Synaptic plasticity mechanisms explain the specificity of DCS

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Disclosure

Lucas Parra is co-founder of Soterix Medial Inc. and co-inventor in patents held by the CCNY. The goal of these efforts is to make High-Definition tDCS broadly available.

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Clinical perspective on mechanism of tDCS

Cathode (-) decreased excitability

Anode (+) increased excitability

Perhaps too simplistic
Detailed models of current flow

- Maximum not always under the electrode
- Polarity inevitably mixed
Model validation in human
Model validation in human

- Individual head anatomy is important

Huang, Liu,...Parra, eLife, in revision
Acurate prediciton of distribution

- Magnitude estimates of existing models generally too high

Huang, Liu,...Parra, eLife, in revision
Can reach deep targets

- Maximum cortical stimulation for 2mA → 0.5 V/m
- Deep targets next to CSF can be equally strong

Huang, Liu, Lafon, Friedman, Dayan, Wang, Bikson, Devinsky, Parra, Measurements and models of electric fields in the in vivo human brain during transcranial electric stimulation, *eLife*, in reversion, October 2016
Fields polarize the membrane linearly

Somatic membrane susceptibility:

\[ \Delta V = cE \]

\[ f(x) = -0.16x + 0.34 \]

\[ R^2 = 0.97 \]

\[ c = 0.1 \frac{V}{V/m} \]

Transient effects – summary

$J = 2 \text{mA}$

$E < 0.5 \text{ V/m}$

$0.1 \text{mV}$

→ 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
LTP/LTD + DC stimulation

Long term synaptic plasticity induced with pulsed-stimulation.

High Frequency → LTP
Low Frequency → LTD

LTP & LTD are both modulated

- dendrite depolarizing (20V/m)
- control

Consistent with dendritic polarization

Activity and NMDA dependent

- dendrite depolarizing (20V/m)
- control

Theta Burst Stimulation, effect consistent with somatic polarization

Theta burst stimulation (TBS)

7Hz bursts

Direction of electric field

SC stim Rec

Relative fEPSP slope

Time (min)

n=12

-20 V/m DCS
+20 V/m DCS
Control

1 mV
5 ms

-20 V/m
+20 V/m

control
soma depolarizing
soma hyper-polarizing

Rahman et al., in preparation
Monotonic, bias to potentiation

![Graph showing relative fEPSP slope vs electric field (V/m). The x-axis represents electric field values from -20 to 20 V/m, and the y-axis represents relative fEPSP slope from 1 to 1.8. The graph demonstrates a monotonic relationship with soma depolarizing and soma hyper-polarizing conditions.]

Rahman et al., in preparation
Repeated TBS boost ceiling of LTP

Rahman et al., in preparation
Strong stimulation known to induced LTP in weakly co-activated pathway.

Rahman et al., in preparation
DCS boosts associative LTP

Asif Rahman

Rahman et al., in preparation
Summary: Lasting Synaptic Effects of DCS

- Require plasticity; do not happen in isolation.
- Polarity effects mixed, but tend to strengthen synapses.
- “Hebbian”: Dependent on activity and NMDA, are pathway specific, follows associative potentiation.

Postulate

Human tDCS effects are specific because DCS modulates Hebbian plasticity, which can be highly task specific.
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