High-Definition transcranial Direct Current Stimulation (HD-tDCS)

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$ NIH (NINDS, NCI), NSF, Epilepsy Foundation, Wallace Coulter Foundation, DoD (USAF, AFOSR)
Disclosure:

Soterix Medical Inc. produces tDCS and High-Definition tDCS. Marom Bikson is co-founder of Soterix Medical. Some of the clinical data presented may be supported by Soterix Medical.

The City University of New York has patents on tDCS and High-Definition tDCS with Marom Bikson as inventor.

tDCS and HD-tDCS are regulated as investigational devices in the USA.
Transcranial Direct Current Stimulation (tDCS)

- Non-invasive, portable, well-tolerated.
- Low-intensity (~2 mA) current passed between scalp electrodes (~20 min).
- For rehabilitation, neuropsychiatric treatment, neuroenhancement.

Questions:
- Can a “simple” intervention modulate brain function?
- How is specificity of action achieved?
Neuromodulation: Electrotherapy Delivery Platforms

- **Deep Brain Stimulation (invasive)**
  - Decreasing Cost
  - Decreasing Risk
  - Increasing Efficacy, Specificity

- **Transcranial Magnetic Stimulation**
  - Deployable, compact
  - Minimal supervision
  - Adverse events: itching, erythema
  - IRB / FDA “NSR”

- **transcranial Direct Current Stimulation**
  - ? tDCS Specificity
What makes tDCS specific?

Given the diversity of tDCS application spanning neuropsychiatric treatment, rehabilitation, and learning in healthy individuals.

• Anatomical targeting (specificity)
  The control of tDCS electrode placement to guide current flow to brain targets
  Design facilitated by current flow models.

• Functional targeting (specificity)
  The use of tDCS *adjunct* to behavioral / cognitive training to facilitate the outcomes of training.
  Design facilitated by animal models of plasticity.
Anatomical targeting with tDCS

- “Conventional” tDCS varies the position of two large electrodes.
- Montage specific effects on behavior and neurophysiology well documented.
- “Shaping” outcomes vs “targeting” brain regions.
Anatomical targeting with tDCS

Conventional bipolar large electrodes
Anatomical targeting with tDCS

High-Definition electrodes in “4x1” configuration

Datta et. al. Brain Stim 2009

Conventional bipolar large electrodes
Non-invasive targeting while maintaining tolerability and deployable advantages.
Anatomical targeting with tDCS

High-Definition electrodes in “4x1” configuration

Dmochowski Neural Engr. 2011

Datta et. al. Brain Stim 2009
Datta et. al. Brain Stim 2009

High-Definition electrodes in “4x1” configuration

Dmochowski Neural Engr. 2011

Optimized tDCS is a “closed” problem

But “best” montage different for:

a) Maximum **intensity** at target.

b) **Focality** (minimizing relative intensity outside of target).
Anatomical targeting with tDCS

Consider a three-electrode setup

1) Linearity of Lead-Fields
2) “Quasi-Uniform Assumption”: Region E α Neuromodulation
Anatomical targeting with tDCS

Optimization algorithm

Linear optimized is “closed” problem: real-time, individualized, and subject to any constraints
Customized targeting with tDCS

Super-obese
Obesity / Craving / Addiction

Pediatric
Epilepsy / ADHD / CP

Stroke
Rehabilitation
(motor, aphasia)

Kessler PLoS ONE 2013
Gillick Frontiers 2014

Datta Brain Stimulation 2011
Dmochowski Neuroimage 2013

Truong Neuroimage 2013
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Neuromodulation comes from secondary non-linear changes

Low-intensity DC
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Low-intensity DC
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Neuromodulation mechanisms:
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Interacting with specific activity in a neural network (Neuromodulation)
Anatomical targeting with brain stimulation

Supra-threshold stimulation
- DBS
- M1s
- TMS


Sub-threshold stimulation
- HD-tDCS
- 4x1

Stimulation primary neuromodulation target. Endogenous circuit.

Quasi-Uniform assumption: Neuromodulation is linear with local electric field magnitude.
From Anatomical Targeting to Functional Targeting

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

Electrode / Coil

Preferential modulation of more active network (activity dependent)

Current flow across entire region
What makes tDCS specific?

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• Functional targeting (specificity)
  
The use of tDCS *adjunct* to behavioral / cognitive training to facilitate the outcomes of training.
  
  Design facilitated by animal models of plasticity.
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.
The theory of Functional Targeting
How does tDCS just enhance the trained task?

Cellular mechanism: Functional Selectivity

Bikson et al. Front Human Neuro 2013
1. tDCS produces a sustained weak polarization of neuronal membranes

2. Weak polarization modulates synaptic efficacy and plasticity
tDCS produces a sustained weak polarization of neuronal membranes

Weak polarization modulates synaptic efficacy
tDSC: Sustained weak polarization

Brain slice: Optical Mapping with Voltage Sensitive Dyes

Bikson J Physiol. 2004
tDCS: Sustained weak polarization

Brain slice: Optical Mapping with Voltage Sensitive Dyes

Bikson J Physiol. 2004
tDCS produces a sustained weak polarization of neuronal membranes

Weak polarization modulates synaptic efficacy
Biophysical basis of tDCS functional selectivity

1. tDCS produces a sustained weak polarization of neuronal membranes

2. Weak polarization modulates synaptic efficacy
Biophysical basis of tDCS functional selectivity

- Theta-burst plasticity session, no tDCS
- Theta-burst session plasticity session with tDCS

Accelerated plasticity when tDCS is present
Biophysical basis of tDCS functional selectivity

- Theta-burst plasticity session, no tDCS
- Theta-burst session plasticity session with tDCS

![Graph showing synaptic strength over time with and without tDCS](image-url)
Biophysical basis of tDCS functional selectivity

Non task-related synapse

Task-related synapse

A

B

C

D

No DCS

DCS

No plasticity

No plasticity

Endogenous plasticity

Enhanced plasticity

Depolarization

Glutamate

Calcium

DCS depolarization

Synaptic activity

LTD threshold

LTP threshold

Closed NMDAR

Open NMDAR

Open AMPAR

Synaptic plasticity cascades

Dendritic Spine

Backpropagating action potential

Dendritic spike

Neighboring synaptic current
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