Cognitive Enhancement with tCS

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DIY cognitive enhancement..

Zap Yourself Smarter With This DIY tDCS Brain Stimulator

Kannon Yamada

On 26th November, 2014

[Image of a person wearing a brain stimulation device]

The Depression Treatment Device

Use for 20 minutes, once or twice a day.

[Image of a person using a device]

Oxford Martin Policy Paper

Mind Machines
The Regulation of Cognitive Enhancement Devices

Hannah Maslen, Thomas Douglas, Roi Cohen Kadosh, Neil Levy and Julian Savulescu

The Atlantic

Prepare to Be Shocked
Four predictions about how brain stimulation will make us smarter
Outline

- tCS effects: theories & controversies
- Net-zero sum theory (?)
- Trait – Dependency of tCS effects
- tCS targeting → Networks
Why-What-Where-How Neuroenhancement

Physical activity
- unspecific effects on metabolism and nutrients
- Requires commitment and time (elderly..)

Drugs (modafinil, memantine)
- Side effects
- unspecific effects (all brain)

Dietary regimen
- Same as physical activity

Brain training
- Effect on specific functions
- Effect size is usually small...

Transcranial Current Stimulation (tCS)
- Cheap
- Less commitment
- Wearable
- Easy to use
- Stand-alone intervention OR add-on (enhancer)
- More focal (→ modeling)

Special issue in Current Opinion in Behavioural Sciences 2016
Cognitive Enhancement with tDCS

Reviewed ~ 100 studies
- tDCS (anodal, cathodal)
- healthy participants
- age 18-55
- Sham-controlled

(Coffman et al., 2014; Horvath et al., 2015)
Single session vs training; online-offline...

**ONLINE vs OFFLINE**
- Offline: 33%
- Online: 67%

**ONLINE EFFECTS**
- ↑ ACC: 52%
- ↓ RT: 27%
- ↑ RT: 6%
- ↓ ACC: 15%

**OFFLINE EFFECTS**
- ↑ ACC: 50%
- ↓ RT: 22%
- ↑ RT: 17%
- ↓ ACC: 11%

**SINGLE SESSION vs TRAINING**
- Single: 88%
- Multiple: 12%

Santarnecchi et al. 2015, Curr. opin. in Behav. Sc.
Polarity specific Effects?

Is **anodal** tDCS more effective?  
Is **cathodal** tDCS detrimental?

Santarneechi et al. 2015, Curr. opin. in Behav. Sc.
Non-specific effects?

**Cognitive Functions**
- Language: 19%
- WM: 30%
- STM: 14%
- LTM: 16%
- Problem solving: 5%
- Verbal learning: 4%
- Creativity: 3%
- Implicit learning/memory: 5%
- Aritmetical reasoning: 2%
- Cognitive control: 3%
- Attention: 3%

**Stimulation Site**
- Left DLPFC: 56%
- F3: 13%
- CP5: 7%
- CP6: 2%
- F4: 2%
- C3: 2%
- P5: 2%
- P4: 2%
- P3: 4%
- P8: 2%
- T3: 2%

**Montages..?**
Enhancement of Working Memory

- The N-back working memory task (Fregni et al., 2005)

3-back task

Key region: dorsolateral prefrontal cortex
Enhancement of Working Memory

- **Anodal** tDCS of left DLPFC enhances performance on 3-back working memory task (Fregni et al., 2005)

- **Anodal** tDCS of the left DLPFC, combined with N-back working memory task, enhances digit span (Andrews et al., 2011)
  - Neither tDCS nor N-back testing alone was sufficient
Enhancement of Explicit Learning

- Enhancement of explicit learning consolidation during sleep (Marshall et al., 2004)
  - List of words presented to subjects during the day
  - Anodal tDCS of bilateral DLPFC during slow wave sleep
  - Enhanced recall of word list
Enhancement of Attention

- Visual **Attention** Task: Air Traffic Control (Nelson et al., 2014)
Enhancement of Attention

• With sham tDCS, attention decreases over time (Nelson et al., 2014)
  – Lower target detection rate
  – Slower reaction times
  – Reduction in cerebral blood flow velocity

• Anodal tDCS of DLPFC (left or right) enhances attention
  – Higher target detection rate
  – Maintained blood flow velocity
  – Increased cerebral oxygenation
Enhancement of Complex Cognition: Eureka!

• **Remote associates test** (Cerruti & Schlaug, 2009)
  – Given 3 words, have to find a word associated with all 3
  – E.g., “Child, Scan, Wash” → “Brain”

• **Anodal** tDCS of the left DLPFC enhances performance
Overlapping effects and stimulation sites...

Implicit Learning

Explicit Learning

Motor Learning

Attention

Language

Working Memory

Complex Cognition
1) Stimulating Different Networks?

