Disturbi funzionali in neurologia - l'apporto della neurofisiologia

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Outline

- Weakness/paralysis

- Sensory loss
  - Somatic sensation
  - Vision
  - Hearing

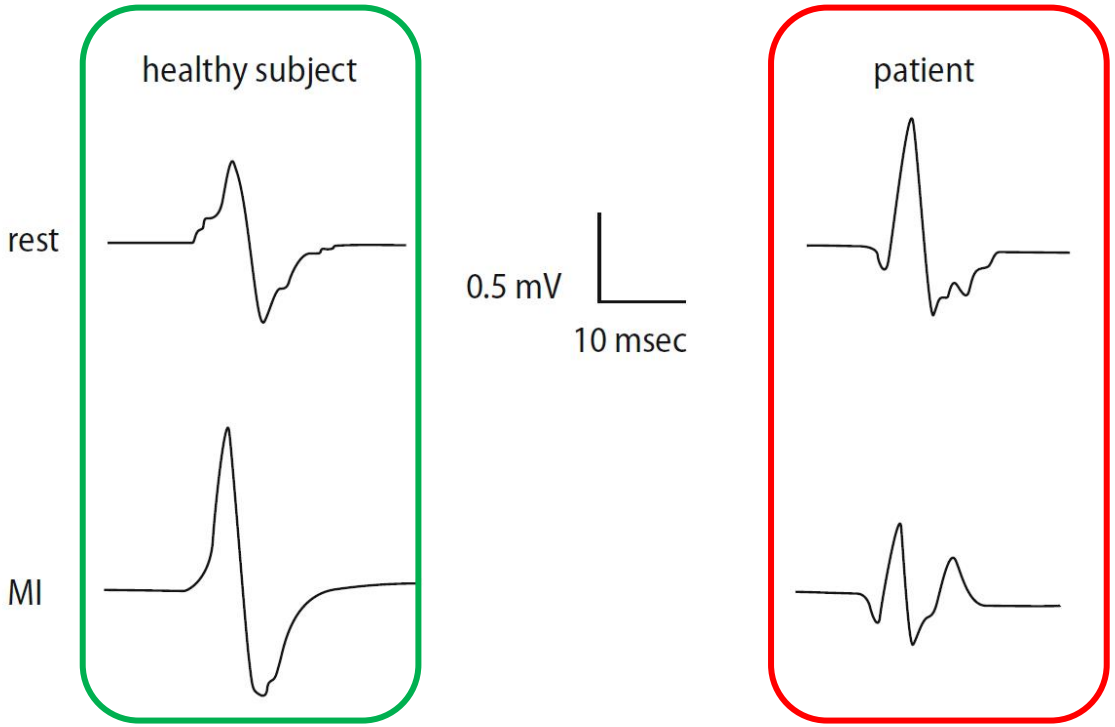
- Movement disorders
  - Myoclonus
  - Tremor
  - Dystonia

- Treatment

Weakness/paralysis

- Normal nerve conduction studies
- Electromyographic pattern compatible with decreased activation (indistinguishable from reduced effort)
- Normal latency of motor evoked potentials obtained with transcranial magnetic stimulation

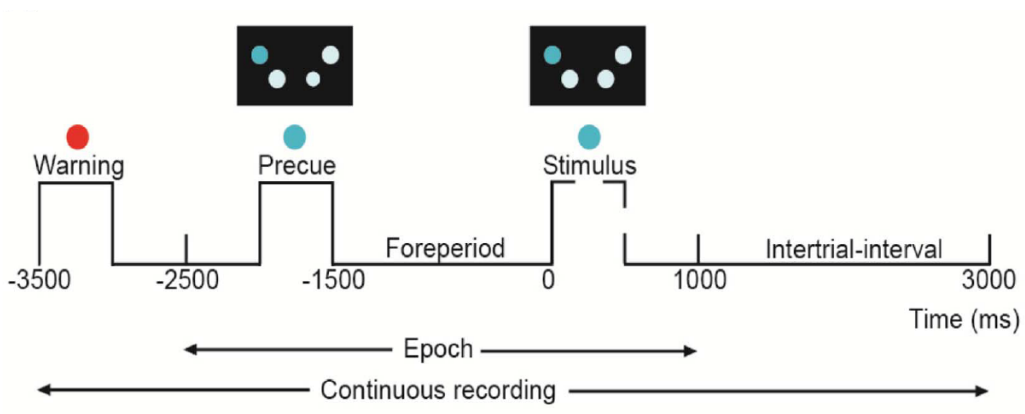
  → integrity of descending corticospinal pathways

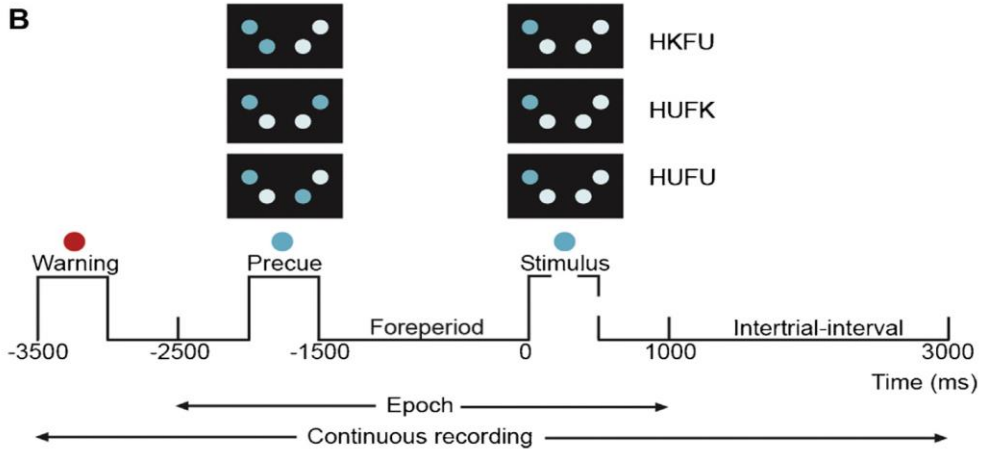


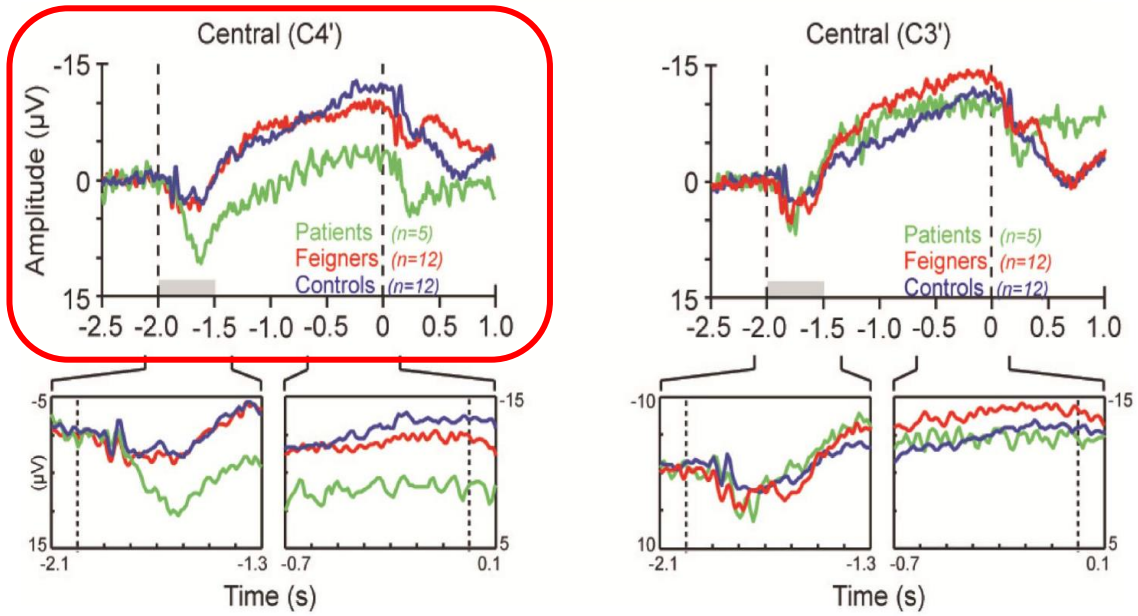
- Suppression of MEP amplitude during motor imagery
- Possible down-regulation of cortical excitability by an active inhibitory process

