Paired-Pulse TMS to one Brain Region

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Paired-Pulse Paradigms

• Sequential pulses applied to the same cortical region
  – Variable intensities
  – Various inter-stimulus intervals (ISIs)

• Terminology
  – Conditional Pulse
  – Test Pulse
Reviewing...
D-waves and I-waves
Paired-Pulse TMS... Why?

“Black box” 1
- Paired-Pulse TMS

“Black box” 2
- H-Reflexes
Main intracortical circuits

- SICI (short-interval intracortical inhibition)
- ICF (intracortical facilitation)
- LICI (long-interval intracortical inhibition)
SICI (short-interval intracortical inhibition)

1. Conditioning TMS
2. Test TMS

Control

Interstimulus interval = 2 ms

Subthreshold CS
Suprathreshold TS
ISI 1-6 milliseconds
SICI attributed to the activation of intracortical processes

• Electrophysiologic evidence

• The conditioning stimulus is sub-threshold
  – No MEP is elicited
  – The activation of this CS did not modulate H-Reflexes (that assess excitability at the level of the spinal motor neuron)

• Thus, effect caused by interneuron activation within motor cortex

SICI attributed to the activation of GABA-a mediated circuits

- Duration of inhibition (20ms) consistent GABA-a-mediated inhibitory postsynaptic potentials in animal preparations.

- SICI (short-interval intracortical inhibition)
  - Benzodiazepine (GABA-a agonist) increases SICI

(Krnjevic et al, 1964; 1965; Ziemann et al, 1996)
Methods (things to look out for...)

• Voluntary contraction reduces SICI
  – Test under resting conditions
  – Monitor the EMG activity
  – Clinical populations

• Intensity of the CS
  – Subthreshold for activation of corticospinal projections
  – Optimal at 70-80% RMT

(Ridding et al, 1995; Di Lazzaro et al, 1998; Kujirai et al, 1993)
SICI in Neurological Populations

• Parkinson’s Disease
• SICI Reduced
• Reduction in SICI correlated with reduced blood-flow in the basal ganglia
• Normalized after dopaminergic treatment
  
• Dystonia
• SICI reduced

(Hanajaima et al, 1996; Ridding et al, 1995)
Main intracortical circuits

• SICI (short-interval intracortical inhibition)
• ICF (intracortical facilitation)
• LICl (long-interval intracortical inhibition)
ICF (intracortical facilitation)

Subthreshold CS
Suprathreshold TS
ISI 8-30 milliseconds
SICI attributed to the activation of intracortical processes

• Electrophysiologic evidence

• The conditioning stimulus is sub-threshold
  – No MEP is elicited
  – The activation of this CS did not modulate H-Reflexes (that assess excitability at the level of the spinal motor neuron)

• Thus, effect caused by interneuron activation within motor cortex

(Ziemann et al., 1996)
ICF attributed to net-facilitation in NMDA mediated intracortical circuits

- Net-facilitation: combination of prevailing facilitation and weaker inhibition

- Mediated by glutamatergic NMDA receptors
  - Decreased ICF with NMDA receptor antagonists

- Less consistent between-individuals

- Clinical usefulness??

(Ziemann et al, 1998)
Main intracortical circuits

- SICI (short-interval intracortical inhibition)
- ICF (intracortical facilitation)
- LICI (long-interval intracortical inhibition)
LICI (long-interval intracortical inhibition)

CS suprathreshold
TS suprathreshold
ISIs 50-200 milliseconds

(Valls-Sole et al, 1992)
LICI attributed to the activation of GABA-b mediated intracortical circuits

- Electrophysiologic evidence indicating that spinal networks were not affected by LICI

- Pharmacological evidence
  - Baclofen (GABA-b receptor agonist) enhances LICI

(Nakamura et al, 1995; 1997; Mc Donnel et al, 2006)
LICI in clinical neurologic conditions

• Parkinson’s disease
  – LICI enhanced
  – Correlation between enhanced LICI and severity of bradykinesia

• Cerebellar ataxia
  – LICI enhanced

(Berardelli et al, 1996; Tamburin et al, 2004)
Practical step-by-step guide

1. Determination of the “hot-spot” for target muscle
2. Determination of motor threshold for target muscle
3. Baseline MEPs at threshold (typically 50 responses)
4. Paired-pulse measures (typically 50 responses also)
Thank you!

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