Practical for transcranial Direct Current Stimulation (tDCS)

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Complete references and sources at end.
Some questions about tDCS....
What does tDCS look like?
What does tDCS look like?

Here’s an electrode
Head-gear to hold them in specific places
Two cables to the device
Here’s another one
The most fundamental mistake in tDCS is assuming equipment and accessories selection does not matter, electrode preparation does not matter, training does not matter.

Control and documentation of details underpins reproducibility, tolerability, efficacy...

What is the “dose” of tDCS?

- Size, position, and current applied to electrodes
- Example: 5x5 cm\(^2\) electrodes, C3 Anode, SO Cathode, 2 mA for 20 minutes

Peterchev, Bikson et. al.
*Brain Stim*
2012
tDCS waveform is easy to describe

Intensity (mA), Duration (minutes)

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

Current intensity vs. Time
tDCS montage pretty easy to describe

Number, position, and shape.

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

“Lateralized” Montage

Extra-cephalic Montage

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So: **regular tDCS** uses large sponge based electrodes connected to a 2-channel device (one anode, one cathode)

**Practical training** is just how to prepare these sponge electrodes and set-up 2-channel device.

**Theory** is where you should place them and device settings (dose) along with other intervention design factors (tasks, inclusion/exclusion...)

DaSilva et al. Electrode positioning and montage in transcranial direct current stimulation. *JOVE* 2011
What is the High-Definition tDCS?

• Use of small “HD” gel-electrodes, instead of sponges
• Categorical increase in control on brain targeting
• Useful with EEG

Dmochowski, Bikson et al

*J. Neural Engr.* 2011
What is the 4x1 HD-tDCS?

- Five HD electrodes (one center, four surround)
- Used for focal unidirectional cortical modulation

Datta, Bikson et al

*Brain Stimulation* 2009
So regular **tDCS** uses large sponge-based electrodes connected to a 2-channel device (one anode, one cathode)

**Practical training** is just how to prepare these sponge electrodes and set-up 2-channel device. **Multi-channel**

**Theory** is where you should place electrodes and device settings (dose) along with other intervention design factors (task, inclusion/exclusion)

Villamar et al. Technique and considerations in the use of 4x1 ring HD-tDCS. *JOVE* 2013
Is tDCS safe?

- Consensus YES: No serious adverse effect in >30,000 sessions in (diverse) patients or healthy volunteers
- Requires certified equipment and protocols
Is tDCC tolerated?

- Consensus YES: but when standard protocols are followed
- Requires certified equipment (devices, electrodes) and training
Can tDCS be done at home?

• Only with specially designed equipment
• Consensus telemedicine protocols: “Remote-Supervised tDCS”

Remotely-supervised transcranial direct current stimulation (tDCS) for clinical trials: guidelines for technology and protocols

Leigh E. Charvet*1, Margaret Kasschau1, Abhishek Datta2, Helena Knotkova3, Michael C. Stevens4, Angelo Alonzo5, Colleen Loo5, Kevin R. Krull6 and Marom Bikson7
How does tDCS work?

- Low-intensity direct current polarizes neurons
- Change in membrane potential changes processing and plasticity

Jackson, Bikson et. al.  
*Clinical Neurophys.* 2016
Is more dose, more?
Is more dose, more?

Intensity (mA), Duration (minutes)

- Anode (1 mA, 20 min) 30 min)
- Cathode (-1 mA, 20 min) 30 min)
-2 mA

Outcome (behavior)

Linear dose-response

Nitche et. al. J Physiol. 2000
Is more dose, more?

Intensity (mA), Duration (minutes)

Anode (1 mA, 20 min) | 30 min
Cathode (-1 mA, 20 min) | 30 min
-2 mA

Non-linear dose-response (none-monotonic)

Nitche et. al. *J Physiol.* 2013
Lets talk montage...

