Peripheral and Central Stimulation

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Investigating Hebbian principles of neural plasticity in humans
"Cells that fire together, wire together"

How can we induce plastic changes at the brain level?

*Paired Associative Stimulation (PAS)*
*Or when the peripheral stimulation meets the MEP*

How can we induce plastic changes at the spinal level?

*Spinal Associative Stimulation (SAS)*
*Or when the central stimulation meets the H-reflex*
How do we measure cortical excitability? The MEP

**TMS**

M1

**Magnetic Stimulator**

**EMG Instrument**

**MEP**

**STIMULUS**
Induction of plasticity in the human motor cortex by paired associative stimulation

Katja Stefan, Erwin Kunesch, Leonardo G. Cohen, Reiner Benecke and Joseph Classen

Test
pre

Interventional paired stimulation

Test
post

Electrical stimulation of right median nerve

TMS of left M1 hand representation

90 pairs ISI 25 ms
Induction of time-dependent plasticity in the motor cortex

(A) pre post

ISI 25 ms
ISI 100 ms
ISI 525 ms
ISI 5000 ms

(B) Amplitude (mV)

pre post

25 1000 525 5000

ISI (ms)

(C) Amplitude change (percent of baseline)

(D) Silent period duration (ms)

Stefan et al, Brain, 2000
Changes in cortical excitability were no due to changes in spinal excitability: MEPs and F-waves

Stefan et al, Brain, 2000
• The increase of cortical excitability (MEP amplitude) was dependent on the synchronous **timing** between the afferent and the magnetic stimulation.

• Plasticity induced by PAS 1. evolved rapidly (within 30 min), 2. was persistent (minimum duration 30-60 min) yet reversible, and 3. was topographically specific – properties signature of associative **long-term potentiation (LTP)**.
How do we measure spinal excitability? The H-REFLEX
Effect of Stimulus Intensity - M Response & H Reflex

Low Intensity
PNS

M-Response

H-Reflex

Increased Intensity
PNS

Smaller
H-Reflex

Larger
M Response
SAS protocol:

Spinal associative stimulation: A non-invasive stimulation paradigm to modulate spinal excitability

Mar Cortes, Gary W. Thickbroom, Josep Valls-Sole, Alvaro Pascual-Leone, Dylan J. Edwards

Diagram:
- PRE: H-Reflex RC
- INTERVENTION (15 min)
- POST: H-Reflex RC
- 0.1 Hz paired stimuli
- 20 ms interval
- 90 paired stimuli
Peripheral stimulation of somatosensory afferents conditioned by low frequency TMS, increases spinal excitability

SAS protocol:
Repetitive paired stimulation can induce changes in *spinal excitability*.

**Diagram a:**
- TMS
- PNS
- TMS<sub>latent</sub> Only
- PNS Only
- Combined TMS<sub>latent</sub>+PNS
- 100µV
- 20ms

**Diagram b:**
- H-reflex Amplitude (mV)
- NO TMS
- TMS

*Graph:* $y = 0.017x + 0.7742$
$R^2 = 0.97303$

*Cortes et al, Clin Neurophysiology, 2011*
Left shift of the RC post-intervention

Amplitude

Standard Deviation

PRE H-Reflex Recruitment Curve

Individual POST Recruitment Curves

Cortes et al, Clin Neurophysiology, 2011
REFERENCES: