Cognitive Enhancement with Noninvasive Brain Stimulation: Better Living Through Electricity?

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Disclosure Statement

I have no financial or nonfinancial interest in any organization whose products or services are described, reviewed, evaluated or compared in the presentation.
“Zap your brain into the zone: Fast track to pure focus”
New Scientist, 2012

Is Sally right?
What if she is? What if she isn’t?
What else do we need to think about?
Topics: Primer, Promise & Peril

• **The Primer**
  – TMS
  – tDCS

• **The Promise**
  – Cognitive enhancement
  – Manipulation of social cognition

• **The Peril**
  – Safety
  – Character
  – Justice
  – Autonomy
Transcranial Magnetic Stimulation (TMS)

- Based on Faraday Principle
- Rapidly fluxing magnetic field
- Induces current in underlying cortex
- Noninvasive
- Permits focal manipulation of cortical activity
TMS treats depression

- Approved by FDA in 2008

- Definitive RCT
  - 301 medication-refractory patients in 23 sites
  - 5x/week for 4-6 weeks
  - 14.2% remission (vs. 5.5% sham)
  - 23.9% response rate (12.3% sham)
Transcranial Direct Current Stimulation (tDCS)

- Subthreshold stimulation
- Neurons alter firing rates
- Anodal or cathodal stimulation may have different effects.
tDCS: Low spatial/temporal resolution

Datta et al., 2009
Safety & tolerability

- 137 healthy subjects
- 277 tDCS sessions
- No serious adverse effects occurred.
- Mild side effects: mild tingling (76%), itching (68%), burning (54%), and pain (25%).

Kessler et al., *Brain Stimulation*, 2012
Convenience & cost

- Portable
- Can be worn during other therapies
- Costs ranging from $100s-$1000s
- Usable without advanced training
Number of tDCS print media articles and applications described

- Technical
- Investigative
- Therapeutic
- Enhancement

Veljko Dubljević, Victoria Saigle, Eric Racine
Neuron, Volume 82, Issue 4, 2014, 731 - 736
Hope or hype?

Tone of Print Media Articles Per Area of Application

Optimistic Neutral Critical
NIBS and cognitive enhancement

TMS and tDCS have been used to transiently improve cognition across multiple domains...

- Language
- Learning & Memory
- Numerical/Mathematical Reasoning
- Visuospatial Processing
- Frontal/Executive Functions
- Social Cognition

Language

- 25 normal right-handed
- Anode over left pTC; cathode over right pTC
- 2 sessions: (1) real tDCS (1.5mA for 20 min), and (2) sham tDCS.
- Standardized word and nonword reading tests
Motor learning

Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation

Janine Reis\textsuperscript{a,b}, Heidi M. Schambra\textsuperscript{a}, Leonardo G. Cohen\textsuperscript{a,1}, Ethan R. Buch\textsuperscript{a}, Brita Fritsch\textsuperscript{a,b}, Eric Zaran\textsuperscript{c}, Pablo A. Celnik\textsuperscript{c,1,2}, and John W. Krakauer\textsuperscript{c,1,2}

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Numerical competence

• TRNS of bilateral DLPFC with arithmetic training
• Short- and long-term improvements in calculation
• NIRS changes: Enhanced neurovascular coupling efficiency

Snowball et al., 2013
Visuospatial processing

Egocentric Neglect  Allocentric Neglect

Medina et al., 2012
Task-dependent working memory enhancement

Experiment 1

Visit 1
A-PASAT 3 Back A-PASAT

Visit 2
A-PASAT 3 Back A-PASAT

Counterbalanced

> 48 hours

Visit 1
A-PASAT 1 Back A-PASAT

Visit 2
A-PASAT 1 Back A-PASAT

Counterbalanced

Online domain-specific cognitive task + atDCS results in offline improvement in performance within-domain

Gill et al., *Brain Stimulation*. 2015
Frontal lobe functions
Impulse Control, Cognitive Control & Creativity

Novel Uses

“Use it to hammer nails?”

Chrysikou et al., Cognition, 2013
tDCS and causal reasoning

Woods et al., Neuroimage, 2014
Social Cognition

Altruistic punishment

Ultimatum Game

Proposer

Responder

Fairness • Equity
Reciprocity

Self-interest

Stimulation of rDLPFC facilitates acceptance of unfair offer

Acceptance rate for the 16/4 offer in the human offer condition

Knoch et al., Science. 2006
Social Cognition

Deception: Neural mechanisms and ‘lie detecting’

• Greater TMS-induced MEPs generated during deceitful responses vs. truthful ones (Lo et al., 2003)

• Guilty Knowledge Test (Priori et al., 2007)
  – Anodal tDCS over bilateral DLPFC
  – Increased RT for false compared to true responses
Oh Brave New World?
When you have the power to change the way you feel, it changes everything.
Augmenting Visual Search Performance With Transcranial Direct Current Stimulation (tDCS).

