Non-invasive strategies for affective neuromodulation

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Disclosure (relevant to presentation)

The City University of New York: Patents on brain stimulation. Soterix Medical: Co-founder, Produces tDCS and High-Definition tDCS. Boston Scientific: Neuromodulation Scientific Advisory Board GlaxoSmithKline (GSK) Life Science Scientific Advisory Board

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What defines neuromodulation technologies is how energy is delivered to what target.

- **Implants**: Deep Brain Stimulation (DBS), Spinal Cord Stimulation (SCS)
- **In-Hospital**: Transcranial Magnetic Stimulation (TMS), Electroconvulsive Therapy
- **Wearable**: Transcranial Electrical Stimulation (tES), Transcranial Direct Current Stimulation (tDCS)
What defines neuromodulation technologies is how energy is delivered to what target.

- **Implants**
  - Deep Brain Stimulation (DBS)
  - Spinal Cord Stimulation (SCS)

- **In-Hospital**
  - Transcranial Magnetic Stimulation (TMS)
  - Electroconvulsive Therapy

- **Wearable**
  - Transcranial Electrical Stimulation (tES)
  - Transcranial Direct Current Stimulation (tDCS)
tDCS: transcranial Direct Current Stimulation

Cathode (-) Electrode

Anode (+) Electrode

20 minute session 5x per week

“Anodal” / “Cathodal” refer to proximity of target
tDSC: Transcranial Direct Current Stimulation

• Hand-held device, head gear
• 20 minute session, 2 mA via scalp electrodes
• Modulator of brain excitability and plasticity
• > 400 controlled trials across neurological / psychiatric inductions + performance
• Remote supervised (home)
Noninvasive brain stimulation treatments for addiction and major depression

Katharine Dunlop, Colleen A. Hanlon, and Jonathan Downar

Transcranial direct current stimulation to prevent and treat surgery-induced opioid dependence: a systematic review

Alessia Gallucci, Pedro H Lucena, Géraldine Martens, Aurore Thibaut & Felipe Fregni
How does tDCS work?
How does tDCS work?

How should neuromodulation interventions for affective disorders or addiction be designed?
tDCS

Experimentally-verified Anatomical MRI derived models of current flow

tDCS

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tDCS

High Definition tDCS

Circuit therapeutics

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High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow

Circuit therapeutics

Non-invasive electrical targeting

- Software allows you to steer currents to targeted brain regions
- Single programmable device and head-gear

How does tDCS work?

How should neuromodulation interventions for affective disorders or addiction be designed?
tDCS boosts learning
High-intensity Pulses

- Over-driving a neural network
- Neuromodulation comes from secondary non-linear changes

Low-intensity DC

Deep Brain Stimulation | Motor Cortex Stimulation | Transcranial Magnetic Stimulation (TMS)
High-intensity Pulses

Low-intensity DC

Over-driving a neural network
High-intensity Pulses

Over-driving a neural network

Low-intensity DC
High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Interacting with specific activity in a neural network (Neuromodulation)

Transcranial Direct Current Stimulation (tDCS)
Electrode

Network of interest (e.g. depression, math cells)

Other networks – not targets for neuromodulation

Preferential modulation of more active network (activity dependent)

Current flow across entire brain region

tDCS changes excitability
"Cathodal" tDCS
Soma hyper-polarized
Apical dendrite depolarized

"Anodal" tDCS
Soma depolarized
Apical dendrite hyper-polarized
tDCS: Sustained weak polarization

Brain slice: Optical Mapping with Voltage Sensitive Dyes

Bikson et al. Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices. *J Physiol* 2004
Synaptic efficacy is modulated by Direct Current (pathway + polarity specific)

Evoked Response + Cathodal or Anodal Direct Current Stimulation

Synaptic efficacy is modulated by Direct Current (pathway + polarity specific)

- Direct Current stimulation does not generate synaptic activity or neuronal firing (*Functional Targeting*)

tDCS boosts learning
Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current Stimulation (DCS)

Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current Stimulation (DCS)

• DCS does generate synaptic plasticity de novo (Activity Dependent)

Repeated DCS accelerates LTP and boosts the ceiling for synaptic learning

- Hypothesis: Combing Direct Current stimulation with ongoing training of a task may enhance the rate and ceiling learning specifically of that task (Activity Dependent)

tDCS applied with a task. Specificity comes from the task. tDCS makes the task (therapy) more effective.
How does a tool to modulate excitability or plasticity treat addiction?

How should neuromodulation interventions for affective disorders or addiction be designed?
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Novel cellular targets of tDCS support Functional Targeting Coupled Neuro-Vascular Hypothesis of Neuromodulation