Determining the tDCS dose: Electrode Montage and Brain Targeting

Harvard tDCS course Boston, Nov 4, 2013

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$ NIH, NSF, Epilepsy Foundation, Wallace Coulter Foundation, DoD
Disclosure:

Soterix Medical Inc. produces tDCS and High-Definition tDCS. Marom Bikson is founder and has shares in Soterix Medical. Some of the clinical data presented may be supported by Soterix Medical.
This talk slides are online now at:
What is tES dose?

Transcranial Electrical Stimulation (tES 🔄) dose is defined by all parameters of the stimulation device that affect the current flow generated in the brain 🔄:

1. **Electrode Montage**: number, shape, size, position.
2. **Waveform**: Current waveform parameters: pulse width, amplitude, polarity, repetition frequency; and interval between stimulation sessions and total number of sessions.

   **tDCS**: Direct Current

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**Nomenclature defined**: Guleyupoglu, Bikson et al. Classification of methods in transcranial electrical stimulation (tES). *J Neurosci Methods* 2013; 219(2) 287-311

**Dose defined**: Peterchev, Bikson et al. Fundamentals of transcranial electric and magnetic stimulation dose: Definition, selection, and reporting practices. *Brain Stimulation* 2012; (5) 435-53
tDCS dose: Waveform

Intensity (mA), Duration (minutes)  Ramp (e.g. LTE), repetition...

Current intensity

Time

Outcome (behavior)

Linear dose-response

-2 mA  2 mA

Anode (1 mA, 20 min)  30 min

Cathode (-1 mA, 20 min)  30 min

Intensity

-  +

-  +

-2 mA  2 mA
tDCCS dose: Waveform

Intensity (mA), Duration (minutes)  Ramp (e.g. LTE), repetition…

Anode (1 mA, 20 min)  30 min
Cathode (-1 mA, 20 min)  30 min

Intensity

Time

Current intensity

Outcome (behavior)

Non-linear dose-reponse (none-monotonic)
tDCS dose: Electrode montage

Number, position, and shape.

Materials, High-Definition...

5x5 cm, M1 (anode), SO (cathode)

“Lateralized” Montage

Extra-cephalic Montage

....
(1) Electrode design and preparation is the most important factor for consistent set-up, tolerability, and safety.

- Pad fluid leak (e.g. pressure, view obstructed)
- Dry out (e.g. pad material, view obstructed)
- Pad re-use (contamination)
- Critical with High-Definition electrodes (but cannot be ignored with pads)
Simple Goal: To increase excitability in cortex under the anode and decrease excitability under the cathode (ignore rest of brain)

(!) There is a biophysical basis for polarity specific excitability changes. But, this simple dose approach is NOT supported by engineering design (or much clinical testing)
Computational models predict the current flow generated in the brain for a specific stimulation configuration/settings.

Electrical activity (efficacy and safety) is determined by current flow at tissue.

tDCS dose is set by surface application (stimulators and pads/coils).
Computational models predict brain current flow

- 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
Theory of neuron polarization by tDCS
Theory of neuron polarization by tDCS
Theory of neuron polarization by tDCS

Anode (+)

Head Surface

Current Flow

Hyperpolarized cell compartments

Depolarized cell compartments

Current flow

outward

inward

? Increased Excitability / Plasticity
Current flow
inward
outward

Head Surface

Cathode (-)

Current Flow

Depolarized cell compartments

Hyper-polarized cell compartments

Decreased Excitability / Plasticity

Theory of neuron polarization by tDCS
Modulation of “excitability” under DCS

- Depolarized soma
  - Increased Excitability / Plasticity

- Hyperpolarized soma
  - Decreased Excitability / Plasticity

Current flow:
- outward
- inward
Cellular Studies on tDSC (neuralengr.com)


Computational models predict brain current flow

- 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**
Electrode-distance dependent after-effects of transcranial direct and random noise stimulation with extracephalic electrodes

Moliadze V, Antal A, Paulus W

Clinical Neurophysiology 2010 121:2165-71

Electrode montages for tDCS and weak transcranial electrical stimulation: Role of “return” electrode’s position and size

Datta A, Rahman A, Scaturro J, Bikson M

Clinical Neurophysiology 2010 121:1976-8

< A priori assumption: Increased current delivered to brain (decrease scalp shunt)

> Clinical neurophysiological: Decreased motor-cortex modulation (TMS-MEP)

> Model prediction: Temporal current “slip”-reducing intensity at motor cortex.

