Non-invasive Cerebellar Stimulation (tDCS): Background, Methods And Applications

Pablo Celnik, MD
Associate Professor
Vice-Chair for Research, Dept. of Physical Medicine and Rehabilitation
Dept. of Neurology
Dept. of Neuroscience
Johns Hopkins University
Introduction

Since the discovery of electricity and magnets, humans have been curious about stimulating the brain.

Only recently, we have began to understand how this technology works and how we can use it.

transcranial Direct Current Stimulation (tDCS)
tDCS: early animal studies

• Direct stimulation of the surface of the cat brain has a marked effect on spontaneous activity of motor cortex cells.

• Anodal causes an increase

• Cathodal causes cessation

Purpura & McMurtry (1964)
tDCS: early animal studies

- tDCS does not cause direct depolarization as TMS does (blasting the neuron forcing it to fire). However, it increases cell polarity bringing it closer to a depolarized (anodal) or hyperpolarized (cathodal) state.

- Anodal tDCS results in cortical neurones to be depolarized at a subthreshold level (ie) requires less stimulus input.

Purpura & McMurtry (1964)
tDCS: early animal studies

• If prolonged stimulation is applied, increase in EPSP size and evoked synaptic activities (Local field potentials) occur.
tDCS: Early human studies

- 4 seconds of tDCS can change the underlying excitability of the M1, without long lasting aftereffects.

- Sodium (carbamazepine) and calcium (flunarizine) channel blocker inhibit anodal effect.

- This supports the notion that anodal tDCS causes neuronal depolarization through the influx of sodium/calcium into the cell.
tDCS: Long lasting effects

- 9-13 minutes of stimulation generates after-effects that last for an hour (Nitsche et al., 2000).
- Sodium and calcium blockers inhibit anodal aftereffect.
- NMDA receptor antagonist (dextromethorphan) inhibits both anodal/cathodal aftereffect.

tDCS: mechanisms

• Anodal tDCS induces NMDA receptor dependent LTP, and requires coupling of DCS with synaptic activity.

• Combined tDCS and synaptic activity enhances BDNF secretion and TrkB activation.

(Fritsch et al. Neuron 2010)
tDCS: methods

- **tDCS** is applied through two surface electrodes placed on the skull.

- Depending on duration and polarity of the stimulation can increase or depress excitability from minutes to 1-2 hours.
  
  - **Anodal** => INCREASES excitability
  - **Cathodal** => DECREASES excitability
tDCS: methods

• http://youtu.be/hp6bBs16g28?t=1m5s

• http://youtu.be/gWV9tJ_Ccq0?t=50s

tDCS: Applications!!
Can we modulate cerebellar excitability with tDCS?

- Crossover counterbalance design study (n=9)
- Anodal, Cathodal or Sham tDCS (2mA intensity, 25min).
- A neuronavigation device ensured coil positions consistency within and between sessions.

Assessing CB-M1 connections in humans

(Ugawa 1994, 1995; Werhan 1996; Pinto & Chen 2001; Daskalakis & Chen 2004)
Assessing CB-M1 connections in humans

(Ugawa 1994, 1995; Werhan 1996; Pinto & Chen 2001; Daskalakis & Chen 2004)
tDCS modulates cerebellar excitability in a polarity specific manner

Anodal tDCS increased cerebellar excitability
Cathodal tDCS decreased cerebellar excitability
The effect is dose dependent and last up to 30 mins.

Facilitation

Inhibition

Pre anodal tDCS
Post anodal tDCS

Inhibition

Pre
Post

CBI

1mA cathodal
2mA cathodal
Sham (Experiment 1)

Facilitation
Inhibition

Cerebellar tDCS does not affect M1 excitability

M1 excitability assessment

Cerebellar tDCS does **not** affect brainstem excitability

Brainstem excitability assessment

**Brainstem MEP threshold**

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**Right M1**

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<th>Anodal</th>
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**Brainstem MEP amplitude**

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**Eye-blink reflex: R1 amplitude**

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<th>1mA cathodal Pre</th>
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<th>2mA Pre</th>
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<td>R1 amplitude (mV)</td>
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Can we assess cerebellar excitability changes associated to learning?

**Locomotor Adaptation**

- Human locomotor adaptation is thought to involve the cerebellum.
- People with cerebellar damage have difficulty adapting to novel environmental demands (Martin et al., 1996; Smith and Shadmehr, 2005; Morton and Bastian, 2006).
- Neurophysiological studies in animals indicated that this motor adaptation may be mediated via long term-depression (LTD) in cerebellar Purkinje cells (Gilbert and Thach, 1977; Medina et al., 2000).
- We hypothesized that adaption in a split-belt walking paradigm would reduced the excitability of cerebellar-M1 connections (Jayaram et al. Cereb. Cortex 2011)
Locomotor adaptation

(Jayaram et al. Cereb. Cortex 2011)
Locomotor adaptation

(TMS) (Jayaram et al. Cereb. Cortex 2011)
Locomotor adaptation results in reduction of CBI

(Jayaram et al. Cereb. Cortex 2011)
CBI changes correlate with the magnitude of adaptation

Change in CBI vs After-effect

Change in CBI vs Magnitude of Adaptation

more adaptation

Less CBI

Step Symmetry

Catch Trial

More Adaptation

Less CBI

Step Symmetry

Adaptation

r = 0.77

r = 0.79

(Jayaram et al. Cereb. Cortex 2011)
Potential cerebellar substrate to this form of adaptation

The reduction of CBI is consistent with Purkinje cell LTD
Can we enhance motor learning using tDCS?

Since the cerebellum is involved in acquisition, we hypothesized that enhancing cerebellar activity would result in larger acquisition, whereas enhancing M1 would elicit larger retention.

Galea et al. Cereb. Cortex 2011
Cerebellar tDCS enhances adaptive learning

Galea et al. Cereb. Cortex 2011
tDCS enhances adaptive learning and retention

Different motor learning processes can be enhanced by tDCS
- M1 increases retention
- Cerebellum enhances acquisition

Galea et al. Cereb. Cortex 2011
Conclusions

• transcranial Direct Current Stimulation is a useful non-invasive stimulation technique to study CNS physiology and behavior.

• tDCS can modulate (enhance or inhibit) the excitability of different brain regions, including the cerebellum.

• tDCS can enhance different behaviors, i.e. motor learning, and their components, i.e. acquisition or retention.

• tDCS has the potential to become a useful therapeutic intervention for neurological patients.
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