Technical and Mechanistic Foundations of tDCS: Emerging applications in Major Depressive Disorder, May 8. 2014

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Biophysical Foundations of tDCS: Evidence from Computer Models and Animal Studies

Ole Seibt, Lucas Parra, Dennis Truong, Asif Rahman, Thomas Radman, Belen Lafon, Greg Kronberg
tDCS produces current flow in the brain

- Two pad electrodes placed on head and connected to DC current stimulator.
- Current passed between **ANODE(+)** and **CATHODE(-)**
- **DC CURRENT FLOW** across cortex.
- Current is **INWARD** under **ANODE** and **OUTWARD** under **CATHODE**
tDCS current flow: anode and cathode
tDCS current flow: anode and cathode

Current flow

outward  inward

Electrode

Head Surface

Cortical Neuron
tDCS current flow: anode and cathode

- Current flow
  - outward
  - inward

- Head Surface
- Anode (+)
- Hyperpolarized cell compartments
- Depolarized cell compartments
- Increased excitability / Plasticity
Current flow

inward

outward

Head Surface

Cathode (-)

Depolarized cell compartments

Hyper-polarized cell compartments

Decreased Excitability / Plasticity

tDCS current flow: anode and cathode
Animal Studies of Direct Current Stimulation

- >250 pre-clinical studies showing neuromodulation by Direct Current Stimulation (1960-2014)
- Quantification of membrane polarization
- Quantification of modulation of synaptic efficacy and synaptic plasticity
- Quantification of modulation of oscillations
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Neuron Polarization during DCS

Optical Mapping with voltage sensitive dyes

Multi-compartment neuronal modelling

There is a well established mechanistic and quantitative substrate for cellular targets of tDCS

Bikson J Physiol 2004
Neuron Polarization during DCS

Brain slice: Intracellular recording + Morphological reconstruction

Layer II/III Pyramidal
0.1 mV polarization per 1 V/m electric field

Layer I Interneuron
0 mV polarization per 1 V/m electric field

Layer V/VI Bursting Pyramidal
0.3 mV polarization per 1 V/m electric field

DC Current Flow

So little?

Radman Brain Stim 2009
High-intensity Pulses

Over-driving a neural network

Nuance comes from dose (pulse frequency, shape): leading to non-linear changes

Low-intensity DC

Deep Brain Stimulation  Motor Cortex Stimulation  Transcranial Magnetic Stimulation (TMS)
tDCS mechanisms: Neuromodulation

High-intensity Pulses
Over-driving a neural network

Low-intensity DC
tDCS mechanisms: Neuromodulation

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

Transcranial Direct Current Stimulation (tDCS)
Animal Studies of Direct Current Stimulation

- >250 pre-clinical studies showing neuromodulation by Direct Current Stimulation (1960-2014)
- Quantification of membrane polarization
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Direct Current Stimulation modulates synaptic efficacy

Anodal stimulation + evoked synaptic response

fEPSP: metric of cellular synaptic efficacy

Cathodal stimulation (soma Hyperpolarized)

Control

Anodal stimulation (soma Depolarized)

Rahman J Physiol 2013
Direct Current Stimulation modulates synaptic efficacy

- Higher sustained synaptic inputs under anodal stimulation
- Substrate for plasticity
Animal Studies of Direct Current Stimulation

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- Quantification of modulation of oscillations
Direct Current Stimulation of Network Oscillations

Network Gamma Activity

Cathode DCS (-6V/m)

Brain Slice + Computational Model
Reato J. Neurosci 2010

Anode DCS (6 V/m)
Direct Current Stimulation of Network Oscillations

- Boost (anode) or suppress (cathode) ongoing gamma oscillations

Gamma oscillations are a substrate for neuronal plasticity (learning)
Animal Studies of Direct Current Stimulation

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1) tDCS **montage** (electrode position) determines brain current flow pattern.

2) with **Waveform** (duration, intensity) determines dose.
tDCS montages for treatment of Depression

- Brunoni et al.
- SELECT / ELECT
  Anode DPLPC
  2 mA
  Double blind RCT

- Loo et al.
- Multi-Center Trial
  Anode DPLPC
  2 mA
  Double blind RCT
**Neuromodulation: Electrotherapy Delivery Platforms**

- **Deep Brain Stimulation (invasive)**
- **Transcranial Magnetic Stimulation**
- **Transcranial Direct Current Stimulation**

**Decreasing Cost**
- Deployable, compact
- Minimal supervision

**Decreasing Risk**
- Adverse events: itching, erythema
- FDA “NSR”

**Increasing Efficacy, Specificity**

? tDCS Specificity