Plasticity Inducing Protocols
Plasticity: TMS Operational Definition

Plasticity: “The brain’s ability to constantly change, grow and reorganize over the course of a lifetime.”

Any change in the outcome measure that outlasts the TMS application can be thought of as a plastic response of the brain.
Noninvasive Protocols that Lead to Plastic Changes

- TDCS
- Conventional rTMS protocols (inter-pulse interval)
- Patterned rTMS protocols (inter-pulse and inter-train interval)
- Paired Associative Stimulation Protocols
- Combinations
tDCS

- Anodal = generally facilitatory
- Cathodal = generally inhibitory
rTMS protocols

Conventional rTMS

1 Hz eTBS

5 Hz iTBS

10 Hz imTBS

20 Hz QPS

Patterned rTMS

200 ms (3 pulses at 50 Hz)

100 ms

20 s (5 Hz)

8 s

2 s

10 s

5 s

1 s

ISI = 1.5, 5, 10, 30, 50, 100, 1250 ms

5 s

7.5 s - 8.5 s

360 trains
Effects of Conventional rTMS

Maeda et al., 2000
Theta Burst Stimulation

- Theta Burst stimulation
  - 3 Pulses of TMS at 50 Hz with a 200 ms Intertrain Interval (total of 200 trains)
- Continuous Theta Burst Stimulation (40 sec)
- Intermittent Theta Burst Stimulation (190 sec)
  - 2 seconds (10 trains) repeated every 10 seconds

Huang et al., 2005
Why Theta Burst Stimulation?

- Rat Hippocampal cells fire in bursts of theta frequency during learning.
- Human EEG Theta frequency increases during learning.
- Time course of MEP change is similar to LTP and LTD in slice preparations.
- Modulated by GABA and Glutamate, like LTP and LTD.
Theta Burst Stimulation

- Effect of TBS

Huang et al., 2005

im=5 sec train repeated every 15 sec for 110 sec
Computational Model of effects of TBS

Huang et al., 2011
TBS in Aging

A

Genetic factors
environmental factors

Brain plasticity

Expression of certain genes
Insult (e.g., TBI or stroke)
Poor diet
Lack of exercise
Stress
Diabetes mellitus

Cognitive ability
Age

B

Genetic factors
environmental factors

Brain plasticity

Different starting point
Different slope

Cognitive ability
Age
TBS in clinical populations

Red = individuals with autism
Blue = healthy controls

Green = individuals with schizophrenia
Blue = healthy controls
Running is the neurogenic and neurotrophic stimulus in environmental enrichment

CON=control
EEO=enriched environment (only)
RUN=running
EER=enriched environment + running

(Mustroph et al, 2012; Kobilo et al, 2011)
Running enhances LTP

- Training
dose = 4.7km ± 0.41
- Over 10 days
- Neurogenesis
- Morris water maze

(van Praag et al, 2009)
TBS and exercise

Pre-exercise

Responses “pushed out” the 95% confidence interval

Post-exercise
Paired Associative Stimulation: Sensory-Motor Plasticity

Stefan et al., 2000
What you should know...

• Effects are influenced in both duration and direction by:
  – Intensity of Stimulation
  – Duration of Stimulation
  – Location of Stimulation
  – Sensitivity of outcome measure
  – Time of Day (Sale et al., 2007)
  – Attention (Stephan et al., 2004)
  – Hormones (Smith et al., 1999)
  – Brain State

• Inter and intra-individual differences:
  – 1 Hz can be facilitatory in some individuals
  – Only approximately 50% of individuals respond to PAS
  – TBS has high intraindividual reliability, PAS does not.
Example of Brainstate affecting rTMS effect

- 1mA 10mins tDCS
- rTMS at 5Hz 100stim train at AMT – decreases SICI, but not lasting change in excitability as tested by single pulse TMS
- Result = after effects of tDCS can generate opposite effects of rTMS or conversely can alter the after effects of tDCS

Lang et al., 2004
Step-by-Step Procedure

• 1. Find hot-spot
• 2. Find active motor threshold
• 3. Baseline single-pulse measures
• 4. TBS (cTBS or iTBS)
• 5. Post-TBS assessments (single-pulse TMS)
  – T5
  – T10
  – T20
  – T30