The frontier of tDCS in psychiatry and the role of new technologies

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Disclosure:

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

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What defines neuromodulation technologies is how energy is delivered to what target.
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tDCS: Transcranial Direct Current Stimulation

- Hand-held device, head gear
- 20 minute session, 2 mA via scalp electrodes
- Modulator of brain excitability and plasticity
- > 400 controlled trials across neurological / psychiatric inductions + performance
- Remote supervised (home)
tDCS methods matters

1) Century of clinical testing, poor reproducibility:


tDCS: Transcranial Direct Current Stimulation

- Mixed clinical results
- Too many indications
- Too low intensity to trigger neuronal firing
- Direct current is not a physiologic signals
- Not spatially target
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tDCS

Experimentally-verified Anatomical MRI derived models of current flow
tDCS

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Circuit therapeutics
tDCS

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High Definition tDCS

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High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow

Circuit therapeutics

Non-invasive electrical targeting
• Software allows you to steer currents to targeted brain regions
• Single programmable device and head-gear
• Target optimized solved. Question is what target?
transcranial electrical targeting papers


4) Model validation: Huang et al. Measurements and models of electric fields in the human brain during transcranial electric stimulation. Elife 2017
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High-intensity Pulses | Low-intensity DC

Over-driving a neural network

Neuromodulation comes from secondary non-linear changes

Deep Brain Stimulation | Motor Cortex Stimulation | Transcranial Magnetic Stimulation (TMS)
High-intensity Pulses

Over-driving a neural network

Low-intensity DC
High-intensity Pulses | Low-intensity DC

Over-driving a neural network
High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Interacting with specific activity in a neural network (Neuromodulation)

Transcranial Direct Current Stimulation (tDCS)
Electrode

Current flow across entire brain region

Network of interest (e.g. depression, math cells)

Other networks – not targets for neuromodulation

Preferential modulation of more active network (activity dependent)
Functional Targeting:
Activity dependent sensitivity to brain stimulation
Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current Stimulation (DCS).
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- DCS does generate synaptic plasticity de novo (Activity Dependent)
- Directions of changes by anodal/cathodal depends on LTP types
Repeated DCS accelerates LTP and boosts the ceiling for synaptic learning

- Hypothesis: Combing DCS with ongoing training enhances the rate and ceiling learning specifically of that task (Activity Dependent)
tDCS applied with a task. Specificity comes from the task. tDCS makes the task (therapy) more effective.


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The challenge for tDCS is not feasibility, but optimization to meaningful applications
• Software allows you to steer currents to target brain region
• Single programmable device and head-gear
• **Target optimized solved. Question is what target?**
Maybe one size does not fit all?

What is biomarker?

What is intensity?

What is inclusion?

What is the timing?

What is the task?

• Target optimized solved. Question is what target?
Personalized Therapy
Personalized Therapy Iterative
Personalized Therapy

- Tunable
- Fast Iterations
- Minimal risk
Personalized Therapy

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Drugs
Molecular

Implants
In-Hospital

Apps

Wearable
neuromodulation
Personalized Therapy

- Effective
- Tunable
- Minimal risk

Drugs Molecular

Implants In-Hospital

Apps

Wearable neuromodulation
Software allows you to steer currents to targeted brain regions

- Single programmable device and head-gear
- Target optimized solved. Question is what target?
EEG automatically and instantly “inverted” to optimal HD-tDCS montage

- Decades old “reciprocity” hypothesis, but with closed head model
- Activity guided targeting, does not require source localization
Phase II (Harvard/Spaulding) **Fibromyalgia pain**
Daily in-clinic sessions of EEG Guided HD-tDCS, open label
Phase II (Harvard/Spaulding) Fibromyalgia pain
Daily in-clinic sessions of EEG Guided HD-tDCS, open label
Targeted (Image Guided) tDCS


2) **EEG + HD-tDCS Fibromyalgia**: Castillo-Saaavedra et al. Clinically Effective Treatment of Fibromyalgia With High Definition tDCS. J Pain 2016

3) **EEG to HD-tDCS reciprocity**: Dmochowski et al. Optimal use of EEG recordings to target active brain areas with transcranial electrical stimulation. Neuroimage 2017
Personalized Neuromodulation Therapy at Home
Personalized Neuromodulation Therapy at Home

Head-gear ($R_x +$ sensors)

App

Medical wearable

3x Measure

Historical data

decision
ElectraRx – Prescription

Adaptive questions optimized to select daily treatment (not diagnose)

How are you?

What is bothering you?

What kind of pain?

How’s work?

Option 1 Rx

Option 2 Rx
Adaptive Questionnaires for Personalized Neuromodulation
Adaptive Questionnaires for Personalized Neuromodulation

I'm sorry to hear that. Can you tell me what is bothering you? (click all that apply)

- Anxiety
- Sadness
- Pain
- Headache
- Lack of focus
- Lack of energy
- Lack of appetite
- Lack of sleep
- Ringing or buzzing in the ears

Is there anything else you would like me to share with your doctor?

Continue
Adaptive Questionnaires for Personalized Neuromodulation

Taking everything into consideration, during the past week how satisfied have you been with your family relationships?

- Very Poor
- Poor
- Fair
- Good
- Very Good
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Responsive Measures for Personalized Neuromodulation

- Head gear – EEG, EOG, fNIRS, GVS
- HealthDot Sensors - PPG, ECG, Respiration, IMU, EDA, EMG

HealthDot (chronic) → Vital sign, Brain measures → Option 1 Rx
Headgear (during session) → Raw data → Cloud → Option 2 Rx
Personalized Neuromodulation Therapy

**Fast Iterative**

**Tunable targeted**

- Head-gear ($R_x +$ sensors)
- App
- Medical wearable
- Measures

**Responsive Adaptive Q**

[Raw Data]

**Historical data**

decision
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Tunable targeted

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Measures

Responsive Adaptive Q
[Raw Data]

Historical data

decision
Personalized Neuromodulation is Personalized
Personalized home-based tDCS


2) Pediatric Epilepsy: Meiron et al. HD-tDCS in early onset epileptic encephalopathy. J Brain Inj 2017

2) Multiple Sclerosis: Kasschau et al. tDCS Feasible for Remotely Supervised Home Delivery in MS. Neuromod 2016

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