The promise and pitfalls of transcranial Direct Current Stimulation

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tDCS : The Elephant in the Room

- Wide range of indications for cognitive enhancement and treatment
- Yet a very simple intervention ("9V battery")

Maybe, It’s not so simple.
tDCS is not simple:
Electrode montage for Anatomical Targeting
Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad

Abhishek Datta, MS, Varun Bansal, BS, Julian Diaz, BS, Jinal Patel, MS, Davide Reato, MS, Marom Bikson, PhD
< 1 V/m Brain Electric Field
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
"Cathodal" tDCS
Soma hyper-polarized
Apical dendrite depolarized

"Anodal" tDCS
Soma depolarized
Apical dendrite hyper-polarized

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 $\rightarrow$ directional polarization $\rightarrow$ directional excitability and plasticity changes

- **ANODE**
- **Brain Current flow**
  - outward
  - inward
- **CATHODE**

**Brain Current flow**

- **Depolarized soma**
- **Hyperpolarized soma**

** 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

But are the models right?
Stimulation of the cerebral cortex in the intact human subject

P. A. Merton & H. B. Morton
Physiological and modeling evidence for focal transcranial electrical brain stimulation in humans: A basis for high-definition tDCS
Subject specific models predict MEP
+ Imaging of current flow
+ Intracranial recording
+ Clinical neurophysiology
+ .....
But are the models right?

After dozens of direct and indirect validation, seem so
tDCS is not simple:  
Task/Training for Functional Targeting
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)

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)
Optimize both Anatomical + Functional Targeting
EEG guided-tDCS:
Anatomically targeting the function
- Any EEG can be automatically “inverted” to an optimal HD-tDCS montage
• 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 (!)
tDCS is not simple: Cellular targets
“Cathodal” tDCS
Soma hyper-polarized
Apical dendrite depolarized

“Anodal” tDCS
Soma depolarized
Apical dendrite hyper-polarized

Axon (synapse) terminals are most sensitive to stimulation.
High Rate Stimulation generates LTP which is modulated by concurrent Direct Current

LTP from high rate stim

“Cathodal” or “Anodal” Direct Current Stimulation

EPSP

Axon Pathway specific testing

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
The folded brain.
Physics: Cortical folding results in alternating pattern of inward ("excitatory") and outward ("inhibitory") current flow

• Gyri level changes in outward/inward polarity

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

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

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

Indirect Mechanisms
Limited output transcranial electrical stimulation (LOTES-2017): Engineering principles, regulatory statutes, and industry standards for wellness, over-the-counter, or prescription devices with low risk
During tES, there is always more current in the skin than brain.
Cranial Nerves
(back to models)
• Simulation driven montage design with HD-tDCS
• Functional Targeting - LTP specific modulation
• Boosting rate and ceiling of LTP
• Image (EEG) based Targeting
• Axon and Dendrite Compartments
• Mixed polarization
• Cranial nerve targets?
• Non-linear response on the brain ”preference” for excitatory