Would you let someone zap your brain? Why electronic brain stimulation is trending | LA Times

Noob cable question (foc.us v2 to amrex) (self.tDCS)

Can somebody sell me a tDCS that goes to 4mA (self.tDCS)

Any montage suggestions for improving focus and attention? (self.tDCS)

Making sponge electrodes (self.tDCS)
Neuroethical concerns of enhancement with NBS

- Safety
- Character
- Justice
- Autonomy

*Hamilton et al., 2010*
Theoretical concerns of unregulated public use of tDCS

1. Wrong placement
2. Wrong intensity/duration
3. Device-medication interactions
4. Unintended consequences of “correct” use

Maslen et al., 2014
Kuersten & Hamilton, 2014
tDCS & psychopharmacology

- **Glutamate/NMDA modulators**
  - Blocking receptors eliminates aftereffects; enhancement enhances facilitatory plasticity
- **GABA modulators (e.g. lorazepam)**
  - Delayed then enhanced & prolonged anode-induced excitability
- **Monoamine modulators (e.g. amphetamines)**
  - May enhance facilitatory plasticity
- **Dopamine modulators**
  - L-dopa: converts facilitatory plasticity to inhibition, prolongs inhibitory plasticity
  - D2 antagonists: abolish induced plasticity; D2 agonists: variable dose-dependent effects
- **Acetylcholinergic modulators**
  - Reuptake inhibitor: similar effect to L-dopa
- **Serotonergic modulators**
  - Reuptake inhibitor enhances facilitatory plasticity, converts inhibitory plasticity to facilitation

Brunoni et al., 2013
Gains in some performance measures may have a cost...

**Novel Uses:**
Left PFC cathodal

“Use it to hammer nails?”

**Working memory:**
Left PFC anodal

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**Experiment 1**

Visit 1
A-PASAT 3 Back A-PASAT

> 48 hours

Visit 2
A-PASAT 3 Back A-PASAT

Counterbalanced

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**Experiment 2**

Visit 1
A-PASAT 1 Back A-PASAT

> 48 hours

Visit 2
A-PASAT 1 Back A-PASAT

Counterbalanced

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Chrysikou et al. 2013

Gill et al., 2014
Unintended tradeoffs...

Iuculano & Cohen Kadosh, 2013

6 days of training + TES
• Posterior parietal cortex
• Dorsolateral prefrontal cortex

• PPC: Increased learning but reduced automaticity
• DLPFC: Increased automaticity but decreased learning
Trait and individual-specific outcomes...

Sarkar et al., 2014
Not a global ‘brain booster’

- 41 Subjects
- WAIS-IV Testing baseline & post-stimulation
- Bilateral and unilateral conditions vs sham

Sellers et al., 2015
Are cognitive neuroscience studies the wrong investigative framework?

More safety-driven & long-term studies needed:

• Mediators
• Modulators
• Parameters
• Dose-response
Character

• Issues of identity and meaning in life
• Enduring discomfort linked to concept of personal growth
• Painful experiences may engender valuable qualities
• Painful experience may be important for developing empathy
• Clearly, we do not believe in enduring all suffering
• Who decides?

That which does not kill you makes you stronger.

NO PAIN, NO GAIN
Justice

• Equitable distribution of resources
• Boutique cognitive enhancement
• Problematic but not unique
• Brain stimulation may be less problematic than pharmacologic agents

“The future is here. It’s just not evenly distributed yet.”
-William Gibson
Autonomy
Freedom from stimulation

“Hard” & “soft” coercion

• Hard (explicit) coercion
• The “greater good”
• Historical precedent
• Forced mood or attitude adjustment
  • Military applications
  • Prison populations
• Forced revelation of cognitive states
  • Lie detection
Autonomy
Freedom from stimulation
“Hard” & “soft” coercion

• Soft (implicit) coercion
• Demand for competitive advantage
• Progress defined by ever-improving performance/productivity
• Examples:
  • Professional sports
  • Stimulants use among students and professionals
Autonomy
Freedom to stimulate

• Liberty to do what one thinks is best for oneself
• Impossible/impractical to ban
  • Communication and education
  • Gain insight into self-enhancement community
  • Promote ethos of responsible use

Fitz & Reiner, 2013
Next steps?

• Learning from other examples of self-enhancement:
  – Cosmetic surgery
  – Cosmetic neuropharmacology

• Systematic research into safety & efficacy
  – Animal models
  – Cognitive neuroscience

• Open lines of communication
• Public education & discourse
• Monolithic policies unlikely to be useful (and ineffective)
Conclusions

• Neither snake oil nor panacea
• Potential for a different kind of harm/risk?
• Different kinds of research (mechanisms & mechanics)
• If you can’t beat ‘em… teach ‘em?
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FDA focus on intention influences tDCS marketing

- Not currently regulated as medical devices.
- Manufacturers’ language circumvents device regulations.
- Analogous to food and supplement regulations vs. drugs.

*Wexler, 2014

“An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
1. Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
2. Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
3. Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.”
Is regulating tDCS as a clinical medical device for nonclinical uses the solution?

**PRO:** Enforces more rigorous approach to safety and risk in commercial entities.

**CON:** Potentially stifling effect on innovation.

- Numerous potential intended uses; coverage of all indications and unforeseen eventualities may be impractical.

- Regulatory authorities/infrastructure not well-equipped to address enhancement instead of treatment.

- Regulation of DIY-tDCS may have paradoxical effects:
  - Tight regulation may drive public use further underground
  - Ignoring self-stimulation ignores responsibility to educate and respond to citizens.

Unlikely to affect the public use of other available devices:

- Repurposed Iontophoresis Units
- tDCS Device Kits
- Homemade Devices