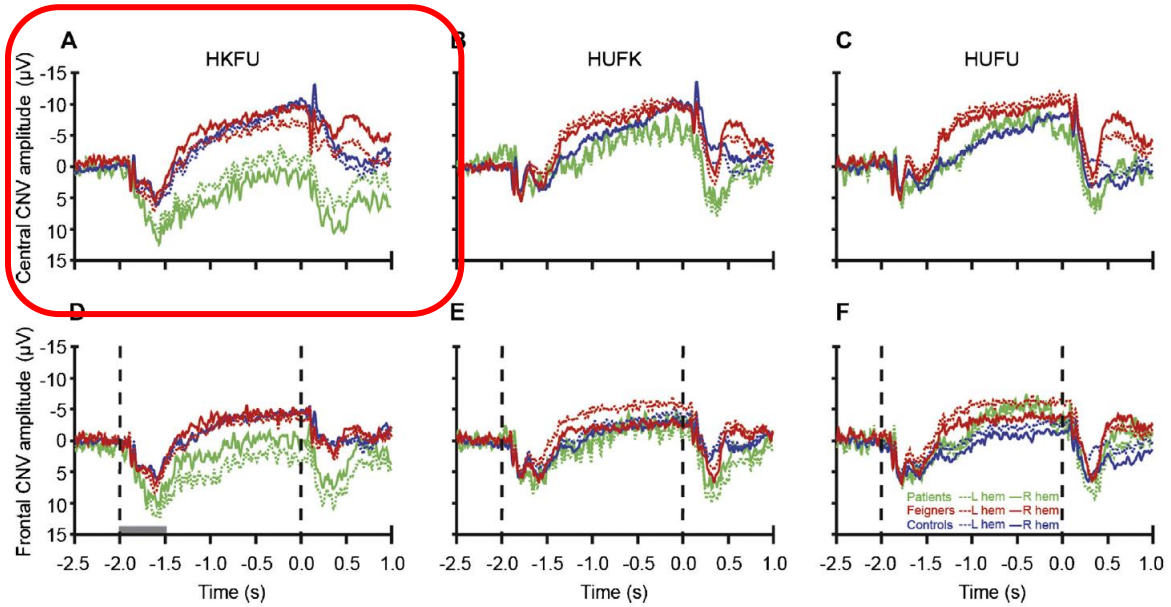
Liepert et al., 2009

Weakness/paralysis









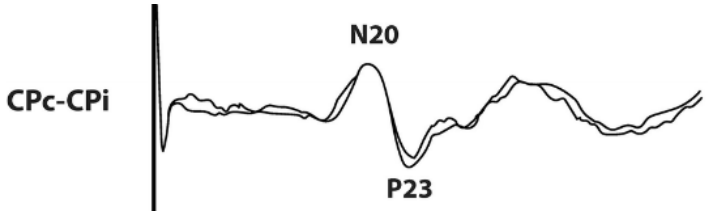
- Abnormal preparatory motor activity only with the impaired limb and only with prior knowledge of the required action

Blakemore et al., 2013, 2015

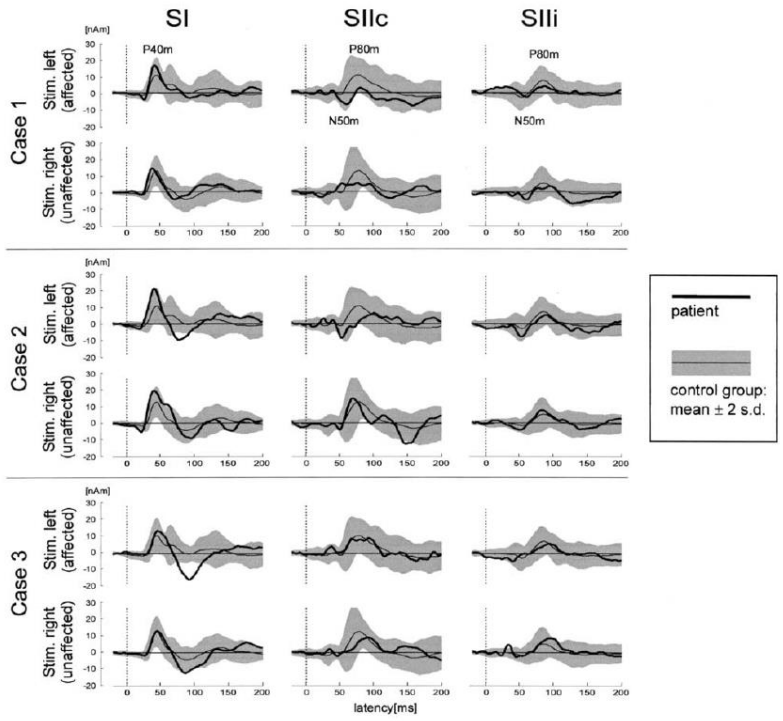
Sensory loss – somatic sensation

- Normal short-latency somatosensory evoked potentials (SEP)

  → integrity of large fibres, dorsal column – medial lemniscus system



- Anecdotal reports of low-amplitude short latency SEP, normalised either with general anesthesia or increase in stimulation intensity → deranged top-down control of sensory input?

