Does Increasing Current Intensity of tDCS Boosts Outcomes?

Marom Bikson
Lucas Parra, Jacek Dmochowski, Hanoch Kaphzan, Asif Rahman, Niranjan Khadka, Mark Jackson, Dennis Truong, Belen Lafon, Gregory Kronberg, Devin Adair, Nigel Gebodh, Mohamed Fallah Rad, Zeinab Esmaeilpour, Devin Adair, Thomas Radman

The 17th Annual International Conference on Dose-Response

PRECONDITIONING IN BIOLOGY AND MEDICINE
Mechanisms and Translational Research

The Annual Meeting of the International Dose-Response Society

April 18, 2018
Disclosure

The City University of New York has patents on brain stimulation with Marom Bikson as inventor.

Marom Bikson was equity in Soterix Medical Inc.

Marom Bikson serves on the Boston Scientific neuromodulation scientific advisory board.

Support

NIH (BRAIN), Harold Shames, DoD
Transcranial Direct Current Stimulation (tDCS)

• Non-invasive, portable (9V), well-tolerated neuromodulation.
• Low-intensity (1-2 mA) current passed between scalp electrodes.
• Tested for cognitive neuroscience and neuropsychiatric treatment and neurorehabilitation.

~2000 trials since 2005

Very abbreviated list of tDCS indications and applications:

Medical: Depression, Pain, Migraine, Parkinson's, Alzheimer’s, Epilepsy, PTSD, Schizophrenia, Tinnitus, Neglect, Rehabilitation (motor, aphasia), TBI, OCD, MS...

Performance: Attention / Vigilance, Accelerated learning (reading, motor skills, math, threat detection), Memory, Creativity, Sleep (SW, Lucid dreaming, Threat detection, Impulsivity, Compassion, Jealousy, IQ, Prejudice...
Training or Therapy ➔ Benefit

tDCS + Training or Therapy ➔
More Benefit on Specific Task or Indication
Almost all tDCS trials use between 1 or 2 mA ... because almost all tDCS trials use 1 or 2 mA.

- Is 2 mA better then 1 mA?
- Do currents greater than 2 mA boost outcomes?
Mechanisms and Effects of Transcranial Direct Current Stimulation

James Giordano¹, Marom Bikson², Emily S. Kappenman³, Vincent P. Clark⁴, H. Branch Coslett⁵, Michael R. Hamblin⁶, Roy Hamilton⁵, Ryan Jankord⁷, Walter J. Kozumbo⁸, R. Andrew McKinley⁷, Michael A. Nitsche⁹, J. Patrick Reilly¹⁰, Jessica Richardson¹¹, Rachel Wurzman⁵, and Edward Calabrese¹²
Incomplete evidence that increasing current intensity of tDCS boosts outcomes

Zeinab Esmaeilpour a,b,*, Paola Marangolo c, Benjamin M. Hampstead d,e, Sven Bestmann f, Elisabeth Galletta g, Helena Knotkova h,i, Marom Bikson a

a Department of Biomedical Engineering, The City College of New York of CUNY, New York, NY 10031, USA
b Biomedical Engineering Department, Amirkabir University of Technology, Tehran, Iran
c Dipartimento di Studi Umanistici, University Federico II, Naples and IRCCS Fondazione Santa Lucia, Rome Italy
d VA Ann Arbor Healthcare System, Ann Arbor, MI 48105, USA
e Department of Psychiatry, University of Michigan, Ann Arbor, MI 48105, USA
f Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, University College London, UK
g Rusk Rehabilitation Medicine, New York University Langone Medical Center, USA
h MJHS Institute for Innovation in Palliative Care, New York, NY, USA
i Department of Family and Social Medicine, Albert Einstein College of Medicine, The Bronx, NY, USA
Approach: Monotonic dose response across scales?

Not monotonic (linear) at any scale than potentially not in totality
Monotonic dose response across scales

Current flow intensity (Electric field) in brain
- Peak = 0.426 V/m
- Peak = 0.852 V/m
- Peak = 0.28 V/m

Membrane polarization
- Radial Field = 0.08 V/m
- Radial Field = 0.16 V/m
- Radial Field = 0.14 V/m

Excitability and synaptic efficacy (plasticity)

Network activity

Cognition and Behavior
- 1X Change?
- 2X Change?
- -2X Change?
- 2X Change?

Technology/Outcome measure

Biophysical Modeling
- Current flow modeling
- Neuron model
- Network model
- Computational neurostimulation

Animal Modeling
- Intracellular recording
- Voltage sensitive dyes
- Excitatory Post Synaptic Potential (EPSP)
- Calcium imaging

Human Neurophysiology
- Transcranial Magnetic Stimulation (TMS) / Motor Evoked Potential (MEP)
- Transcranial Magnetic Stimulation (TMS)/ Electroencephalography (EEG)

Neuroimaging
- Spectroscopy
- Functional Magnetic Resonance Imaging (fMRI)
- Arterial Spin Labeling (ASL)

Behavioral/Clinical Measures
- Questionnaire
- Visual Analogue Scale (VAS)
- Task performance (rate)
Monotonic dose response across scales.
Applied current for a given electrode montage and brain electric fields
Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad

Abhishek Datta, MS, Varun Bansal, BS, Julian Diaz, BS, Jinal Patel, MS, Davide Reato, MS, Marom Bikson, PhD
• Electrode montage (number and size) determines brain current flow pattern

• Electric field in any brain region linear with applied current
Individual variation and dose response with diffuse tDCS and focal HD-tDCS
Physiological and modeling evidence for focal transcranial electrical brain stimulation in humans: A basis for high-definition tDCS
Validated: Subject specific models predict MEP
Monotonic dose response across scales

Current flow intensity (Electric field) in brain
- Peak = 0.426 V/m
- Peak = 0.852 V/m
- Peak = 0.28 V/m

Membrane polarization
- Radial Field = 0.08 V/m
- Radial Field = 0.16 V/m
- Radial Field = 0.14 V/m

Excitability and synaptic efficacy (plasticity)

Network activity

Cognition and Behavior
- 1X Change?
- 2X Change?
- -2X Change?
- 2X Change?

