Downloading Personalized Brain Stimulation

Marom Bikson
Disclosure (relevant to presentation)

The City University of New York: Patents on brain stimulation. Soterix Medical: Co-founder, Produces tDCS and High-Definition tDCS. Boston Scientific: Neuromodulation Scientific Advisory Board GlaxoSmithKline (GSK) Life Science Scientific Advisory Board

Support

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Slides and References @MaromBikson
What defines neuromodulation technologies is how energy is delivered to what target

- Spinal Cord Stimulation (SCS)
- Transcranial Magnetic Stimulation (TMS)
- Transcranial Electrical Stimulation (tES)
- Deep Brain Stimulation (DBS)
- Electroconvulsive Therapy
- Transcranial Direct Current Stimulation (tDCS)

Implants
In-Hospital
Wearable
What defines neuromodulation technologies is how energy is delivered to what target.

- Deep Brain Stimulation (DBS)
- Spinal Cord Stimulation (SCS)
- Transcranial Magnetic Stimulation (TMS)
- Electroconvulsive Therapy
- Transcranial Electrical Stimulation (tES)
- Transcranial Direct Current Stimulation (tDCS)
- Implants
- In-Hospital
- Wearable
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)
Effects of Transcranial Direct-Current Stimulation on Neurosurgical Skill Acquisition: A Randomized Controlled Trial.

Ciechanski P¹, Cheng A², Lopushinsky S³, Hecker K⁴, Gan L⁵, Lang S⁶, Zareinia K⁷, Kirton A⁸.

Utilizing Transcranial Direct Current Stimulation to Enhance Laparoscopic Technical Skills Training: A Randomized Controlled Trial

Morgan L Cox, Zhi-De Deng, Hannah Palmer, Amanda Watts, Lysianne Beynell, Jonathan R Young, Sarah H Lisanby, John Migaly, Lawrence G Appelbaum

doi: https://doi.org/10.1101/455329

Effects of transcranial direct-current stimulation on laparoscopic surgical skill acquisition

P. Ciechanski, A. Cheng, O. Damji, S. Lopushinsky, K. Hecker, Z. Jadavji, and A. Kirton
tDSC boosts learning
High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Neuromodulation comes from secondary non-linear changes
High-intensity Pulses

Over-driving a neural network

Low-intensity DC
High-intensity Pulses

Over-driving a neural network

Low-intensity DC
High-intensity Pulses
Over-driving a neural network

Low-intensity DC
Interacting with specific activity in a neural network (Neuromodulation)
Electrode / Coil

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

Current flow across entire brain region

Preferential modulation of more active network (activity dependent)
Direct Current
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 (Activity Dependent)

1 hour after TBS
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 (Activity Dependent)
tDCS applied with a task. Specificity comes from the task. tDCS makes the task (therapy) more effective.
1) Decades of mechanistic studies in animals (original LTP):  
   Jackson et al. Animal Models of transcranial Direct 
2) Safety from >30k sessions: Bikson et al. Safety of 
   Transcranial Direct Current Stimulation: Evidence 
3) Methods and application guide: Woods et al. A technical 
   guide to tDCS, and related non-invasive brain 
Sub-threshold DBS?
Sub-threshold SCS?

A neuromodulation penumbra
Low Intensity Stimulation

Preferential modulation of more active network (activity dependent)
High Intensity Stimulation

Supra-threshold pacing
High Intensity Stimulation

Supra-threshold pacing

Low Intensity Area

Preferential modulation of more active network (activity dependent)
Are implants needed for targeting?

Non-invasive targeted electrical stimulation
tDCS

Experimentally-verified
Anatomical MRI derived
models of current flow
tDCS

Experimentally-verified
Anatomical MRI derived
models of current flow
tDCS

Experimentally-verified Anatomical MRI derived models of current flow

Circuit therapeutics
tDCS

Experimentally-verified Anatomical MRI derived models of current flow

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Experimentally-verified Anatomical MRI derived models of current flow

High Definition tDCS

Circuit therapeutics
tDCS

High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow

Circuit therapeutics
tDCS

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?
- Target optimized solved. Question is what target?
High-Definition tDCS
Anatomical + Functional Targeting
Core transcranial inventions papers

4) Model validation: Huang et al. Measurements and models of electric fields in the human brain during transcranial electric stimulation. Elife 2017
Personalized Therapy
Personalized Therapy

Iterative

measurement

decision
Personalized Therapy

- Tunable
- Fast Iterations
- Minimal risk
Personalized Therapy
• Tunable
• Fast Iterations
• Minimal risk

Drugs
Molecular

Implants
In-Hospital

Apps
Wearable
neuromodulation
Personalized Therapy
- Effective
- Tunable
- Minimal risk

Drugs
Molecular

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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

2) **EEG + HD-tDCS Fibromyalgia**: Castillo-Saavedra 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
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
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
Personalized Neuromodulation Therapy at Home

Head-gear ($R_x +$ sensors)

App

Medical wearable

3x Measure

decision

Historical data
Responsive Measures for Personalized Neuromodulation

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

HealthDot (chronic)
Headgear (during session)
[ Raw data ]
Vital sign
Brain measures

Option 1 Rx
Option 2 Rx
Personalized Neuromodulation Therapy

Fast Iterative

Tunable targeted

Head-gear ($R_x +$ sensors)

Medical wearable

Measures

Responsive Adaptive Q
[Raw Data]

Historical data

decision
tDCS applied with a task. Specificity comes from the task. tDCS makes the task (therapy) more effective
Personalized Neuromodulation Therapy

- Fast Iterative
- Tunable targeted

Head-gear ($R_x +$ sensors)

App

Medical wearable

Measures

Decision

Historical data

Responsive Adaptive Q [Raw Data]
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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Digital Neuro Symposium, Mount Sinai, Dec 8, 2018
Novel cellular targets of tDCS support Functional Targeting Coupled Neuro-Vascular Hypothesis of Neuromodulation