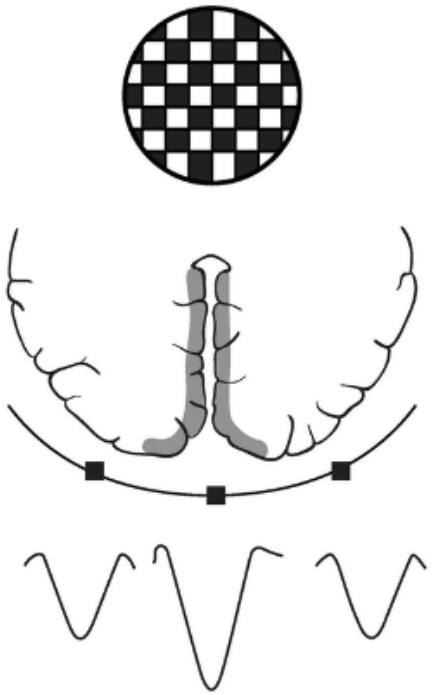


- Normal somatosensory evoked fields from the primary and secondary somatosensory cortices
- Absent P300 from somatosensory stimulation
- Spinothalamic system not assessed (e.g. laser evoked potentials)

Lorenz et al., 1998; Hoechstetter et al., 2002

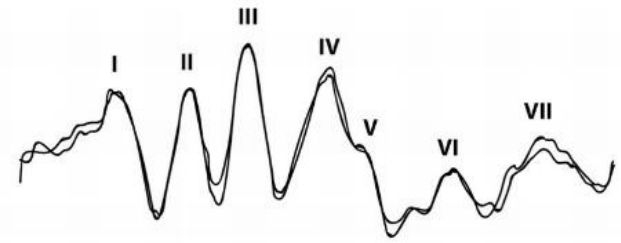
Sensory loss - vision

- P100 component of the standard pattern-reversal visualevoked potentials (VEP) usually reported to be normal
- Anectodal reports of smaller P100 amplitude, but difficult to exclude voluntary defocusing
- Small P300 in some cases



Sensory loss - hearing

- Normal brainstem auditory evoked responses
- Smaller amplitude of P300 and mismatch negativity

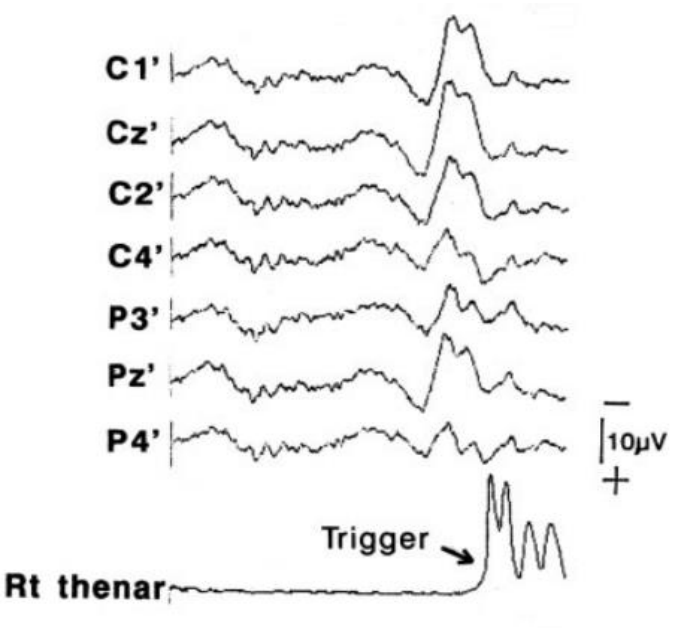


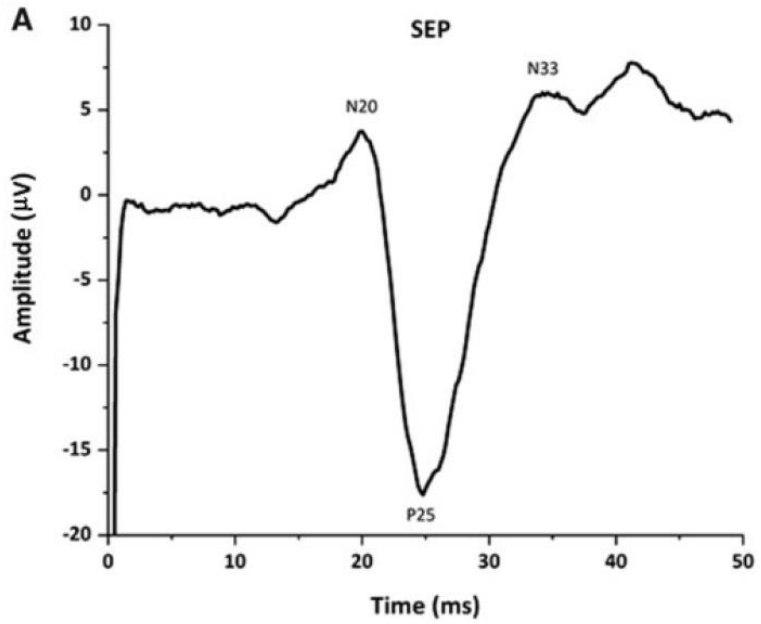
- Processing in primary sensory cortices mostly intact
- Possible impairment in higher-order sensory elaboration

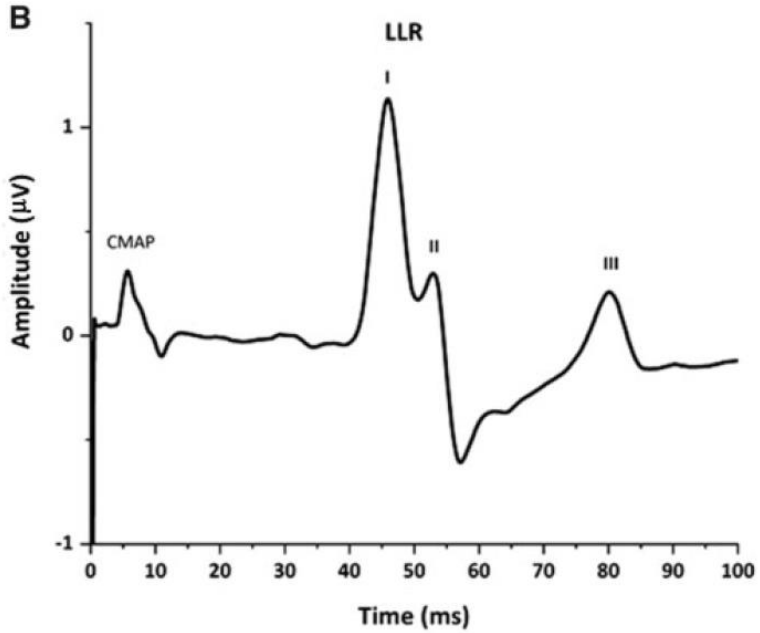
James et al., 1989; Fukuda et al., 1996; Manresa et al., 1996; Schoenfeld et al., 2011