(and all the mistakes people make and all the potential people don’t leverage)
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**
Transcranial Direct Current Stimulation (tDCS)

Radman et al.  
*Brain Stim.* 2009
Transcranial Direct Current Stimulation (tDCS)

Current flow
outward  inward

Electrode
Head Surface
Cortical Neuron

Radman et al.
Brain Stim. 2009
Transcranial Direct Current Stimulation (tDCS)

Current flow: inward, outward

Anode (+)

Head Surface

Hyperpolarized cell compartments

Depolarized cell compartments

Increased Excitability / Plasticity

Transcranial Direct Current Stimulation (tDCS)

Current flow
outward      inward

Head Surface

Cathode (-)

Current Flow

Depolarized cell compartments

Hyper-polarized cell compartments

Decreased Excitability / Plasticity

Radman et al.  
*Brain Stim.* 2009
Central assumption: Inward/Outward current flow produces Excitation/Inhibition

Then, classic tDCS design:

- “Active” electrode placed over the target and polarity selected to Excite (Anode) or Inhibit (Cathode)
- “Return” ("reference") electrode placed somewhere else, and ignored

Physics of current flow does not support this approach
Montovani Montage (tested for OCD)
“Active” electrode over the pre-Supplementary Motor Area
“Return” on the right shoulder
Current flows in and out of brain

Physics

• Current goes from anode to cathode
• All current that enters the cortex must exit

TDCS design implications

• Must consider both electrodes
• No such thing “anodal” or “cathodal” tDCS

Datta et al. *Clinical Neurophys.* 2010
Current does not stop at cortex

Physics
• Current is conserved when passing through grey matter
• Electric fields can increase based on anatomy

tDCCS design implications
• Deep brain structures cannot be ignored
• Spine sometimes cannot be ignored

Dasilva et al. *Headache*. 2012
Current does not stop at cortex

Physics

• Hot-spots around deep structures
• Cellular morphology is varied

tDCS design implications

• Difficult to predict “increase” or “decrease” in deep structures
• Details idiosyncratic
Current direction at cortex complex

Physics
• Cortical folding results in alternating pattern of inward ("excitatory") and outward ("inhibitory") current flow

Physics
• Cortical folding results in alternating pattern of inward ("excitatory") and outward ("inhibitory") current flow

TDCS design implications
• Direction at target idiosyncratic (individualized)
• Excitability reverses across regions and within gyri
High-Definition electrodes in “4x1” configuration

Conventional bipolar large electrodes

Datta et. al. Brain Stim 2009
4x1 High-Definition tDCS

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

Center electrode: CATHODE

Center electrode: ANODE

Outward current (inhibitory)  

Inward current (excitatory)
Conclusions: Current flow design in tDCS

- tDCS is rationalized based on increasing / decreasing cortical excitability with inward / outward current flow
- Conventional tDCS uses two large electrodes (one anode, one cathode) producing diffuse and deep brain current flow, with peak brain intensity somewhere between electrodes
- 4x1 High-Definition tDCS (HD-tDCS) allows targeting of just cortex with a largely uni-directional pattern
- Other High-Definition montages can be designed and optimized

Datta et. al. Brain Stim 2009
Dmochowski Neural Engr. 2011
How do we Optimize Brain Stimulation?
( how to do it “right” )
How do we optimize brain stimulation?

**Who:** Subject selection
   (inclusion, exclusion)

**Where:** Targeted brain region
   (primary, secondary)

**What:** Adjunct therapies
   (training, drugs)

**When:** Timing
   (repetition)

**Why:** Mechanism driven design
   (disease etiology)
How do we optimize brain stimulation?

**Who:** Subject selection (inclusion, exclusion)

**Where:** Targeted brain region (primary, secondary)

**What:** Adjunct therapies (training, drugs)

**When:** Timing (repetition)

**Why:** Mechanism driven design (disease etiology)

Individual anatomy and physiology determine response

Datta, Truong, Bikson et al. Inter-individual variation during transcranial Direct Current Stimulation. Front Psychiatry 2012
How do we optimize brain stimulation?

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(disease etiology)

Where we put the electrode or coil

How do we optimize brain stimulation?

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  (disease etiology)

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**Adjunct interventions to change brain state**

Bestmann and Feredoes. Combining neurostimulation and neuroimaging in cognitive neuroscience Ann N Y Acad Sci 2013
How do we optimize brain stimulation?

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Where: Targeted brain region
   (primary, secondary)
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   (training, drugs)
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Why: Mechanism driven design
   (disease etiology)

Relative to absolute time (time of day, repetition...)
or responsive (biomarker, symptoms...)
How do we optimize brain stimulation?