- Stimulation of DLPFC as a “Gate” to other regions/networks

- tDCS can alter functional connectivity between brain regions (Coffman et al., 2014), as demonstrated with fMRI and EEG

Zahele et al. 2011 (EEG)
2) Stimulating Overlapping Cognitive Skills?

- Enhancement of **explicit learning** with tDCS correlates with enhancement of **attention** (Coffman et al., 2012)

- Enhancement of **working memory** with tDCS mediated by enhancement of selective **attention** (Gladwin et al., 2012)

- **Learning** (memory acquisition/consolidation) linked to **working memory** and **attention** (Coffman et al., 2014)

**Common denominator** → Improvement of **attention**, therefore reaction times, and filtering ability, working memory, etc.....

![Left Executive Control](image1.png) ![Right Executive Control](image2.png)
Net Zero Sum effect?
tDCS effects → Net zero-sum?

- Net zero-sum derived from notion of conservation of energy
- A gain in function is accompanied by an equal loss of function
- Is brain enhancement a zero-sum game?
  - Distribution of processing power
  - Example: Trade-offs (e.g. speed-accuracy)

Brem et al., 2014
Evidence for Zero-Sum?

Study of numerical learning in healthy participants.

6 Days of training combined with:
1) tDCS over Dorsolateral Prefrontal Cortex

2) tDCS over Posterior Parietal Lobe

Luculano & Cohen Kadosh, 2013
Trait Dependency
Effect of tES reflect **individual differences** → “Phenotype”, related to pre-existing oscillatory patterns (higher/lower gamma?)

Important for the **personalization of tES protocol** and for the **ethical evaluation** of cognitive enhancement interventions.

tACS=1.0 mA, tRNS=1.0 mA
Unleashing Potential: Transcranial Direct Current Stimulation over the Right Posterior Parietal Cortex Improves Change Detection in Low-Performing Individuals

Philip Tseng, Tzu-Yu Hsu, Chi-Fu Chang, Ovid J.L. Tseng, Daisy L. Hung, Neil G. Muggleton, Vincent Walsh, Wei-Kuang Liang, Shih-kuen Cheng, and Chi-Hung Juan

Right Posterior Parietal cortex Anodal tDCS

Change Detection Task (visual short term memory)

EEG recording during the task
Trait Dependency of tCS effects

Low and High Baseline performers

Performance indexes
N2pc = Negative parietal contralateral wave (200ms)
SPCN = Sustained parietal contralateral negativity

High performers at baseline cannot push their physiological limit → Higher Intensity?
Timing, State dependency and Network Targeting
State-Dependency: Can tDCS alone increase intelligence?

Intelligence Quotient assessment Day 1 → tDCS (20') → Intelligence Quotient assessment Day 2

Sellars et al. 2015
tDCS decreases IQ?

Modeling of electric fields

Effect on Intelligence Quotient

Effect on specific indexes of cognitive performance
Cognitive networks

Fluid Intelligence
(20 functional units)

Verbal and Visuospatial
Fluid Intelligence

Processing stages
• Rule Inference
• Rule Application

Santarnecchi et al., 2018
Brain connectivity

- Brain is organized in distinct networks (Zhang et al., 2010)
- Negatively correlated networks (Fox et al., 2005)

Task positive and Default Mode Networks

Resting-State Networks
fMRI-based Multifocal tCS

Optimization of multifocal transcranial current stimulation for weighted cortical pattern targeting from realistic modeling of electric fields

Ruffini et al. 2013
Bifocal vs Multifocal tDCS: effect on Cortical Excitability

Fischer et al. 2016, Neuroimage
How to measure tCS effects: changes in corticospinal excitability

First evidence of tDCS after effect from Nitsche and Paulus, 2000

Changes in cortical excitability assessed using TMS-EMG,

anodal tDCS increases excitability, cathodal tDCS decreases excitability
Bifocal vs Multifocal tDCS

Fischer et al. 2016, Neuroimage

Change in cortical Excitability during and after tDCS
Bifocal vs Multifocal tDCS: effect on fMRI connectivity

**Within-Network Effect**

**Network-to-Network Effect**
Towards Network-based targeting for clinical applications

Ruffini, Wendling, Sanchez, Santarnecci
Current Opinion in Biomedical Engineering 2018
Combine tCS with Psychotherapy

Pachorek et al., submitted
Multichannel tCS targeting connectivity patterns

Pachorek et al., submitted
Combine tCS with Psychotherapy: Timing

Pachorek et al., submitted

Baseline Assessment

Priming (e.g. 30' before)

Synergistic effect

Consolidation (Within / Between sessions/cycles)

Outcome

TMS

Predictive Biomarkers
- Cortical excitability
- Plasticity levels
- Connectivity
- Brain Oscillations

Multifocal tES

EEG

Outcome Measures
- Cortical excitability
- Plasticity levels
- Connectivity
- Brain Oscillations