Movement disorders - myoclonus

Definitive electrophysiological criteria for cortical myoclonus





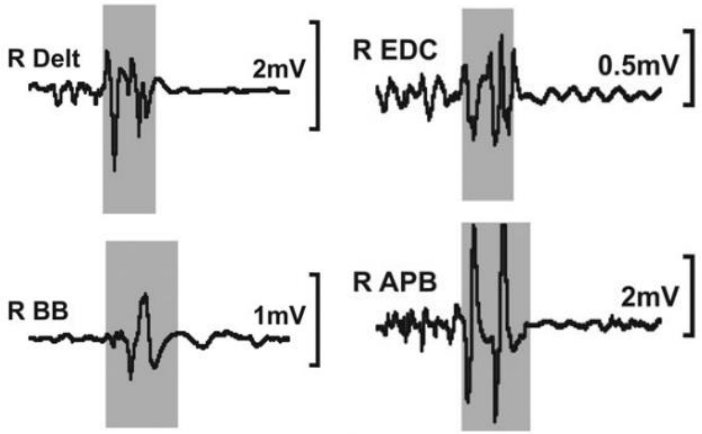


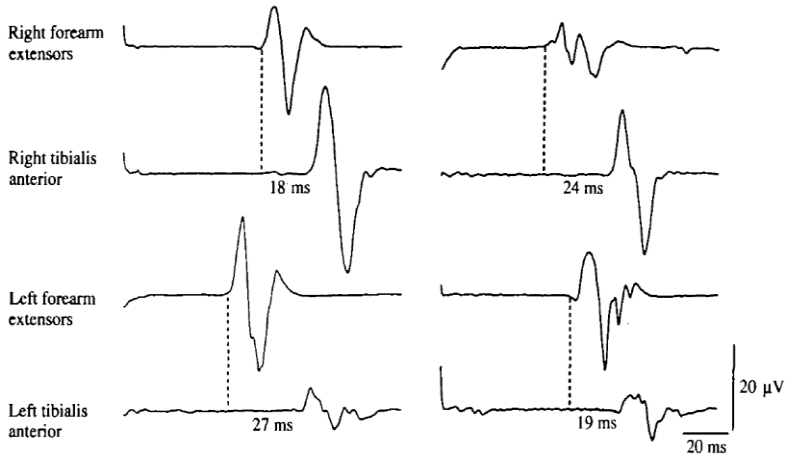
- Jerk-locked back averaging → Sign of organic myoclonus
- Giant somatosensory evoked potentials → Amplitude cutoff not entirely reliable
- C-reflex (long-latency reflexes) → Too fast to be compatible with voluntary activity

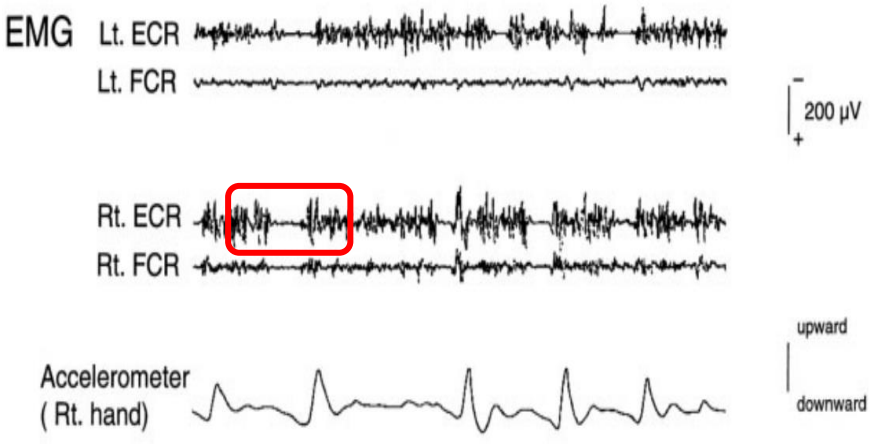
Latorre et al., 2018, 2021

Movement disorders - myoclonus

Supportive electrophysiological criteria for cortical myoclonus



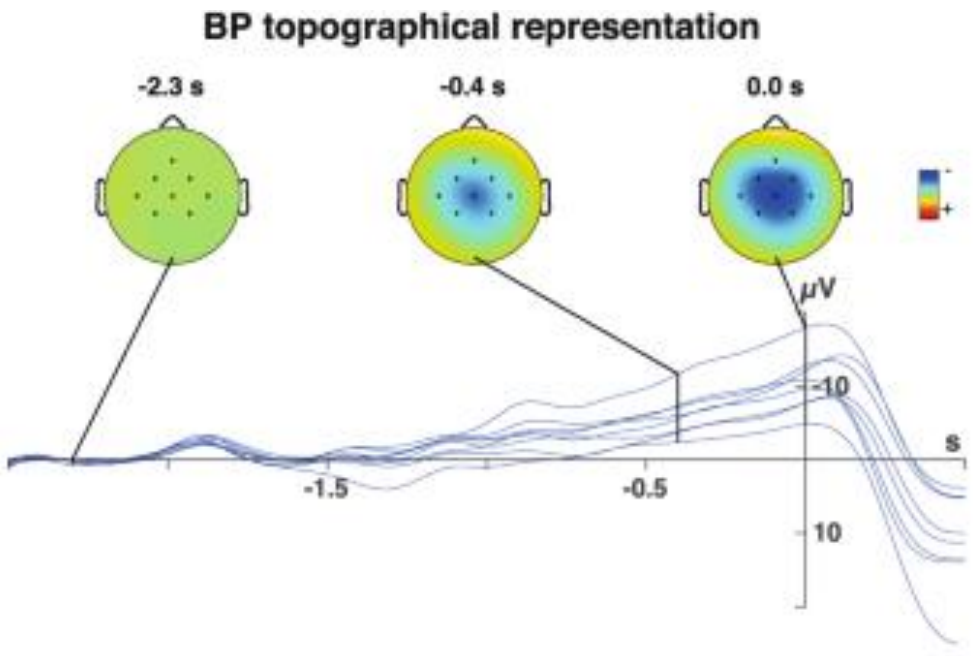


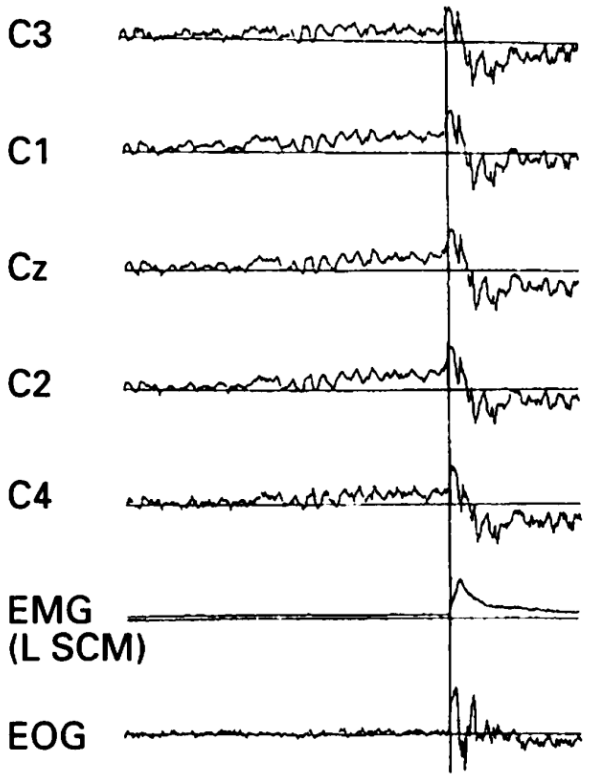


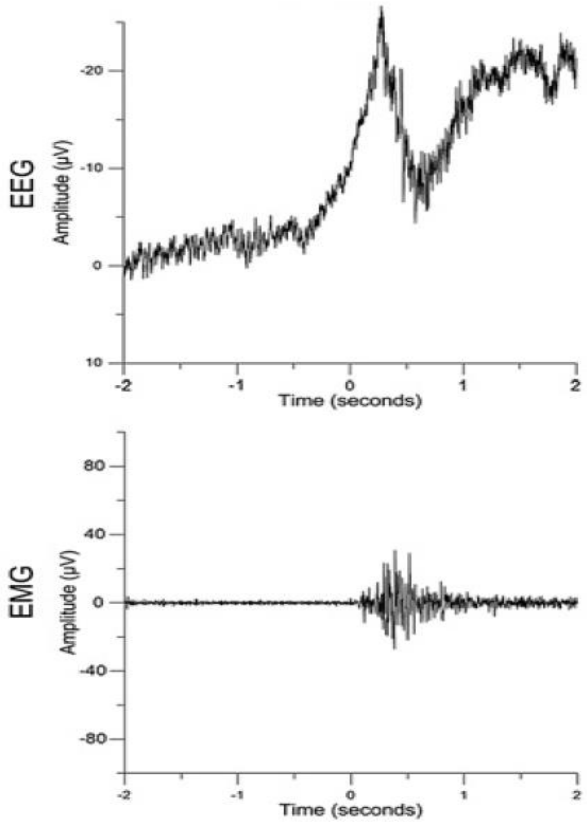
- EMG burst duration < 50-100 ms → Can be present in healthy subjects
- Cranial-caudal progression → Latency progression probably impossible to feign
- Both positive and negative myoclonus → Silent period probably impossible to feign

