Frontiers of Neuromodulation Technologies

8th Annual Psychology Research Day

UNIVERSITY OF NEW MEXICO
April 18, 2013

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$ NIH, NSF, Epilepsy Foundation, Wallace Coulter Foundation, DoD  COI: Soterix Medical Inc.
What is Neuromodulation?

- Definition: Use of applied electricity to modulate brain function.
- The name of neuromodulation technology is defined by how electricity is delivered (some letters ending with “s”).
- More specifically, the “dose” of neuromodulation is set by two things:
  - The position and shape of the electrodes / coil
  - The electrical waveform (shape) applied to the electrodes / coil
- Whatever neuromodulation outcomes: are a function of the dose combined with relevant subject parameters (e.g. brain state)
What is Neuromodulation?

- Whatever neuromodulation outcomes: are a function of the **dose** combined with relevant subject parameters (e.g. brain state)

**Deep Brain Stimulation (DBS)**
- **Dose:** electrodes inside brain, high intensity
  - Very Targeted
  - Safety + Reversibility Concerns
  - Costly

**Transcranial Magnetic Stimulation (TMS)**
- **Dose:** Coil outside head, high intensity
  - Somewhat Targeted
  - Mostly Safe (limited clinic)
  - Not cheap (equipment, resources)

**Transcranial Direct Current Stimulation (tDCS)**
- **Dose:** Electrodes outside head, low intensity
  - Somewhat Targeted
  - Safe and cheap (deployable)
  - Well tolerated (Adjunct to other therapies)
Why Neuromodulation?

Goal: Treatment of neuropsychiatric disorders, enhance rehabilitation, modulate learning, study brain function* …

*using electricity to probe and elicit responses is foundational to discoveries on brain function

Rationale:
• Brain is an electrical organ and so responds to electricity.
• Brain function and disease have electrical analogues.
• Efficacy and safety derive from control of dose and subject parameters.
• Achieves outcomes not possible with other techniques (on their own).

Frontiers

- Specify of outcome by targeting brain regions implicated in behavior/disease.
- Unique and powerful outcomes through electrical sensitive processes.
- Individualized therapy tunable and customized
- Safe, tolerated, with minimal side-effects (reversible, no residue)
- Cost / Access (battery: hundreds of subjects/years of treatment)
Transcranial Direct Current Stimulation (tDCS)

- Non-invasive, portable, well-tolerated neuromodulation.
- Low-intensity (mA) current passed between scalp electrodes.
- Investigated for cognitive neuroscience and neuropsychiatric treatment.

- How can a “simple” intervention modulate brain function?
- How is specificity of action achieved?
Transcranial Direct Current Stimulation (tDCS)

- Two pad electrodes placed on head and connected to DC current stimulator.
- Current passed between ANODE(+) and CATHODE(-)
- DC CURRENT FLOW across cortex.
- Current is INWARD under ANODE and OUTWARD under CATHODE

MRI derived computational model
Transcranial Direct Current Stimulation (tDCS)
Transcranial Direct Current Stimulation (tDCS)
Transcranial Direct Current Stimulation (tDCS)

Anode (+)

Current flow
outward → inward

Head Surface

Hyperpolarized cell compartments

Depolarized cell compartments

Increased Excitability / Plasticity
Transcranial Direct Current Stimulation (tDCS)

Cathode (-)

Head Surface

Current Flow

Inward

Current flow

Outward

Decreased Excitability / Plasticity

Hyper-polarized cell compartments

Depolarized cell compartments
Transcranial Direct Current Stimulation (tDCS)

Current flow

- Inward
- Outward

Depolarized soma

Increased Excitability / Plasticity

Hyperpolarized soma

Decreased Excitability / Plasticity
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MRI derived computational model

Brain current intensity

Brain current direction

LEFT SIDE VIEW

RIGHT SIDE VIEW
tDCS Dose is those parameters controlled by operator
Electrode number, size, current at each electrode

- Tremendous flexibility in dose selection (with a single device).
- tDCS dose determines brain current flow and so which regions are targeted. **Specificity.**
tDCS dose: Targeted modulation of cortex

- Total of 5 small “HD” electrodes (4+1)
- 1 Center electrode over target determines polarity (anode, cathode)
- 4 return electrodes - Ring radius determines modulation area
tDCS dose optimization

How do you select an electrode montage?

**tDCS Dose**: Number, shape, location, current at each electrode

Practical limitations:
Hardware (number of electrodes) and safety limitations (total current)

Given a brain target, where to apply current on the scalp
Given a brain region of interest, which electrodes should be activated?

- Target brain region is selected.
- Targeting software automatically determines “best” dose (current applied to each electrode).
- Dose perception delivered through programmed tDCS device.
• Given a brain region of interest, which electrodes should be activated?
• Dose be customized and optimized to individuals? (obesity, extremes of age, injury, stroke…)
  ➢ Subject specific MRIs processed
  ➢ Dose adjusted (normalized) to account for individual differences
tDCS dose: Turn-key targeting software

- Given a brain region of interest, which electrodes should be activated?
- Dose be customized and optimized to individuals? (obesity, extremes of age, injury, stroke…)

[Diagram showing process flow of treatment and configuration]
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Targeting brain regions with electrotherapy

*Therapeutic electricity is delivered through electrodes*

- **Electrodes implanted near brain targets**
  - Medtronic

- **Non-invasive electrodes positioned on scalp**
  - Soterix Medical
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tDCS mechanisms
tDCS mechanisms: Neuromodulation
tDCS mechanisms: Neuromodulation

High-intensity Pulses  Low-intensity DC

Over-driving a neural network
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Low-intensity DC

Over-driving a neural network
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Low-intensity DC

Over-driving a neural network
tDGS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Interacting with specific activity in a neural network
tDCS mechanisms: Neuromodulation

Low-intensity DC + specific network activation
tDCS mechanisms: Neuromodulation

Low-intensity DC + specific network activation

Current flow across entire region
tDCS mechanisms: Neuromodulation

Low-intensity DC + specific network activation

Current flow across entire region

Modulation (plasticity) of only co-activated neurons
tDCS mechanisms: Neuromodulation

- Synapse level specificity of direct current stimulation shown in rat cortical brain slice.
tDCS mechanisms: Neuromodulation

- Quantitative multi-scale models of tDCS modulated learning in sleep
- Full cellular to human behavior/learning integration
tDCS mechanisms: Animal, Neuron modeling, and Human studies

- tDCS produces low-intensity brain currents well below action potential firing threshold.
- Ongoing neuronal activity is sensitive to small perturbations by electrical current – including oscillations and synaptic processing.
- Neuromodulation may be specific to coactivated normal or pathological networks – providing specificity.
- Plasticity may be promoted by weak electric current.
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