How does Direct Current Stimulation (DCS) work?

DCS boosts **Hebbian** plasticity

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Disclosure

Co-inventor in patents held by the City University of New York.

Co-founder of Soterix Medical, Neuromatters and Kcore Analytics – startup efforts to make neurotechnology broadly available.
Clinical perspective on mechanism of tDCS

Anode (+) increased excitability

Cathode (-) decreased excitability

Perhaps too simplistic
Direct currents cause complex E-fields

- Strongest E-field not always under the stimulation electrodes
  
- Cortical gyration cause mixed polarity E-fields

Datta, *Brain Stimulation*, 2009

Rahman, *J Physiology*, 2013
Model validation in human

Huang, Liu, eLife, 2017
E-field models are generally accurate.

- Magnitude and spatial distribution of E-field generated by TES reasonably well predicted.

Huang, *eLife*, 2017
TES can reach deep targets

- Maximum cortical stimulation for 2mA → 1 V/m
- Deep targets can be equally strong
- Individual subject anatomy matters

Huang, eLife, 2017
The ROAST pipeline is a method for realistic volumetric approach to simulate transcranial electrical stimulation.

- **Free**
- **Fast**: 10~30 min
- **Fully automated**
- **Easy to use**


```
>> roast('subject.nii', {'F1', 2, 'P2', -2})
```

Available at: parralab.org/roast
Stimulation intensity

- “Intersectional Pulsed Stimulation” (IPS) uses multiple 1mA electrodes to achieve stronger stimulation in depth.
- Targeting of IPS is equivalent to High Definition TES which can be optimized.

Huang, *Brain Stimulation*, 2018
Fields polarize the membrane linearly

![Neuron diagram](image)

\[ \Delta V = f(E) \]

Bikson, *J Physiology*, 2004
Transient effects – summary

\[ \Delta V = V = 0.1 \text{mV} \]

→ 1% firing rate

→ 1% synaptic efficacy

→ 1ms timing → entrainment

Reato, *Frontiers in Human Neuroscience*, 2013
Long term effects?

Hypothesis: Long term effects are mediated by synaptic plasticity

Hypothesized mechanism:
• E-fields polarize the membrane.
• In “Hebbian” plasticity the membrane depolarization captures post-synaptic activity.

Prediction:
• E-field interact with long-term synaptic plasticity via membrane depolarization.

Kronberg, *Brain Stimulation*, 2017
Plasticity induction + DC stimulation

- Induce long term potentiation/depression (LTP/LTD) in vitro in hippocampus.
- Record synaptic efficacy with field excitatory postsynaptic potentials (fEPSP).

High frequency tetanus → LTP
Low frequency tetanus → LTD

Kronberg, *Brain Stimulation*, 2017
LTP & LTD are both modulated

- Cathodal DCS
- control

Kronberg, *Brain Stimulation*, 2017
Depolarizing field → stronger synapses

Greg Kronberg, *Brain Stimulation*, 2017
Depolarizing field → stronger synapses

Kronberg, *Brain Stimulation*, 2017
Affected pathway depends on polarity

Kronberg, *Brain Stimulation*, 2017
DCS effect requires LTP

No activity → no effect

No NMDAR → no effect

Kronberg, *Brain Stimulation*, 2017
Conclusions of tetanus-induced LTP/LTD:

DCS effects on synaptic strength are specific:
• Needs synaptic plasticity to affect plasticity
• Tends to potentiate, not depress synapses
• Cathodal vs anodal effect specific to dendritic location

Kronberg, *Brain Stimulation*, 2017
Polarity interacts with type of activation

Theta burst stimulation (TBS): HF burst repeated at 7Hz. TBS dominated by somatic activity and we target close to the soma.

Kronberg, *bioRxiv*, 2019
Bias towards potentiation

- Soma depolarizing
- Soma hyper-polarizing

Kronberg, *bioRxiv*, 2019
Bias towards potentiation

Human tDCS

→ 1% in 1V/m

Kronberg, bioRxiv, 2019
Instantaneous E-field is relevant
Specific to the potentiated pathway

Kronberg, *bioRxiv*, 2019
Specific to the potentiated pathway

Weakly activated pathway is not enhanced.

Kronberg, bioRxiv, 2019
Associative

Strong stimulation induces LTP in weakly co-activated pathway. This associative effects is preserved and enhanced with DCS.
Conclusion

DCS boosts Hebbian plasticity:
- Effect dependent on potentiating neural activity
- Specific to activated pathway
- Follows associative rule of learning
Clinical implications

**Postulate**
Human tDCS effects are highly task specific because they inherit exquisite specificity of Hebbian plasticity.

**Predictions on tDCS:**
- Efficacy improves when paired with a learning task instead of rest.
- Specificity comes from the task not focality of stimulation.
- Performance gains should be specific to the trained task.
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Code, data, papers: parralab.org

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