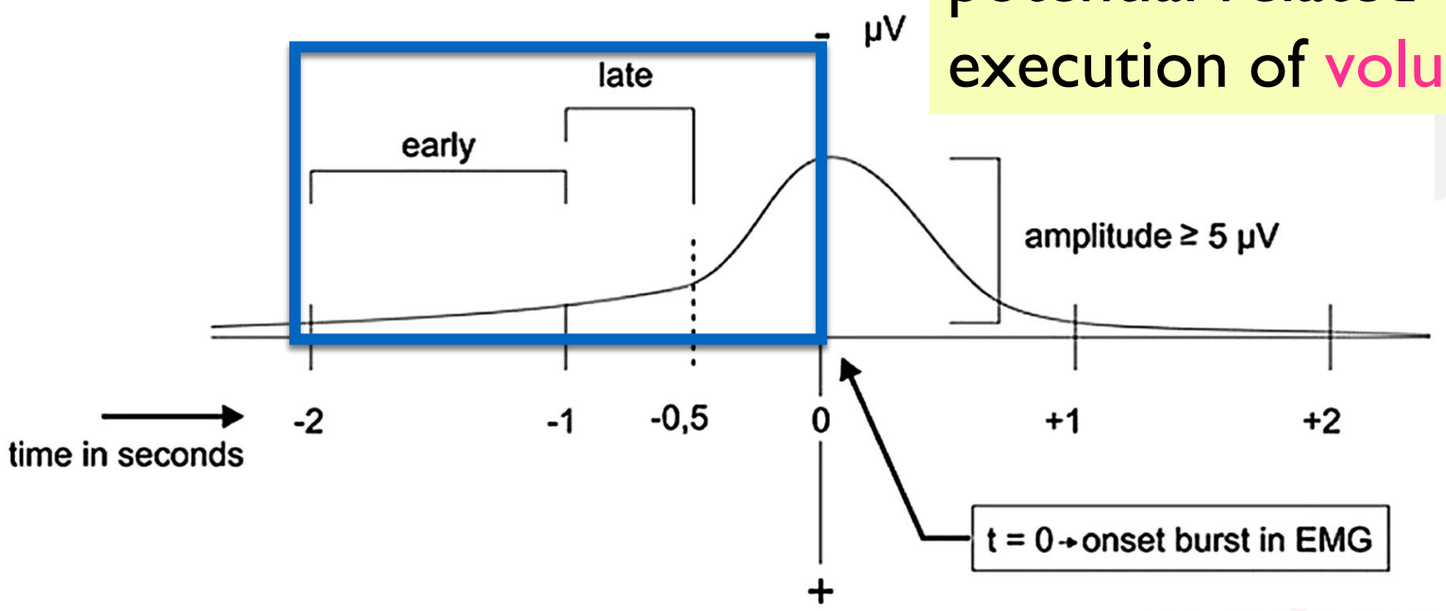
[1]Hallett M & Rothwell J. 2011

[2]Hallett 2010, Apartis 2013

Psychogenic movement disorders

- Myoclonus – EMG, simultaneous EEG with EMG[1,2]
  - Simultaneous EEG with EMG: Bereitschaftspotential

