How the Busy and Folded Brain Responds to tDCS

Marom Bikson
Lucas Parra, Jacek Dmochowski Asif Rahman, Niranjan Khadka, Mark Jackson, Dennis Truong, Zeinab Esmaeilpour, Thomas Radman, Gregory Kronberg, Devin Adair, Nigel Gebodh, Belen Lafon
The City College of New York of CUNY, New York, USA

University of New Mexico Health Sciences Center
Albuquerque, NM
October 4-6, 2017
Disclosure:

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

Support:

NIH (NIMH, NINDS, NCI, NIBIB) – BRAIN initiative, NSF, Epilepsy Foundation, Wallace Coulter Foundation, DoD (USAF, AFOSR)
tDCS: The Elephant in the Room

- Wide range of indications for cognitive enhancement and treatment
- Yet a very simple intervention ("9V battery")

Maybe, It’s not so simple.
tDCS is not simple:
Electrode montage for Anatomical Targeting
tDCS electrode position on the head determines which regions are stimulated.

Specificity may be facilitated by positioning electrodes to “target” specific brain regions.

Truong et al. Clinician accessible tools for GUI computational models. “BONSAI” and “SPHERES”. *Brain Stimulation* 2014
"Cathodal" tDCS
Soma hyper-polarized
Apical dendrite depolarized

"Anodal" tDCS
Soma depolarized
Apical dendrite hyper-polarized

tDCS electrode position on the head determines which regions are stimulated

(!) Must consider both anode and cathode electrodes

Datta et al. Electrode montages for tDCS: Role of "return" electrode *Clinical Neurophys* 2010
tDCS: Directional current flow $\rightarrow$ directional polarization $\rightarrow$ directional excitability and plasticity changes

Disclaimer: Rest of talk will show all this can be wrong.
High-Definition tDCS uses arrays of electrodes to focus current to targets.

Software allows you to generate subject and target specific tDCS “formulation”.

“4x1” montage of High-Definition tDCS

Non-invasive electrical targeting of selected cortex

tDCS is not simple:
Task/Training for Functional Targeting
From Anatomical Targeting to Task Targeting

Network of interest (e.g. depression, pain network)

Other networks – not targets for neuromodulation

Current flow across entire region

Preferential modulation of selected active neurons

Bikson et al. Origins of specificity during tDCS. *Front Human Neuro* 2013
Synaptic efficacy is modulated by Direct Current (polarity specific)

Synaptic efficacy is modulated by Direct Current (polarity specific)

- Direct Current stimulation does not generate synaptic activity or neuronal firing (Functional Targeting)

Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current

LTP from theta burst stim

“Cathodal” or “Anodal” Direct Current Stimulation

Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current

- Direct Current stimulation does not itself generate synaptic plasticity **(Functional Targeting)**

Repeated stimulation 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 of that task (Functional Targeting)
Optimize both Anatomical + Functional Targeting
EEG guided-tDCS:
Anatomically targeting the function
Any EEG can be automatically “inverted” to an optimal HD-tDCS montage
• Based on decades old hypothesis of reciprocity, but based on head model

• Activity guided targeting, but does not require source localization (!)

• Integrated and automatic in theory, but practically concurrent EEG + stimulation has ”inherent physiologic” artifacts (!)

tDCS is not simple: Cellular targets
"Cathodal" tDCS
Soma hyper-polarized
Apical dendrite depolarized

"Anodal" tDCS
Soma depolarized
Apical dendrite hyper-polarized

Axon (synapse) terminals are most sensitive to stimulation

High Rate Stimulation generates LTP which is modulated by concurrent Direct Current

High rate stimulation generates LTP which is modulated by concurrent direct current (DC).

- Depolarized dendrites boost plasticity, under anodal or cathodal DCS.

• Interactions between stimulation polarity and activated network determining modulation.

• “Anodal” or “Cathodal” can either inhibit or boost plasticity – depends on type plasticity:
  - High-Rate is dendrite dependent
  - Theta-burst is some dependent

The folded brain.
Physics: Cortical folding results in alternating pattern of inward ("excitatory") and outward ("inhibitory") current flow

• Gyri level changes in outward/inward polarity

Directionality inversion within Gyri (under electrode)

How can polarity specific (or any) effects result with mixed polarization?

• Input / Output sensitive to anodal polarization only

• Input / Output sensitive to anodal polarization only

• On a population level net change in mixed polarization

Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current stimulation 1 hour after TBS.

- Direct Current stimulation does not itself generate synaptic plasticity (Functional Targeting)

• Simulation driven montage design with HD-tDCS
• Functional Targeting
• LTP specific modulation
• Boosting rate and ceiling of LTP
• Image (EEG) based Targeting
• Axon and Dendrite Compartments
• Mixed polarization
• Non-linear response on the brain ”preference” for excitatory

Maybe, It’s not so simple.
How the Busy and Folded Brain Responds to tDCS

Marom Bikson
Lucas Parra, Jacek Dmochowski Asif Rahman, Niranjan Khadka, Mark Jackson, Dennis Truong, Zeinab Esmaeilpour, Thomas Radman, Gregory Kronberg, Devin Adair, Nigel Gebodh, Belen Lafon

The City College of New York of CUNY, New York, USA

University of New Mexico Health Sciences Center
Albuquerque, NM
October 4-6, 2017

New Mexico Clinical Neurostimulation Meeting