Downloading
Personalized Brain Stimulation

Marom Bikson
Disclosure (active or relevant to presentation)


Support (active or relevant to presentation)

NIH (NIMH, NINDS, NCI, NIBIB) – BRAIN Initiative, NSF, Harold Shames, CCNY Fund, 21st Century Fund, Grove Foundation, ElectroCore

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

- **Implants**: Deep Brain Stimulation (DBS), Spinal Cord Stimulation (SCS)
- **In-Hospital**: Transcranial Magnetic Stimulation (TMS), Electroconvulsive Therapy
- **Wearable**: Transcranial Electrical Stimulation (tES), Transcranial Direct Current Stimulation (tDCS)
What defines neuromodulation technologies is how energy is delivered to what target.

- **Implants**
  - Deep Brain Stimulation (DBS)
  - Spinal Cord Stimulation (SCS)

- **In-Hospital**
  - Transcranial Magnetic Stimulation (TMS)
  - Electroconvulsive Therapy

- **Wearable**
  - Transcranial Electrical Stimulation (tES)
  - Transcranial Direct Current Stimulation (tDCS)
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 boosts learning
**High-intensity Pulses**

- Over-driving a neural network

**Low-intensity DC**

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

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.


Experimentally-verified Anatomical MRI derived models of current flow
tDCS

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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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High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow

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tDCS

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Experimentally-verified Anatomical MRI derived models of current flow
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?
tDCS
Anatomical + Functional Targeting
4) Model validation: Huang et al. Measurements and models of electric fields in the human brain during tES. Elife 2017
5) Open source modeling (NIMH ROAST). Realistic vOlumetric-Approach to Simulate tES—ROAST. bioRxiv 217331
Personalized Therapy
Personalized Therapy Interactive

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

Implants
In-Hospital

Apps

Wearable
neuromodulation
Personalized Neuromodulation

Implants
- Deep Brain Stimulation (DBS)
- Spinal Cord Stimulation (SCS)

In-Hospital
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Wearable
- Transcranial Electrical Stimulation (tES)
- Transcranial Direct Current Stimulation (tDCS)
Personalized Neuromodulation

- Implants
  - Deep Brain Stimulation (DBS)
  - Spinal Cord Stimulation (SCS)

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- Wearable
  - Transcranial Electrical Stimulation (tES)
  - Transcranial Direct Current Stimulation (tDCS)
Personalized tDCS

- How much current (1 mA, 2 mA...)
- How much time (10 min, 20 min...)
- Electrode placement
- Task

Most indications trial one dose
Dose response studies not personalized

Will personalized tDCS enhance outcomes? Can’t make it worse if optimized from fixed dose.
Software allows you to steer currents to targeted brain regions

- Single programmable device and head-gear
- Target optimized solved. Question is what target?
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-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
Personalized Neuromodulation Therapy at Home

Head-gear ($R_x +$ sensors)

App

Medical wearable

Historical data

3x Measure

decision
Cloud – 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
Cloud – Prescription

Adaptive questions optimized to select daily treatment (not diagnose)

How are you?

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How’s work?

Option 1
Rx

Option 2
Rx
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Historical data
Responsive Measures for Personalized Neuromodulation

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

Wearable (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)
- App
- **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

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

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

3) **Dry tDCS:** Khadka et al. Tolerability of a novel multilayer hydrogel composite non-adhesive electrode for transcranial direct current stimulation. Brain Stim. 2018
What about peripheral effect (cranial nerves)?

All transcranial electrical/magnetic stimulation produce much higher current densities at the skin.

Just model it.

✔ Target optimized solved. Question is what target?
Personalized Neuromodulation Therapy  Fast Iterative

Tunable targeted

Head-gear ($R_x +$ sensors)

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Models

decision

Responsive Adaptive Q
[Raw Data]

Measures

Historical data
Downloading Personalized Brain Stimulation

Marom Bikson
Details about all brain stimulation meetings at Neuromodec.com