Latorre et al., 2018, 2021

Movement disorders - myoclonus



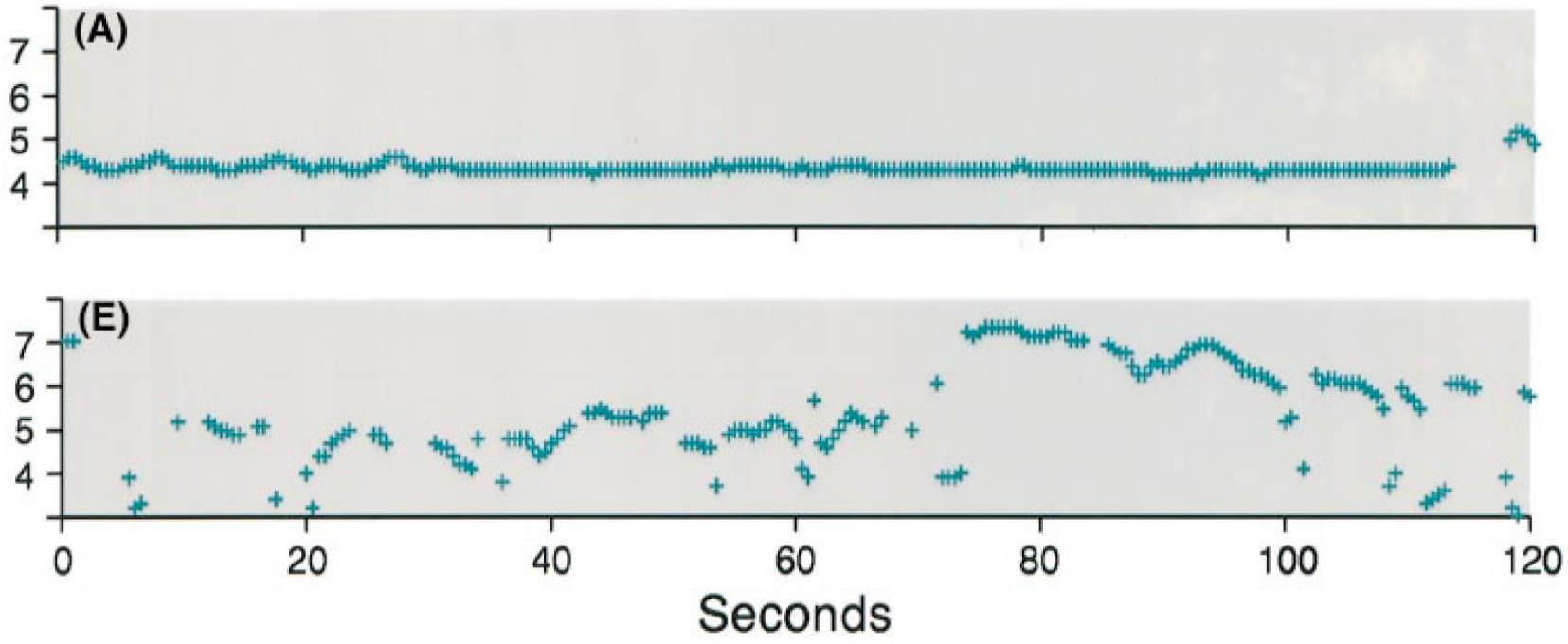


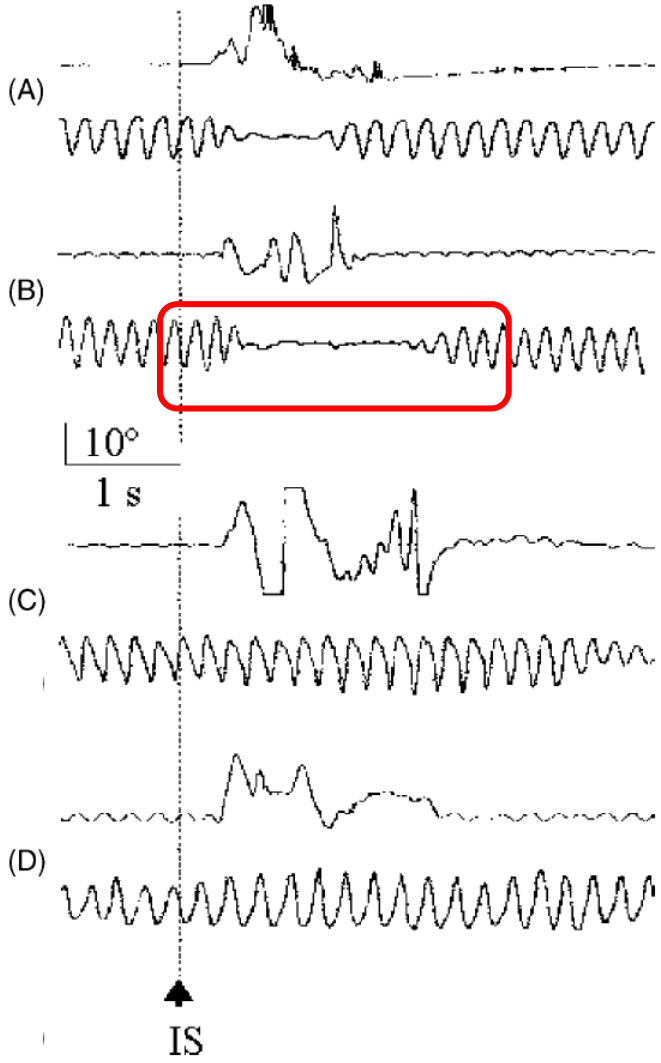


- Very slow potential, distributed around the vertex, preceding spontaneous, voluntary movement
- Likely reflects activity in premotor cortices
- Intact in functional myoclonus
- Requires low-frequency of myoclonus to be recorded

