How non-invasive neuromodulation could change pain management

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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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Neuromodulation

Application of energy, often electricity, to the body on purpose (to restore or enhance function)
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)
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- **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)
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)
Current flow across entire brain region

Electrode/Coil

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

Other networks – not targets for neuromodulation

Preferential modulation of more active network (activity dependent)
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)
Repeated DCS accelerates LTP and boosts the ceiling for synaptic learning

- Hypothesis: Combining 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):


Low Intensity Stimulation

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

Preferential modulation of more active network (activity dependent)

Low Intensity Area
tDCS

Experimentally-verified Anatomical MRI derived models of current flow
tDCS

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High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow
tDCS

High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow
tDCS

High Definition tDCS

Experimentally-verified Anatomical MRI derived models of current flow
- Software allows you to steer currents to targeted brain regions
- Single programmable device and head-gear
- Target optimized solved. Question is what target?

Identify target

Select current per electrode
Target optimized solved. Question is what target?
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
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-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

decision

Historical data

3x Measure

Measure
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

Option 2

Rx

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
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 → Cloud → decision → 3x Measure → Historical data → decision

App
Medical wearable

Head-gear ($R_x +$ sensors)
Responsive Measures for Personalized Neuromodulation

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

HealthDot (chronic)
Headgear (during session)

Vital sign
Brain measures

[ Raw data ]

Option 1 Rx
Option 2 Rx
Personalized Neuromodulation Therapy

- Head-gear ($R_x +$ sensors)
- Medical wearable
- App
- Fast Iterative
- Tunable targeted

Responsive Adaptive Q
[Raw Data]

Historical data

Measures

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

Decision

Responsive Adaptive Q [Raw Data]

Historical data

Measures
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

Implants, Drugs, Cognitive & Physical Therapy, +

Non-invasive neuromodulation (tDCS) as something to make other things work better, plus integrated monitoring technology.
How non-invasive neuromodulation could change pain management

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