> Clinical trial: Decreased analgesic effect

Transcranial DC stimulation in fibromyalgia: optimized cortical target supported by high-resolution computational models

J Pain 2011 12:610-7

Mendonca ME, Santana MB, Baptista AF, Santana MB, Baptista AF, Datta A Bikson M, Fregni F, Araujo CP

(!) Dose design is not trivial because the relation between dose (montage) and current flow is complex.
Dose design for tDCS with computational models (neuralengr.com)

**A**

**B**
Kuo, Nitsche et al. Comparing cortical plasticity induced by conventional and high-definition 4x1 ring tDCS: a neurophysiological study. *Brain Stimulation*. 2013 6(4):644-8

**C**

**D**

**E**
Conventional and High-Definition Electrodes

Conventional bipolar large electrodes

High-Definition electrodes in “4x1” configuration

Datta et. al. Brain Stim 2009
Targeted High-Definition tDCS

- 5 small “HD” electrodes (4+1)
- 1 Center electrode over target determines polarity (anode, cathode)
- 4 return electrodes - Ring radius determines modulation area

Datta et. al. Brain Stim 2009
Targeted High-Definition tDCS

- Any cortical target can be modulated by center electrode
- Area of modulation selected by ring radius
- High-definition focal neuromodulation (>EEG >TMS)
- HD electrode rating is critical (e.g. 2 mA-20 min single; 1 mA-20 min repeated)
The focality of tDCS can be increased using “High-Definition” electrode arrays. Models can be used to design therapies such as 4x1 HD-tDCS. 

Datta et al. Brain Stim 2009

But: The dose of conventional pad tDCS still determines brain current flow at the global and gyri-specific level.

Truong, Bestmann, Nitche
10 minutes of 2 mA 4x1 HD-tDCS produces >2 hour of after-effects
Neuromodulation with diffuse vs. focused tDCS

Conventional tDCS (2 mA)

High-Definition tDCS (2 mA)
The focality of tDCS can be increased using “High-Definition” electrode arrays. Models can be used to design therapies such as 4x1 HD-tDCS.  

Datta et al. Brain Stim 2009

Focal HD-tDCS produces distinct neuromodulation then conventional pad tDCS.  

Kuo et al. Brain Stim 2013

But: 4x1 HD-tDCS optimization, validation + clinical trials are ongoing.

Caparelli-Daquer, Wassermann IEEE 2012 (TMS MEP)
Borckardt, George et al. J. Pain 2012 (Experimental Pain)
Dmochowski, Parra et al. Neural Engr. 2011 (Optimization)
Villamar, Fregni et al Journal of Pain 2012 (Fibromyalgia)
Dmochowski, Fridriksson, Parra et al. Neuroimage (Stoke)
Edwards, Cortes et al. In Prep (Stroke)
Fregni et al. In Prep (Fibromyalgia with biomarkers)
Rothwell et al. In Prep (TMS MEP, focaliity)

....
Validating 4x1 High-Definition tDCS

Transcranial Electrical Stimulation (TES) – short high-intensity pulse that triggers motor response (MEP)

(?) Comparable focality to TMS
Validating 4x1 High-Definition tDCS

Subject specific modeling and experiments

Edwards et. al. Neuroimage 2013
Inter-subject variation in susceptibility >2x

- Change TES intensity to give same MEP response (left)
- Same TES intensity giving different MEP responses (right)
The focality of tDCS can be increased using “High-Definition” electrode arrays. Models can be used to design therapies such as 4x1 HD-tDCS.  

Datta et al. *Brain Stim* 2009

Focal HD-tDCS produces distinct neuromodulation then conventional pad tDCS.  