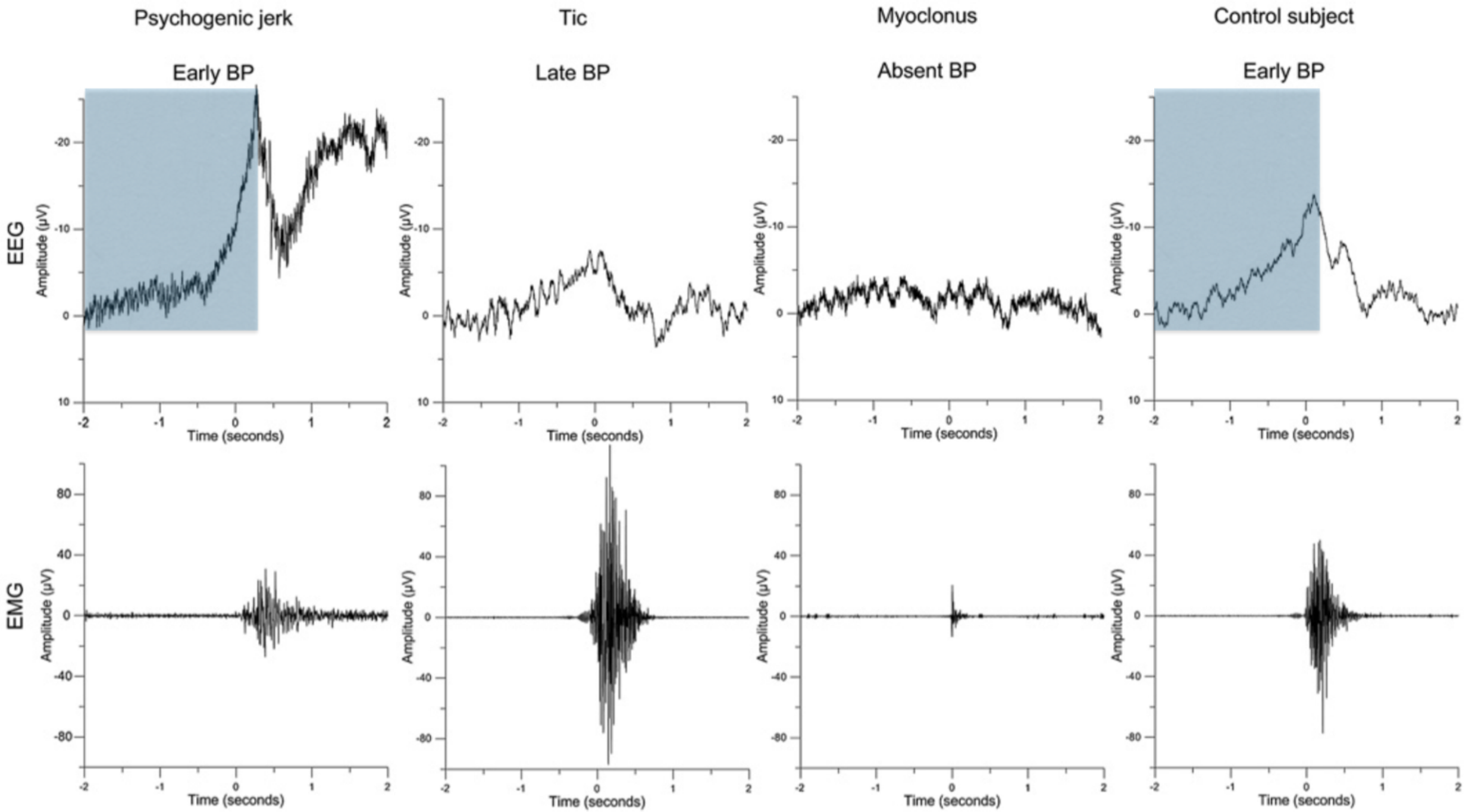
potential related to preparation and/or execution of voluntary movement