Terada et al., 1995; Van der Salm et al., 2012

Movement disorders - tremor

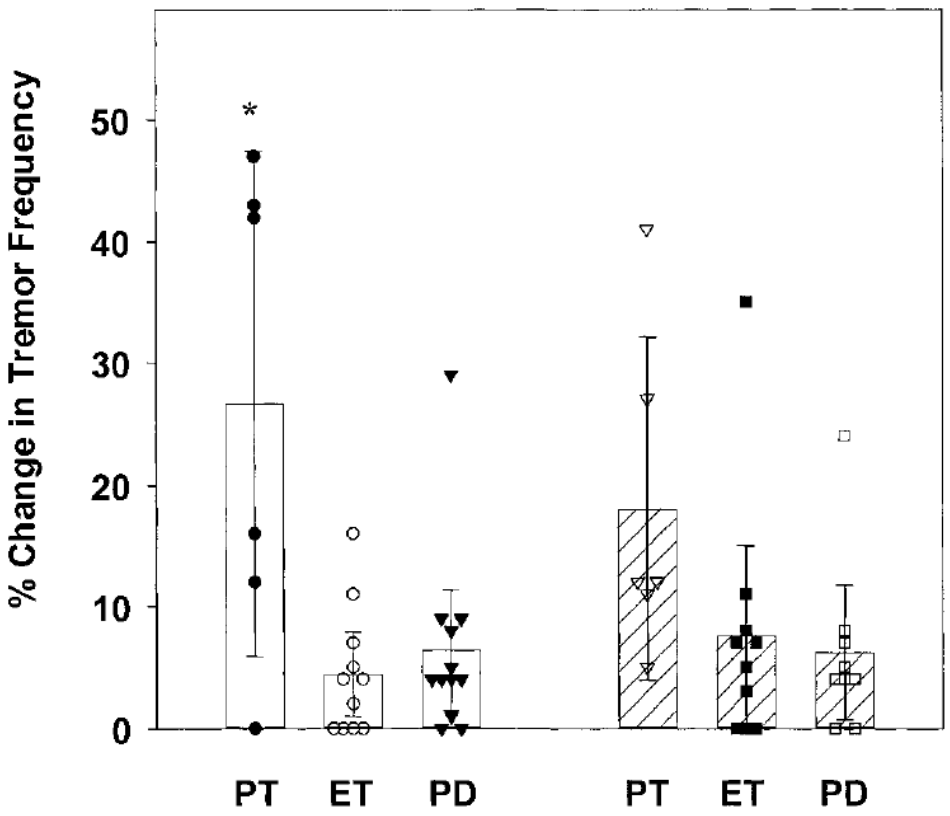


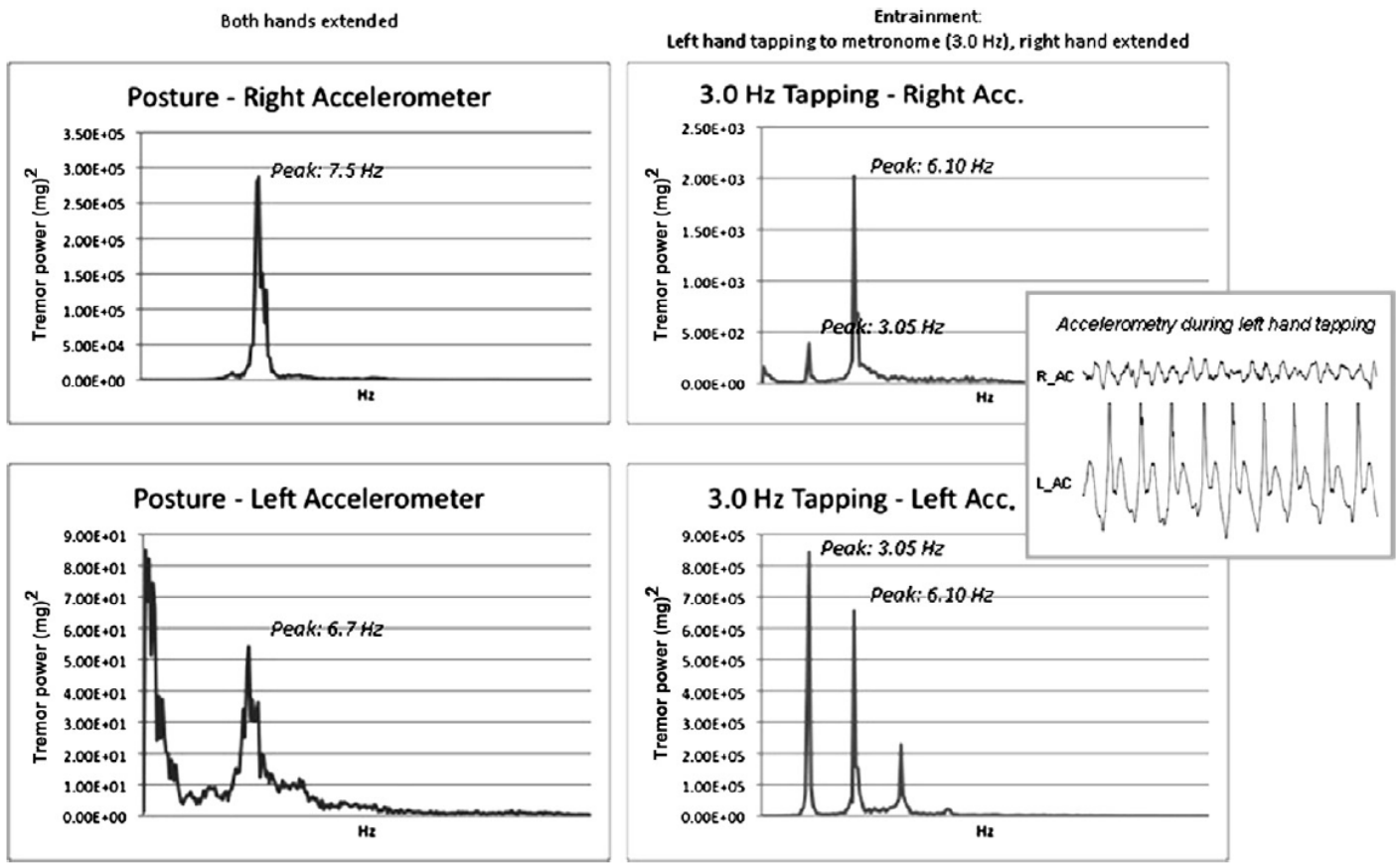


- Compared to other forms of tremor, functional tremor usually shows
  - marked variation in frequency
  - high intermuscular coherence (but orthostatic tremor may as well)
  - pause during ballistic movements with other body parts

O'Suilleabhain and Matsumoto, 1998; Kumru et al., 2004; McAuley and Rothwell, 2004

Movement disorders - tremor





- Tapping test usually results in one of two outcomes

  - increase in frequency variability of functional tremor

  - tremor entrainment

Zeuner et al., 2003; Hallett et al., 2010

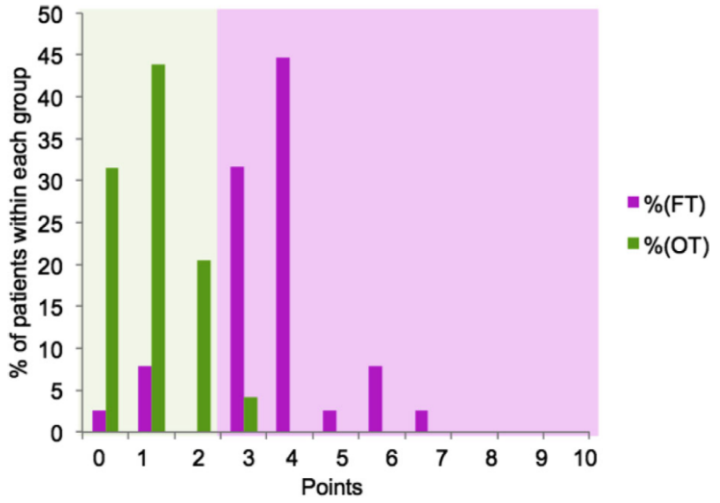
Movement disorders - tremor

- Compared to other forms of tremor, functional tremor usually shows

  - tonic discharge of antagonist muscles approximately 300 milliseconds before tremor onset

