Does tDCS work?

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Carolina Neurostimulation Conference 2018
Disclosure:

(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.

Support:

NIH (NIMH, NINDS, NCI, NIBIB) – BRAIN initiative, NSF, Epilepsy Foundation, Wallace Coulter Foundation, DoD (USAF, AFOSR), Harold Shames, CCNY Fund
tDCS: transcranial Direct Current Stimulation

Cathode (-) Electrode

Anode (+) Electrode

20 minute session
5x per week

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

Cathode

Scalp

Cortex

+  -

"Cathodal" tDCS
Soma hyper-polarized
Apical dendrite depolarized

"Anodal" tDCS
Soma depolarized
Apical dendrite hyper-polarized
Does tDCS work?

Hype, positive or negative, is hype.
— S. Bestmann
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.
Does tDCS work?

When are the **cellular** effects of tDCS meaningful to changing **behavior** and to therapy.
That Direct Current Stimulation inevitably changes cellular function is known, for a long time (~200 years), and is both evident and complex.

Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices in vitro

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tDCS

M1-SO tDCS montage

High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow

4x1 HD-tDCS montage

tDCS

High Definition tDCS

M1-SO tDCS montage

4x1 HD-tDCS montage

Experimentally-verified Anatomical MRI derived models of current flow

Circuit Therapeutics

Non-invasive Targeted

M1-SO tDCS montage

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

Different anatomy → 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.

Realistic vOllumetric-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

TMS is used a probe on motor excitability.

Orientation of TMS and TDCS controlled.

Significant changes in cortical excitability by tDCS - 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)

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

That Direct Current Stimulation inevitably changes cellular function is known, for a long time (~200 years), and is both evident and complex.

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OR and LM are distinct afferent pathways to the same target.
DCS polarity and orientation matter
DCS linearly polarizes neurons (no threshold)

What you can detect depends on how hard you look (n)
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

Functional Targeting

Current flow across entire region

Preferential modulation of selected active neurons

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)

LTP from theta burst stim + Cathodal or Anodal Direct Current Stimulation

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)

Bikson et al. Origin of specificity during tDCS: activity-selective mechanisms. Front Human Neuro 2013
tDCS: Optimize both Anatomical + Functional Targeting
tDCS produces a little current flow across the brain (~1v/m), that produces a little neuronal membrane polarization (~1 mV). A little polarization can influence all aspects of brain function, oscillation, plasticity (see 100 references)....enough to change behavior?
Multi-scale tDCS studies.
Non-monotonic, state-dependent dose response. More it not more.
The breadth of tDCS research and the discovery if complexity is not deficit.

Esmaeilpour et al. Incomplete evidence increasing current intensity of tDCS boosts outcomes. *Brain Stim* 2018
Does tDCS work?

Yeah but it’s complicated... in a way systematically characterized over a decade, but not fully realized in technology and human trial protocols. So positive/negative trials provide signals for ongoing refinement.
neuromodec.com/nycnans2018

Largest meeting spanning neuromodulation and digital healthcare. Dynamic format from basic science, to clinical trials, to technology. Hand-on Courses and Workshops.
• Input / Output sensitive to anodal polarization only

• Input / Output sensitive to anodal polarization only

• On a population level net change in mixed polarization