[1]Hallett M & Rothwell J. 2011

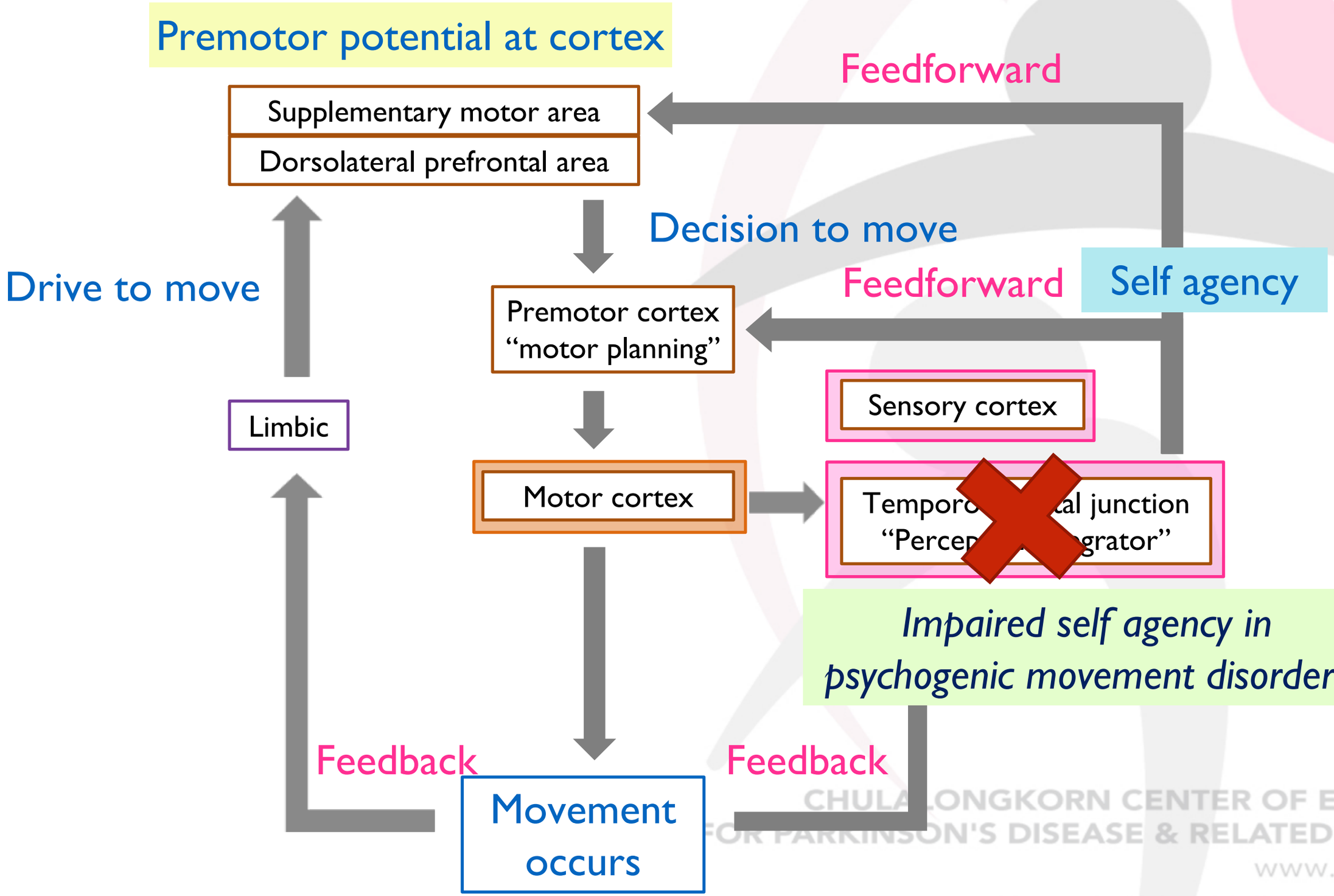
[2]Hallett 2010, Apartis 2013

Voluntary movement



Van de Salm 2012

Framework of movement



Kranick SM & Hallett M, 2013

Learning points

- Neurophysiologic test helps to differentiate organic vs psychogenic movement disorders.
  - Proven in psychogenic tremor and myoclonus
    - Implication for techniques in clinical exam – tapping, ballistic
- Also increase knowledge about pathophysiology of psychogenic movement disorders
  - NOT malingering – conversion, Rx with CBT

Take Home Message

- Neurophysiologic test is an important tool for investigation of complicated movement disorder cases and exclude psychogenic movement disorders (particularly tremor & myoclonus).
    - Should combine with clinical evaluation
- It helps for understanding pathophysiology of normal and abnormal movement.
    - Novel knowledge & therapeutic implication