How to cure any disease and get smart: An overview of tDCS mechanisms
Disclosure:

Soterix Medical Inc. produces tDCS and High-Definition tDCS. Marom Bikson is founder and has shares in Soterix Medical. Some of the clinical data presented may be supported by Soterix Medical. Marom Bikson serves on the scientific advisory board of Boston Scientific Inc.

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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.

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

Depression, pain, migraine, epilepsy, PTSD, schizophrenia, Wnnitus, neglect, rehabilitation (motor, aphasia), TBI, OCD, autism, Accelerated learning (reading, motor skills, math, threat detection), memory, creativity, lucid dreaming…

The Original Cure All

Relieves instantaneously

And Cures: Headaches, Nueralgia, Cough, Cold, Sneezing, Hiccups, Goat, Gonorrhea, Dystheria, Dampflung, Mumps, Measles, Whooping cough, Tuberculosis, And even Bowden's Malady.

For blindness Try Our Rattlesnake Oil!
Is there anything tDCS does not work for?

Vince Walsh
Hype, positive or negative, is still hype.

Sven Bestmann
How could Pharmaceuticals treat so many disorders?
It’s not one thing. Many formulations.

How could Electroceuticals (tDCS) treat many disorders?
It’s not one thing. Many “formulations”.
tDCS electrode position on the head determines which regions are stimulated.

Specific brain regions are associated with specific functions / disease.

Truong et al. Clinician accessible tools for GUI computational models. “BONSAI” and “SPHERES”. Brain Stimulation 2014
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

✓ Allows targeting of selected cortical regions

Datta et al. Gyri-precise model of tDCS: Improved spatial focality using a ring versus conventional pad. *Brain Stimulation* 2009
High Definition tDCS for Stroke Rehabilitation

Dmochowski et al. Targeted transcranial direct current stimulation for rehabilitation after stroke. *Neuroimage* 2013
tDCS montages for treatment of Depression

- Brunoni et al.
  - SELECT / ELECT
  - target: DPLPC
  - 2.0 mA
  - Double blind RCT

- Loo et al.
  - Multi-Center Trial
  - target: DPLPC
  - 2.5 mA
  - Double blind RCT

- Target stimulated but not specifically

Seibt al. The pursuit of DLPFC. *Brain Stimulation* 2015
Transcranial Direct Current Stimulation (tDCS)

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, Jealousy, Reality Filtering, IQ, Prejudice…

Majority of trials use diffuse tDCS

- How can a 9V battery do anything for the complex brain?
- How is specificity of action achieved?
How could weights help with so many sports?
It’s a tool to enhance specific training.

How could Electroceuticals (tDCS) treat many disorders?
It’s a tool to enhance cognitive training and therapy.
tDCS is a tool for the mind that enhances activity and plasticity from cognitive training and therapy

- Human trials with tDCS use brain stimulation as adjunct to the brain training (e.g. math, game)
- Changes in mood that facilitate training (vigilance, relaxation)
- Boosting placebo – real and specific physiological response associated with expectation

Schambra et al. It’s all in your head: reinforcing the placebo response with tDCS. Brain Stimulation 2014
How does tDCS just enhance the trained task?

Cellular mechanism: Functional Targeting

Bikson et al. Origins of specificity during tDCS: anatomical, activity-selectivity, and input-bias mechanisms. *Front Human Neuro 2013*
From Anatomical Targeting to Functional Targeting
From Anatomical Targeting to Functional Targeting

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

Preferential modulation of selected active network (activity dependent)

Current flow across entire region
Supra and sub-threshold electrical stimulation
Supra and sub-threshold electrical stimulation

High-intensity Pulses

- Over-driving neurons (axons)
- Neuromodulation (therapy) derives from secondary system changes

Low-intensity Direct Current

TMS

Invasive cortical

DBS
Supra and sub-threshold electrical stimulation

High-intensity Pulses

- Over-driving neurons (axons)
- Neuromodulation (therapy) derives from secondary system changes

Low-intensity Direct Current
Supra and sub-threshold electrical stimulation

**High-intensity Pulses**

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**Low-intensity Direct Current**
Supra and sub-threshold electrical stimulation

**High-intensity Pulses**

- Over-driving neurons (axons)
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**Low-intensity Direct Current**

- Polarize neurons
- Neuro-modulation: Interacting with specific ongoing neuron activity

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High-intensity Pulses

- High-intensity Pulses

Low-intensity Direct Current

- Low-intensity Direct Current

**tDCS**
① **tDCS produces a sustained weak polarization of neuronal membranes**

② **Weak polarization modulates synaptic efficacy**
① tDCS produces a sustained weak polarization of neuronal membranes

② Weak polarization modulates synaptic efficacy
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
Bikson et al. Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices. *J Physiol* 2004
tDCS: Sustained weak polarization

Intracellular recording and morphology

Radman, Bikson et al. Role of cortical morphology in uniform electric field stimulation. *Brain Stimulation* 2009
tDCS: Sustained weak polarization

Which compartments are polarized by DCS?

- Soma: < 0.3 mV
- Dendrites
- Axon (terminals): < 1 mV

tDCS: Sustained weak polarization

Which compartments are polarized by DCS?

Afferent terminals

There are a lot of terminals and they point every which way

1. tDCS produces a sustained weak polarization of neuronal membranes

2. Weak polarization modulates synaptic efficacy
Weak polarization modulates synaptic efficacy

The amount of postsynaptic current for given pre-synaptic activity

Modulation of on-going synaptic activity, *not* generation

Excitatory postsynaptic currents (field) in brain slice

Weak polarization modulates synaptic efficacy

Excitatory post-synaptic currents (field) in brain slice

Train of synaptic ongoing activity

- Ongoing synaptic activity modulated while tDCS sustained
- Substrate for plasticity
- Modulation of ongoing activity, not generation
Weak polarization modulates synaptic efficacy

- Polarity of modulation depends on many factors

Weak polarization modulates synaptic efficacy

Which compartments are polarized by DCS?
Weak polarization modulates synaptic efficacy

Which compartments are polarized by DCS?
Biophysical basis of tDCS functional selectivity

Fritsch 2010: BDNF dependent + activity dependent induction

- Specific ongoing synaptic activity (no plasticity)
  - tDCS induces plasticity

Rahman 2015: Pathways specific + plasticity dependent modulation

- Ongoing Plasticity
  - tDCS modulates plasticity

"None-active" synapse

No tDCS synaptic plasticity

Synaptic Plasticity in brain slice
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> How can a 9V battery do anything for the complex brain?
> How is specificity of action achieved?
Its more complicated
How does Direct Current change cortical processing?
Direct Current stimulation of ACTIVE network

How does Direct Current change cortical processing?
Direct Current stimulation of ACTIVE networks

Direct Current stimulation changes cortical processing through modulation of network activity
Direct Current stimulation of ACTIVE networks

Reato et al. Transcranial electrical stimulation accelerates human sleep homeostasis. PLOS Computation Biology 2013
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