Transcranial Direct Current Stimulation and the Folded, Active Plastic Brain

Marom Bikson

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Transcranial Direct Current Stimulation (tDCS)

- Non-invasive, portable (9V), well-tolerated neuromodulation.
- Low-intensity (mA) current passed between scalp electrodes.
- Tested for cognitive neuroscience and neuropsychiatric treatment and neurorehabilitation.

Ø How can a 9V battery do anything for the complex brain?
Ø How is specificity of action achieved?

Depression, Pain, Migraine, Epilepsy, PTSD, Schizophrenia, Tinnitus, Neglect, Rehabilitation (motor, aphasia), TBI, OCD, Attention / Vigilance, Accelerated learning (reading, motor skills, math, threat detection), Memory, Creativity, Sleep (SW, Lucid dreaming, Threat detection, Impulsivity, Compassion, Jelousy, Reality Filtering, IQ, Prejudice…
How can a 9V battery do anything for the complex brain?
How is specificity of action achieved?
How can a 9V battery do anything for the complex brain?
How is specificity of action achieved?

Through **anatomical targeting** of specific brain regions.

Can be studied using computational models of current flow.
tDCS electrode position on the head determines which regions are stimulated.

Specificity may be facilitated by positioning electrodes to “target” specific brain regions.

Truong et al. Clinician accessible tools for GUI computational models. “BONSAI” and “SPHERES”. Brain Stimulation 2014
tDCS electrode position on the head determines which regions are stimulated.

(!) Must consider both anode and cathode electrodes.

Datta et al. Electrode montages for tDCS: Role of "return" electrode *Clinical Neurophys*. 2010
tDCS: Directional current flow → directional polarization → directional excitability and plasticity changes

Disclaimer: Rest of talk will show all this can be wrong.
High-Definition tDCS uses arrays of electrodes to focus current to targets.

Software allows you to generate subject and target specific tDCS “formulation”.

“4x1” montage of High-Definition tDCS

Non-invasive electrical targeting of selected cortex

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How can a 9V battery do anything for the complex brain?
How is specificity of action achieved?

Through **functional targeting** of specific brain regions.

Can be studied using brain slices models of synaptic efficacy and plasticity.
From Anatomical Targeting to Task Targeting

Network of interest (e.g. depression, pain network)  Other networks – not targets for neuromodulation

Current flow across entire region

Preferential modulation of selected active neurons

Bikson et al. Origins of specificity during tDCS. *Front Human Neuro* 2013
Synaptic efficacy is modulated by Direct Current (polarity specific)

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

Direct Current has sustained effects on synaptic efficacy despite synaptic depression

• While Direct Current stimulation is on, ongoing synaptic activity boosted (Functional Targeting)

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

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

- Direct Current stimulation does not itself generate synaptic plasticity *(Functional Targeting)*

Repeated stimulation 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 of that task (Functional Targeting)
- How can a 9V battery do anything for the complex brain?
- How is specificity of action achieved?

Through **anatomical targeting** of specific brain regions.
  - Can be studied using computational models.

Through **functional targeting** of specific brain networks.
  - Can be studied using brain slices models.
How can tDCS be optimized?

- For translation, models are only useful in predicting outcomes.

Computational models for **anatomical targeting** of brain regions.

Animal models for **functional targeting** of specific brain activity.
How can tDCS be optimized?

- For translation, models are only useful in predicting outcomes.

**Computational models for anatomical targeting of brain regions.**

**Animal models for functional targeting of specific brain activity**

- Sophisticated tDCS optimization integrates anatomical and functional targeting.
Sophisticated tDCS optimization integrates Anatomical and Functional targeting.

The anode and the cathode.
“Cathodal” tDCS
Soma hyper-polarized
Apical dendrite depolarized

“Anodal” tDCS
Soma depolarized
Apical dendrite hyper-polarized

Synapses are on both depolarized and hyper-polarized compartments.

Axon terminals are also polarized.

High Rate Stimulation generates LTP which is modulated by concurrent Direct Current

High Rate Stimulation generates LTP which is modulated by concurrent Direct Current

- Depolarized dendrites boost plasticity, under anodal or cathodal DCS

- Interactions between stimulation polarity and activated network determining modulation.

- "Anodal" or "Cathodal" can either inhibit or boost plasticity – depends on type plasticity:
  - High-Rate is dendrite dependent
  - Theta-burst is some dependent
Sophisticated tDCS optimization integrates Anatomical and Functional targeting.

Using EEG.
Any EEG can be automatically “inverted” to an optimal HD-tDSCS montage

Sophisticated tDCS optimization integrates anatomical and functional targeting.

- Based on decades old hypothesis of reciprocity, but based on head model
- Activity guided targeting, but does not require source localization (!)
- Integrated and automatic in theory, but practically concurrent EEG + stimulation has "inherent physiologic" artifacts (!)

Sophisticated tDCS optimization integrates Anatomical and Functional targeting.

The folded brain.
Concentric sphere models of tDCS

Rush & Driscoll (1968) Current distribution in the brain from surface electrodes

**Analytical Solution**

Miranda et al. (2006) Modeling the current distribution during transcranial direct current

**Finite Element Method**

Datta et al. (2008) : Transcranial current stimulation focality using disc and ring electrode configurations: FEM analysis.

**Montage optimization**


neuralengr.com/spheres
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Montage optimization


neuralengr.com/spheres
Datta et al. (2008)
• Complete current path from Anode to Cathode
• Inward under Anode, Outward under Cathode
• Tangential between electrodes
• Asymmetric pyramidal neurons in cortical columns
• Directional current flow relevant to cortical surface (columns and pyramidal neurons)

- Polarity specific pyramidal polarization with radial current
- At any polarity: No such thing as a “depolarizing” tDCS
- Tangential current flow polarizes afferent axons
- Neuromodulation at all directions of current flow

Physics: Cortical folding results in alternating pattern of inward (“excitatory”) and outward (“inhibitory”) current flow.

• Gyri level changes in outward/inward polarity

- Majority of current tangential
- Directionality inversion within Gyri (under electrode)

How can polarity specific (or any) effects result with mixed polarization?

• Input / Output sensitive to anodal polarization only

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• On a population level net change in mixed polarization

Non-linear response on the brain rectifies directional polarization, ”preference” for excitatory

Net population response under even or uneven mixed polarization

Anodal / cathodal produce consistent net (uneven) regional polarization

• Network activity (oscillations) “binds” opposite polarized regions to produce a coherent effects
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