  - paradoxical increase in tremor amplitude in response to weight loading

	FT			OT		
	Normal (%)	Abnormal (%)	NA (%)	Normal (%)	Abnormal (%)	NA (%)
Tapping performance at 1 Hz	60.5	39.5	0	100	0	0
Tapping performance at 3 Hz	52.6	47.4	0	86.3	13.7	0
Tapping performance at 5 Hz	60.5	39.5	0	76.7	23.3	0
Tapping response at 1 Hz	68.4	28.9	2.6[a]	80.8	6.8	12.3[a]
Tapping response at 3 Hz	50.0	47.4	2.6[a]	84.9	2.7	12.3[a]
Tapping response at 5 Hz	73.7	23.7	2.6[a]	83.6	6.8	9.6[a]
Ballistic movement response	44.7	52.6	2.6[a]	86.3	1.4	12.3[a]
Tonic coactivation	26.3	39.5	34.2[b]	56.2	1.4	42.5[b]
Coherence test	60.5	18.4	21.1[c]	65.8	5.5	28.8[c]
Loading test	76.3	23.7	0	64.4	35.6	0

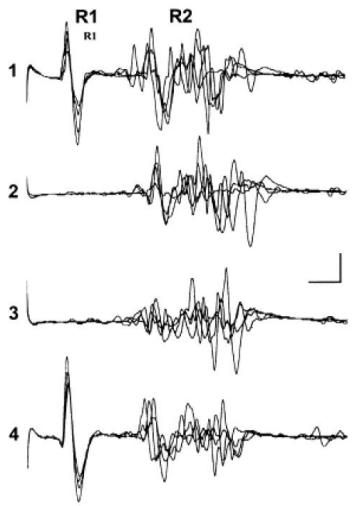


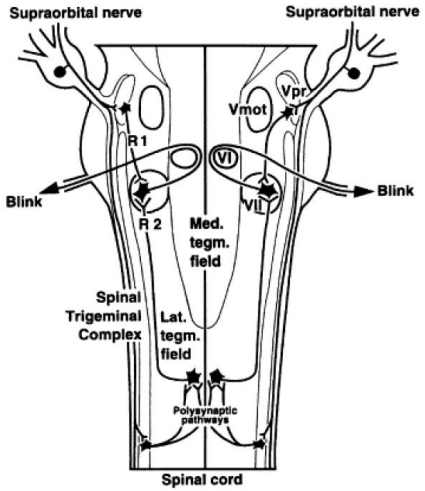
- With an arbitrary cut-off score, the test battery yielded a sensitivity of 89.5% and a specificity of 95.9% in differentiating functional tremor from orthostatic tremor

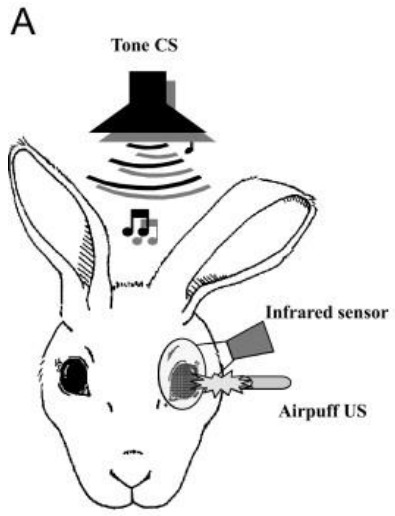
Schwingenschuh et al., 2016

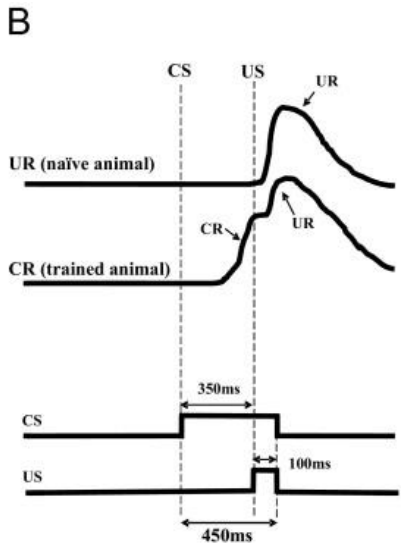
Movement disorders - dystonia

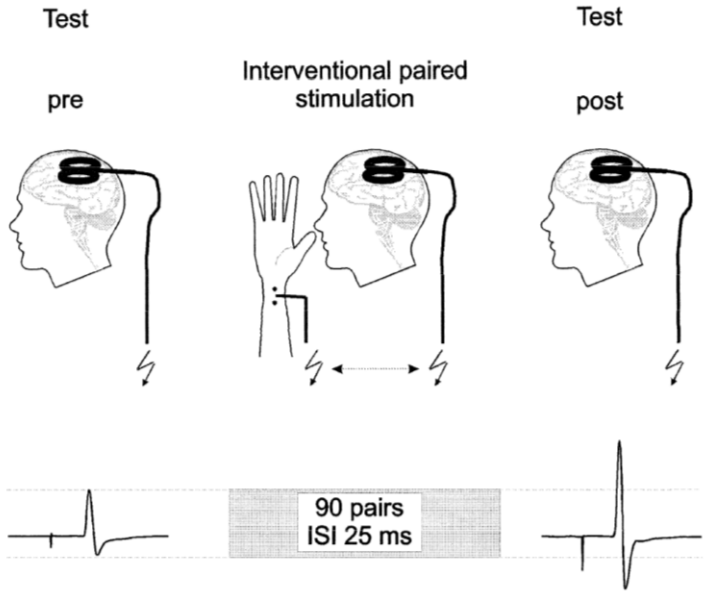
- Most neurophysiological hallmarks of organic dystonia seem to be shared by functional dystonia (e.g., short intracortical inhibition, reciprocal inhibition, somatosensory temporal discrimination threshold)











