Understanding the benefits and uses of tDCS

Marom Bikson
Lucas Parra, Jacek Dmochowski, Asif Rahman, Niranjan Khadka, Mark Jackson, Dennis Truong, Zeinab Esmaeilpour, Thomas Radman, Gregory Kronberg, Devin Adair, Nigel Gebodh, Belen Lafon
The City College of New York of CUNY, New York

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(Patents) The City University of New York on brain stimulation. (Equity) Soterix Medical Inc. produces tDCS and High-Definition tDCS. (Scientific Advisory Board) Boston Scientific Inc. produces neuromodulation products.

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Slides and References @MaromBikson
tDCS: transcranial Direct Current Stimulation

Cathode (-) Electrode

20 minute session 5x per week

“Anodal” / “Cathodal” refer to proximity of target

Anode (+) Electrode
"Cathodal" tDCS
Soma hyper-polarized
Apical dendrite depolarized

"Anodal" tDCS
Soma depolarized
Apical dendrite hyper-polarized
tDSC: Status

Panacea | Snake Oil

It's complicated.
Simplicity in tDCS technology does not justify trivial simplistic mechanisms of action or lack of sophistication in use.

That tDCS in its mode of application, mechanisms, and outcomes is **complicated** is not a deficiency, but inevitable given complexity of brain (dys)function.
tDCS

High Definition tDCS

M1-SO tDCS montage

Experimentally-verified Anatomical MRI derived models of current flow

4x1 HD-tDCS montage

tDCS

M1-SO tDCS montage

Experimentally-verified Anatomical MRI derived models of current flow

High Definition tDCS

4x1 HD-tDCS montage

Circuit Therapeutics

M1-SO tDCS montage

Non-invasive Targeted

Experimentally-verified Anatomical MRI derived models of current flow

4x1 HD-tDCS montage

Different tDCS electrode montages may be as functionally distinct as different drugs

High-Definition tDCS uses arrays of electrodes to focus current to targets.

Software allows you to generate subject and target specific (HD) tDCS “formulation”

Individual Differences

Different anatomy $\rightarrow$ Different brain current flow.

Including for atypical anatomy (neurodegenerative disorders, brain injury), extremes of age...

When applying the same tDCS across a population, aggregate response reflect individual variability.

High Definition tDCS for Stroke Rehabilitation

Dmochowski et al. Targeted transcranial direct current stimulation for rehabilitation after stroke. *Neuroimage* 2013
Realistic vO lumetric-Approach-based Simulator for Transcranial electrical stimulation

BRAIN initiative: NIMH 1R01MH111896. Free (Matlab), Open Source, One command line, validated outcomes.

Huang et al. ROAST -- a fully automated open-source pipeline, bioRxiv 217331, Nov 10, 2017
Gyri level changes in outward/inward polarity

• Input / Output sensitive to anodal polarization only

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• On a population level net change in mixed polarization

TMS is used as a probe on motor excitability.

Orientation of TMS and TDCS controlled.

Significant changes in cortical excitability by tDSCS - but highly pathway specific.

Rawji, Rothwell et al. tDCS changes in motor excitability are specific to orientation. Brain Stim. 2018
Analysis of tDCS must be based on (individual) brain current flow, not just “nominal” target.
(and gyri-level modeling tools for this exist, e.g. NIMH “ROAST”)

Brain effects of tDCS are pathway specific
(collapsing across different tDCS approaches and outcomes can produce null meta-analysis)

That tDCS is low intensity is not news. And is a mechanistic virtue.
tDCS

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. Origin of specificity during tDCS: activity-selective mechanisms. Front Human Neuro 2013
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)

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 (Functional Targeting)
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 (Functional Targeting)

tDCS: Optimize both Anatomical + Functional Targeting
How could weights help with so many sports?
It's a tool to enhance specific training.

How could tDCS treat many disorders?
It's a tool to enhance cognitive training and therapy.
It’s complicated... in a way systematically characterized over a decade, and which has not been fully realized in technology and human trials. Ongoing clinical trial provide signals.
Monotonic dose response across scales

Current flow intensity (Electric field) in brain

Membrane polarization

Excitability and synaptic efficacy (plasticity)

Network activity

Cognition and Behavior

1X Change?  2X Change?  -2X Change?  2X Change?

Biophysical Modeling
- Current flow modeling
- Neuron model
- Network model
- Computational neurostimulation

Animal Modeling
- Intracellular recording
- Voltage sensitive dyes
- Excitatory Post Synaptic Potential (EPSP)
- Calcium imaging

Human Neurophysiology
- Transcranial Magnetic Stimulation (TMS) / Motor Evoked Potential (MEP)
- Transcranial Magnetic Stimulation (TMS)/Electroencephalography (EEG)
- Electroencephalography (EEG)

Neuroimaging
- Spectroscopy
- Functional Magnetic Resonance Imaging (fMRI)
- Arterial Spin Labeling (ASL)

Behavioral/Clinical Measures
- Questionnaire
- Visual Analogue Scale (VAS)
- Task performance (rate)
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 (!)

Dmochowski, et al. Optimal use of EEG recordings to target active brain areas with tES BioRxIv 2016
**Home-based extended therapy**

1) Better for subjects, Better for operators. Convenience and volume of sessions.

2) Digital therapeutics. Apps and Web-based therapy. Task-control (engage network)

3) Integrated sensors / wearables (biomarkers, feedback targets engaged networks).

Axon (synapse) terminals are most sensitive to stimulation
During tES, there is always more current in the skin than brain.
Cranial Nerves
(back to models)
Largest meeting spanning neuromodulation and digital healthcare. Dynamic format from basic science, to clinical trials, to technology. Hand-on Courses and Workshops.
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