**Who:** Subject selection  
(inclusion, exclusion)

**Where:** Targeted brain region  
(primary, secondary)

**What:** Adjunct therapies  
(training, drugs)

**When:** Timing  
(repetition)

**Why:** Mechanism driven design  
(neuromodulation)

Waveform (pulse frequency, DC...) and intensity (supra-threshold, sub-threshold)
How do we optimize brain stimulation?

**Who:** Subject selection  
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(disease etiology)
From Anatomical to Functional Targeting

Network of interest (e.g. therapy, brain function)  Other networks – not targets for neuromodulation

Current flow across entire region

Preferential modulation of more active network (Activity Selective Targeting)

Bikson and Rahman, Origins of specificity during tDCS, anatomical, activity-selective, and input-bias mechanisms. Frontiers Human Neuroscience 2013
How do we optimize brain stimulation?

Who: Subject selection
   (inclusion, exclusion)

Where: Targeted brain region
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Functional Targeting: Only brain regions primed by training are sensitive to stimulation

Bikson and Rahman, Origins of specificity during tDCS, anatomical, activity-selective, and input-bias mechanisms. Frontiers Human Neuroscience 2013
How do we optimize brain stimulation?

**Who:** Subject selection  
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**Where:** Targeted brain region  
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   (disease etiology)
Anatomical targeting with brain stimulation

**Supra-threshold stimulation**
- DBS
- Cortical stim
- TMS


**Sub-threshold stimulation**
- HD-tDCS
- 4x1

Stimulation primary neuromodulation target. Endogenous circuit.

Bestmann and Feredoes. Combining neurostimulation and neuroimaging in cognitive neuroscience Ann N Y Acad Sci 2013
How do we optimize brain stimulation?

Who: Subject selection
(inclusion, exclusion)

Where: Targeted brain region
( primary, secondary)

What: Adjunct therapies
(training, drugs)

When: Timing
(repetition)

Why: Mechanism driven design
(disease etiology)

Focality determined by waveform
Change in outcomes with electrode/coil position ≠ focality

Bestmann and Feredoes. Combining neurostimulation and neuroimaging in cognitive neuroscience Ann N Y Acad Sci 2013
How do we optimize brain stimulation?

Who: Subject selection
   (inclusion, exclusion)

Where: Targeted brain region
   (primary, secondary)

What: Adjunct therapies
   (training, drugs)

When: Timing
   (repetition)

Why: Mechanism driven design
   (disease etiology)

Combination of modalities

How do we optimize brain stimulation?

**Who**: Subject selection (inclusion, exclusion) X

**Where**: Targeted brain region (primary, secondary) X

**What**: Adjunct therapies (training, drugs) X

**When**: Timing (repetition) X

**Why**: Mechanism driven design (disease etiology)

!!!! Large parameter space of combinations
Need to optimize + individualize brain stimulation?

• Despite the **theoretical** flexibility of stimulation, treatments are remarkably invariant across diverse indications (individuals)
  
  (number of pulses, current intensity, hardware...)

• Assume: refining brain stimulation to patient group or individual will enhance tolerability and efficacy
  
  We can only do better, and often need to

• Essentially every brain stimulation that developed from investigational to broadly disseminated (FDA approval) includes individualized therapy
  
  (DBS, TMS...
Computational Models of Brain Stimulation

• Given the large parameter space of brain stimulation, and inevitable limits (cost, risk) of clinical treatment and trials, cannot just “try everything”

• **Computational Models of Brain Stimulation are quantitative tools (software, protocols) that facilitate optimization.**

• **Optimization**: Specific patients groups or individuals receive interventions based on unique characteristics.

• **Tools**: Software or protocols that given patient specific data, suggest treatment strategy. Evolving and iterative.
Those papers with Bikson co-author can be downloaded here
http://bme.ccny.cuny.edu/people/faculty/mbikson


Dasilva AF, Volz MS, Bikson M, Fregni F. Electrode positioning and montage in transcranial direct current stimulation. JOVE . 2011; (51)


Dasilva AF, Mendonca ME, Zaghi S, Lopes M, Dossantos MF, Spierings EL, Bajwa Z, Datta A, Bikson M, Fregni F. tDCS-Induced Analgesia and Electrical Fields in Pain-Related Neural Networks in Chronic Migraine. Headache. 2012; 52(8) 1283-95