- Blink reflex recovery cycle

  Paired-pulse electrical stimulation of the supraorbital nerve

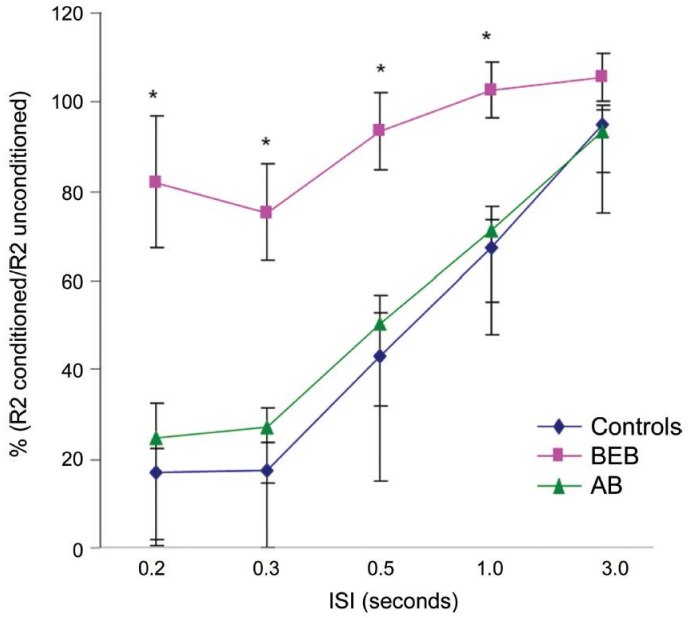
- Eyeblink classical conditioning

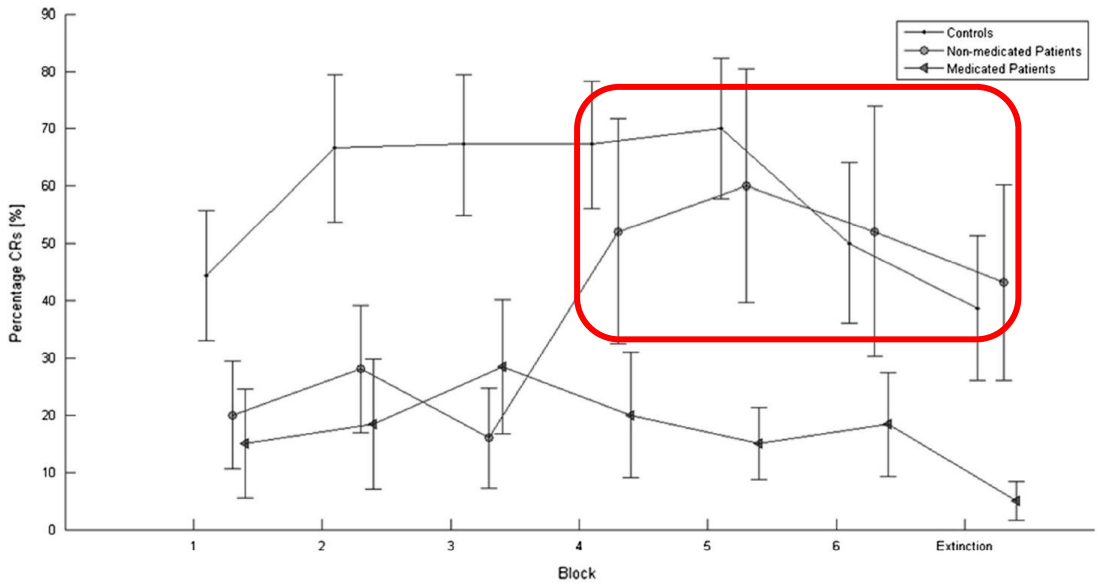
  Coupling between auditory and electrical stimulation

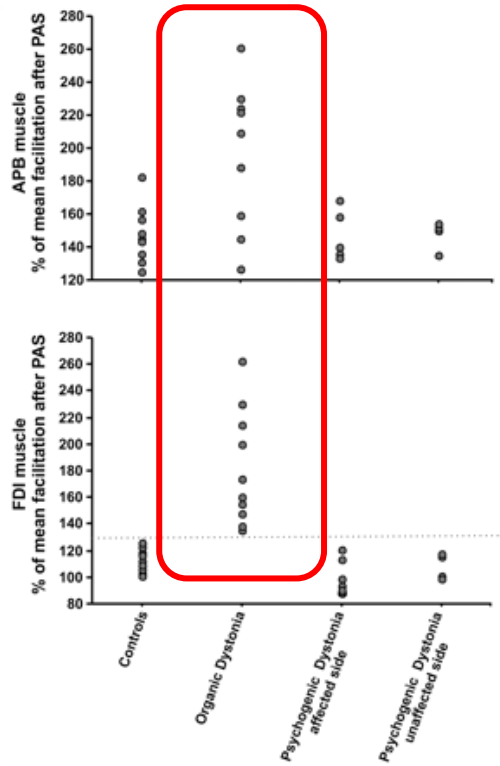
- Paired associative stimulation

  Association between peripheral nerve stimulation and TMS

Movement disorders - dystonia



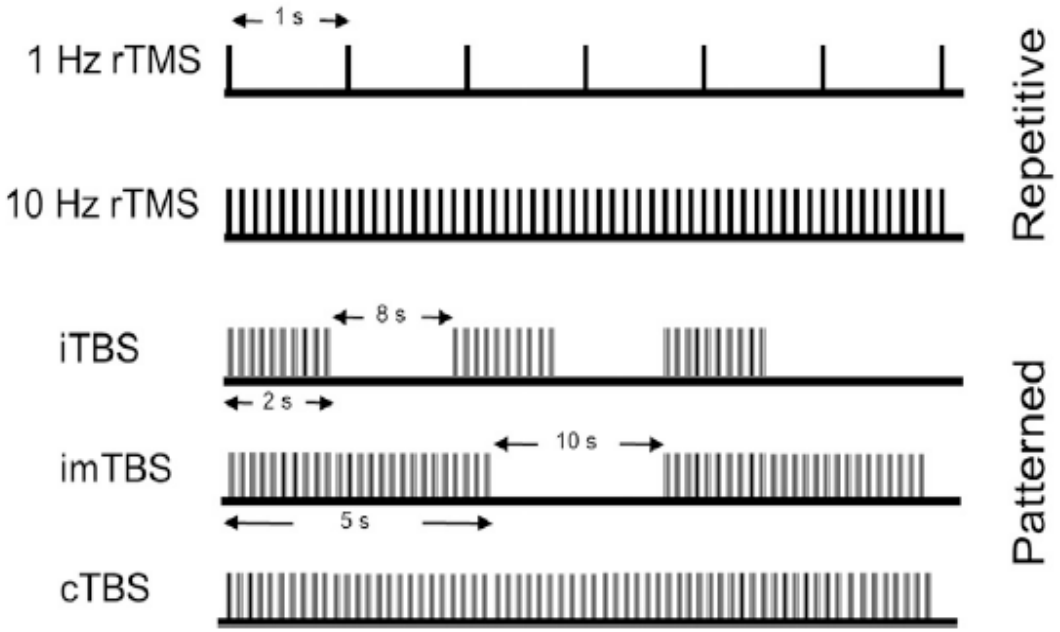




- Blink reflex recovery cycle normal in psychogenic blepharospasm
- Eyeblink classical conditioning and paired associative stimulation normal in suspected psychogenic (mostly fixed) limb dystonia
- Weak evidence

Quartarone et al., 2009; Schwingenschuh et al., 2011; Janssen et al., 2014

Treatment



- small studies (2-20 patients), mostly case series
- often dealing with motor symptoms (weakness/movement disorders)
- heterogeneous TMS protocols – usually low-frequency (≤1 Hz), rarely high-frequency (≥5 Hz)
- different cortical areas targeted, the most common being the primary motor cortex)
- <u>improvement in function generally very good</u>

- Controversies
  - lack of controlled trials (double-blind design, sham stimulation)
  - TMS mostly delivered together with rehabilitation → difficult to assess specific effects
  - placebo effect?

Grazie per l'attenzione

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