Bifocal tES

tES
Safety & Feasibility of Multifocal tDCS in Glioblastoma and Metastasis

Sprugnoli et al., accepted

**Experimental Design.** (A) Patients underwent a clinical MRI in order to define and characterize the brain tumor, including standard and CET1w, T2w, FLAIR, ASL and resting-state fMRI images. Regions of Interest (ROIs) were defined by parcellating the solid component as the necrotic core of the tumor (metastasis in this example) using CET1w sequences, and the edema surrounding the tumor by using FLAIR images. (B) Conductivity values were assigned to each ROIs as well as to healthy brain tissue according to existing literature (lower panels), then E-field distribution of current was calculated (upper panel). (C) The personalized multielectrode solution maximizing the E-field on the solid-edema interface was selected. The experimental session was planned 3-5 days preceding the surgical intervention and multichannel tES was performed inside the MRI scanner by means of an MRI-compatible brain stimulation device. The stimulation session included the acquisition of (i) T1w, FLAIR, ASL and rs-fMRI sequences before tES, (ii) rs-fMRI and ASL during tES, and (iii) FLAIR images after tES. (D) Roughly 1 week after the pre-surgery MRI, patients underwent neurosurgery with subsequent histological classification and immediate post-surgery CT acquisition. (E) Finally, one month after neurosurgery, selected patients underwent a new MRI acquisition and ROIs segmentation in order to perform a second MRI-tES session (F), aiming at evaluating the safety and feasibility of applying tES after neurosurgery. Additional modeling based also on CT scan was performed to account for the effects of skull defects created by cranietomy. This was important to ensure safety and to study/quantify changes in electric field distribution in the presence of skull breaches.
Tumor Tracing, Modeling and Optimization. (A) MRI images were manually segmented by two independent investigators using MRIcro software and 3DSlicer. Following the RANO recommendations, the solid part (red) of the tumor (GBM in this example) as well as the necrotic core (blue) were identified on CET1w images. The edema (green) was segmented using FLAIR images. In the post-surgery phase, T2 TSE scans were used in order to correctly identify the vacuum created by the surgical intervention. (B) Conductivity values were assigned to each ROIs as well as to healthy brain tissue according to existing literature: grey and white matter, CSF, skin, skull. A multi-electrode solution maximizing stimulation over the edema-solid tumor interface was identified for each patient, with the corresponding E-field distribution calculated on patients’ head models (B, lower panel). Resulting E-field was overlaid onto individual anatomical T1w scans, showing specificity of the tES solution targeting the solid tumor (C). (D) T1w MRI of the subject was segmented into multiple tissue classes using MARS, the SPM-8 segmentation toolbox and FreeSurfer (left). Models of PITRODE electrodes (cylinders, 1 cm radius) were placed in the scalp positions corresponding to the 10/10 EEG system (green circles, center). A genetic algorithm was then used to estimate the best multi-electrode solution among those possible using 32 positions on the scalp (center), with the final personalized tES montage including up to 8 electrodes (right).
Post-surgical modeling. (A) Structural MRI and CT images were used to model the impact of tES after surgery (shown: complete resection of a GBM). Ad-hoc ROIs and 3D renderings were created for both skull breaches and metallic clips that could respectively favor current shunting and affect electrodes positioning. (B) New tissue conductivity values were derived by assigning skull defects a conductivity equal to that of the CSF (left), and the amount of current (i.e. E-field) shunting through them was estimated (right). (C) A new multi-electrode stimulation solution was implemented to maximize stimulation over the resection borders, showing high spatial specificity and control of induced E-field. (D) In details, new geometries of the different head tissues (healthy ones and ROIs) were computed after surgery, leading to a new optimized montage maximizing the current on the surgical borders.
RESULTS: Reduction of intratumoral perfusion (solid part)

1) No Adverse Events or Side Effects, neither Pre- nor Post- surgery
2) Selective Decrease of Intratumoral perfusion during stimulation (~36%)

Perfusion changes. (A) Significant reduction in white matter-corrected CBF was observed in the solid tumor during stimulation for both patients with GBM and MTX (p.<0.001), as compared to no changes in the edema (p.<0.328) and necrotic core (p.<0.294). (B) Control ROIs in the contra- and ipsilateral hemispheres to each tumor did not show significant changes in CBF.
Controversy about efficacy

Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations From Single-session Transcranial Direct Current Stimulation (tDCS)

Jared Cooney Horvath*, Jason D. Forte, Olivia Carter

- Included every study of the cognitive effects of tDCS among healthy adults (59)
- Cognitive tasks must be used by 2 or more groups
- Included only studies of single session tDCS
- Spanned executive function, memory, language, and other
- No significant effects of any.

A few studies in each category (~3)  ?
Small sample size  ?
Anodal & Cathodal tDCS
Thank you

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