Kuo et al. *Brain Stim* 2013

Validation: HD-tDCS produces focal current flow. Anatomical variability is important for tDCS (as for TMS) and can be controlled with computational models.  

*Edwards et al. Neuroimage* 2013
• Evaluated range of conventional and HD tDCS montages
• Male/female, super-obese/low-BMI…
• Considered magnitude of peak current in brain
• Location of peak current inside brain
• Maximum stimulator voltage (safety)
• Current density at scalp (sensation)
The focality of tDCS can be increased using “High-Definition” electrode arrays. Models can be used to design therapies such as 4x1 HD-tDCS.

Kuo et al. *Brain Stim* 2013

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Validation: HD-tDCS produces focal current flow. Anatomical variability is important for tDCS (as for TMS) and can be controlled with computational models.

*Edwards et al. Neuroimage* 2013

Anatomical variability can change magnitude and location of peak current. 4x1 HD-tDCS magnitude more sensitive, but location is robust across individuals.

Truong *Neuroimage Clinical* 2013
tDCS in children

4x1 HD-tDCS

8 year old
2.5 cm separation

8 year old
5 cm separation

12 year old
2.5 cm separation

12 year old
5 cm separation

Adult
5 cm separation

Scalp potential

Electric Field/Current Density

0 33% 66% >0.3 V/m
The focality of tDCS can be increased using “High-Definition” electrode arrays. Models can be used to design therapies such as 4x1 HD-tDCS.  

Focal HD-tDCS produces distinct neuromodulation then conventional pad tDCS.

Validation: HD-tDCS produces focal current flow. Anatomical variability is important for tDCS (as for TMS) and can be controlled with computational models.

Anatomical variability can change magnitude and location of peak current. 4x1 HD-tDCS magnitude more sensitive, but location is robust across individuals.

Anatomical variability aggravated at extremes of age. 4x1 HD-tDCS features same.
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Extra Slides on Cellular Studies on tDCS (neuralengr.com)


Mechanisms and rational design of tDCS

Clinical trials, cognitive neuroscience, neurophysiology, imaging

Animal DCS

Tissue / brain slice DCS
The “sliding scale” explanation for tDCS (and brain function)

Brain function and disease as a change in regional “excitability”

As explained by:
- fMRI
- Lesion studies
- Drugs
- TMS….

Implies monolithic function of each brain region
Implies individuals vary in baseline or max “excitability”

tDCS as a universal modulator of regional brain “excitability”

“Cathodal” stimulation
- “Less” function, less neuronal activity
- “Less” excitatory plasticity (inhibition)

“Anodal” stimulation
+ “More” function, neuronal activity
“More” excitatory plasticity (excitatory)
Transcranial Direct Current Stimulation (tDCS)

- 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

MRI derived computational model
Modulation of sensitivity to synaptic input under DCS

Anodal stimulation + evoked response

fEPSP: metric of cellular synaptic efficacy

Rahman et. al. J Physiol 2013

Cathodal stimulation (soma Hyperpolarized)

Control

Anodal stimulation (soma Depolarized)

Synaptic efficacy
Modulation of sustainable synaptic processing

Higher sustained synaptic inputs under anodal stimulation

Rahman et. al. J Physiol 2013
Alternating Current Stimulation of Network Oscillations

**Network Gamma Activity**

- AC stimulation
- Brain oscillations

**Entrainment**

**Modulation**

- Entainment
- Frequency increased
- Subharmonics
- Frequency decreased
- Power modulation
- Spiking resonance

Increasing AC amplitude

Increasing AC frequency

Gamma peak (25Hz)

Double gamma peak (50Hz)
tDCS mechanisms: Neuromodulation

Low-intensity DC + specific network activation
tDCS mechanisms: Neuromodulation

Low-intensity DC + specific network activation

Electrode

Current flow across entire region
tDCS mechanisms: Neuromodulation

Low-intensity DC + specific network activation

Current flow across entire region

Modulation (plasticity) of only co-activated neurons