Non-Invasive Brain Stimulation and Behavioral Therapy

Considerations

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Limitations and advantages of restorative methods….?

- Pharmacology
- Brain Stimulation
- Behavioral Intervention

- Smaller Coil
- Focality / Specificity
- Network activation

Adaptive
Plasticity
Maladaptive

How does repetitive behavior affect motor cortex?
Rapid formation and selective stabilization of synapses for enduring motor memories

Simple repetitive finger movements increase excitability

Motor map changes with skilled practice

How does NIBS affect motor cortex?

Effects of Repetitive Motor Training on Movement Representations in Adult Squirrel Monkeys: Role of Use versus Learning

Extensive training of elementary finger tapping movements changes the pattern of motor cortex excitability

How does NIBS affect motor cortex?
**Rate-dependent TMS protocols**

Rate-dependent TMS protocols can be categorized into three main types: Excitatory, Inhibitory, and rate-dependent protocols. Excitatory TMS protocols include high-frequency TMS (~10Hz) and intermittent TMS, which can be further divided into 2 sec and 8 sec intervals. Inhibitory TMS protocols include low-frequency TMS (~1Hz) and continuous TMS.

**TMS correlates**

- **Resting MT**
- **Transcallosal Inhibition**
- **MEP Amplitude**

**Functional Improvements**

- **sRT/cRT**
- **Pinch force acceleration**
- **Fingers/thumb AROM**
- **Movement accuracy**
- **Purdue Pegboard**
- **JTT**

**IMPROVED CORTICOMOTOR OUTPUT FROM IPSI-LESIONAL M1 & IMPROVED MOTOR BEHAVIOUR**

- **Webster et al. (2006)**
- **Hummel et al., 2005**
- **Khedr et al., 2005**
- **Talelli et al., 2007**
- **Kim et al., 2006**
- **Hummel et al., 2006**
- **Khedr et al., 2005**
- **Boggio et al., 2006**
- **Mansur et al., 2005**
- **Takeuchi et al., 2005**
- **Fregni et al., 2005**
- **Fregni et al., 2006**
- **Werhahn, et al., 2003**

**“An excited neuron tends to decrease its discharge to inactive neurons, and increase this discharge to any active neuron, and therefore to form a route to it, whether there are intervening neurons between the two or not. With repetition, this tendency is prepotent in the formation of neural routes”**

(Hebb, 1932, p.13).
How does combined intervention affect motor cortex?

Is coupling NIBS with therapy good?

Alteration cortical excitability before repetitive synaptic activity


• tDCS: 1mA 10min tDCS
• rTMS at 5Hz 100stim train at 1.0tDCS – 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

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Motor systems example

If...

Motor Training = improvement in function ‘X’
and...
tDCS = improvement in function ‘X’
does...

Motor Training + tDCS = improvement in function 2X, X^2, or 0??
Anodal tDCS combined with robotic motor training

Movement Speed (peak, mean)
Movement Smoothness
Aim Deviation

Highest correlation with clinical function

“Kinematic Robot-Based Evaluation Scales and Clinical Counterparts to Measure Upper Limb Motor Performance in Patients With Chronic Stroke” (Boscher et al, 2009)

Combined tDCS-Robotic Training Study Design

- 60 patients, Right hemiparesis
- >6mnths post first ischemic stroke
- Robotic protocol alternates S/E-wrist robot across sessions
- tDCS 2mA, 35cm² 0.9% NaCl soaked sponges

Robotics with brain stimulation in patients with motor dysfunction

Superior functional gains with Nexstim NBT

Navigation makes a difference; Upper extremity Fugl-Meyer scores

Preclinical data for Nexstim NICHE Trial 2014
Conclusions

- Brain state influences the response to neuromodulation
- Homeostatic mechanisms may oppose further enhancement when interventions are combined
- Combined neuromodulation & behavioural therapy can be effective
- The optimal circumstances require further investigation

Other cortical areas?