Technology/Outcome measure

Biophysical Modeling
- Current flow modeling
- Neuron model
- Network model
- Computational neurostimulation

Animal Modeling
- Intracellular recording
- Voltage sensitive dyes
- Excitatory Post Synaptic Potential (EPSP)
- Calcium imaging

Human Neurophysiology
- Transcranial Magnetic Stimulation (TMS) / Motor Evoked Potential (MEP)
- Transcranial Magnetic Stimulation (TMS)/ Electroencephalography (EEG)
- Electroencephalography (EEG)

Neuroimaging
- Spectroscopy
- Functional Magnetic Resonance Imaging (fMRI)
- Arterial Spin Labeling (ASL)

Behavioral/Clinical Measures
- Questionnaire
- Visual Analogue Scale (VAS)
- Task performance (rate)
Monotonic dose response across scales
Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices in vitro

Marom Bikson¹, Masashi Inoue², Hiroki Akiyama², Jackie K. Deans¹, John E. Fox¹, Hiroyoshi Miyakawa² and John G. R. Jefferys¹

¹Department of Neurophysiology, University of Birmingham, Birmingham, UK
²Department of Life Science, Tokyo University of Pharmacy and Life Science, Tokyo, Japan
Linear membrane polarization with Electric Field intensity
Translational studies on dose response
Dose response in animal models
A.1 Fixed Electric Field (in-vitro animal model)

A.2 Fixed current over skull (in-vivo animal model)
Dose response with diffuse tDCS
Fixed current vs Fixed Electric Field
B.1 Fixed Electric field inside brain (conventional electrodes)

- Individualized current
- tDCS
- Brain EF
- Outcome measure:
  - Neurophysiology
  - Clinical Imaging
  - Behavioral measure

B.2 Fixed stimulator output (conventional electrodes)

- Fixed current
- tDCS
- Brain EF
- Outcome measure:
  - Neurophysiology
  - Clinical Imaging
  - Behavioral measure

- Same EF in ROI
- 0.5 (V/m) Brain EF
- 1 (V/m) Brain EF

- Different EF in ROI
- 1 mA
- 2 mA
- 0.5
- 0.3
- 0.6

Post-hoc modeling
- ROI EF (V/m)
Dose response with focal HD-tDCS
Fixed current vs Fixed Electric Field
C.1 Fixed Electric field inside brain (HD-electrodes)

- Individualized current
- tDCS
- Brain EF
- Outcome measure:
  - Neurophysiology
  - Clinical Imaging
  - Behavioral measure

C.2 Fixed stimulator output (HD-electrodes)

- Fixed current
- tDCS
- Brain EF
- Outcome measure:
  - Neurophysiology
  - Clinical Imaging
  - Behavioral measure

- Same EF in ROI
- 0.5 (V/m) Brain EF
- 1 (V/m) Brain EF

- Different EF in ROI
- 0.3 Brain EF
- 0.6 Brain EF
- 0.3 ROI EF
- 0.5 ROI EF
- 0.6 ROI EF
Monotonic dose response across scales

- Anodal - 1 mA
- Anodal - 2 mA
- Cathodal - 2 mA
- HD-4X1 - 2 mA

Current flow intensity (Electric field) in brain
- Peak = 0.426 V/m
- Peak = 0.852 V/m
- Peak = 0.852 V/m
- Peak = 0.28 V/m

Membrane polarization
- Radial Field = 0.08 V/m
- Radial Field = 0.16 V/m
- Radial Field = 0.16 V/m
- Radial Field = 0.14 V/m

Excitability and synaptic efficacy (plasticity)

Network activity

Cognition and Behavior
- 1X Change?
- 2X Change?
- -2X Change?
- 2X Change?

Technology/Outcome measure

Biophysical Modeling
- Current flow modeling
- Neuron model
- Network model
- Computational neurostimulation

Animal Modeling
- Intracellular recording
- Voltage sensitive dyes
- Excitatory Post Synaptic Potential (EPSP)
- Calcium imaging

Human Neurophysiology
- Transcranial Magnetic Stimulation (TMS) / Motor Evoked Potential (MEP)
- Transcranial Magnetic Stimulation (TMS)/ Electroencephalography (EEG)
- Electroencephalography (EEG)

Neuroimaging
- Spectroscopy
- Functional Magnetic Resonance Imaging (fMRI)
- Arterial Spin Labeling (ASL)

Behavioral/Clinical Measures
- Questionnaire
- Visual Analogue Scale (VAS)
- Task performance (rate)
Monotonic dose response across scales

- Anodal - 1 mA
- Anodal - 2 mA
- Cathodal - 2 mA
- HD-4X1 - 2 mA

Current flow intensity (Electric field) in brain
- Peak = 0.426 V/m
- Peak = 0.852 V/m
- Peak = 0.852 V/m
- Peak = 0.28 V/m

Membrane polarization
- Radial Field = 0.00 V/m
- Radial Field = 0.16 V/m
- Radial Field = 0.14 V/m
- Radial Field = 0.14 V/m

Excitability and synaptic efficacy (plasticity)

Network activity

Cognition and Behavior

1X Change?  2X Change?  -2X Change?  2X Change?
Brain state dependent dose response
tDCS combined with task (brain state)
Does tDCS “boost” brain function or “pre-condition”

Should tDCS be applied during or before training?

Is more-current more?
Additional references
available at neuralengr.org/bikson


