LCNS LABORATORY FOR COGNITION AND NEURAL STIMULATION

CENTER FOR COGNITIVE NEUROSCIENCE

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.

9-Volt Nirvana

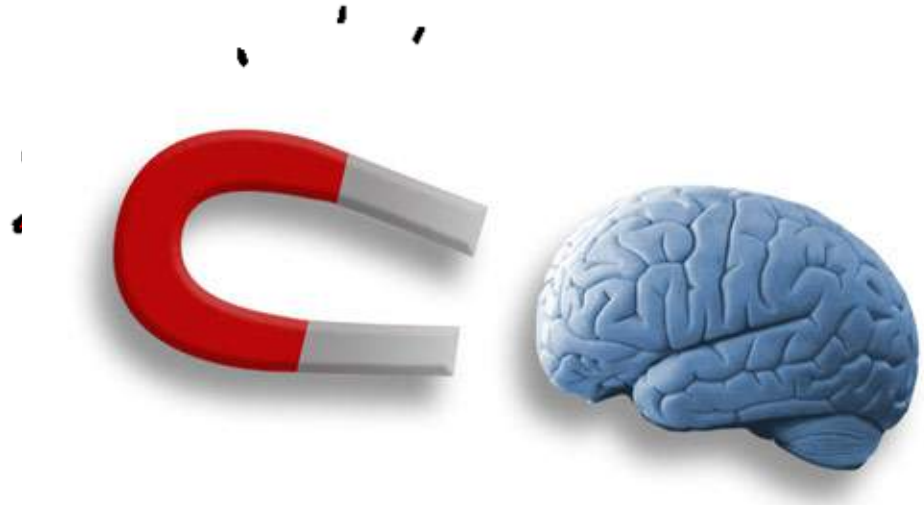
"Zap your brain into the zone: Fast track to pure focus"
New Scientist, 2012

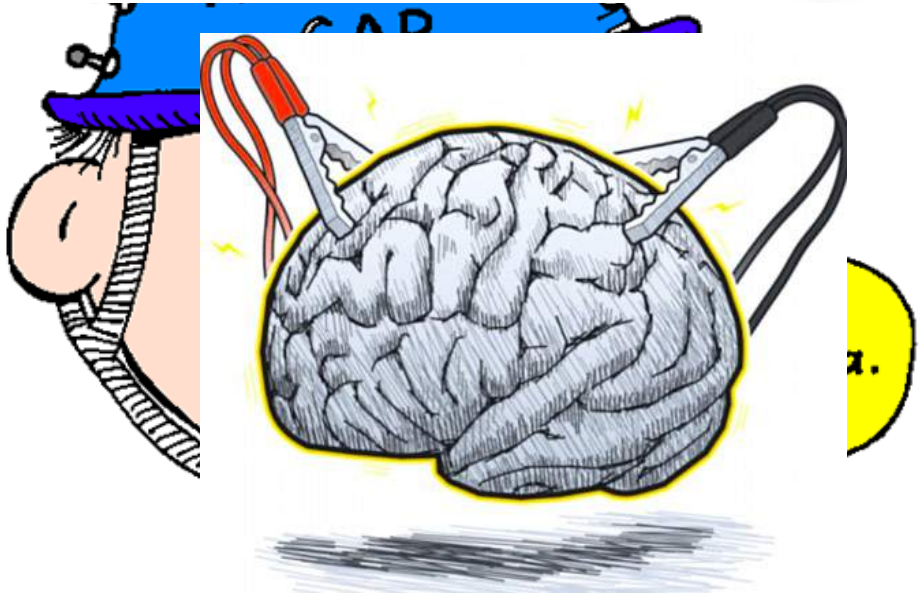
Is Sally right?
What if she is? What if she isn't?
What else do we need to think about?

RADIOLAB

Topics: Primer, Promise & Peril

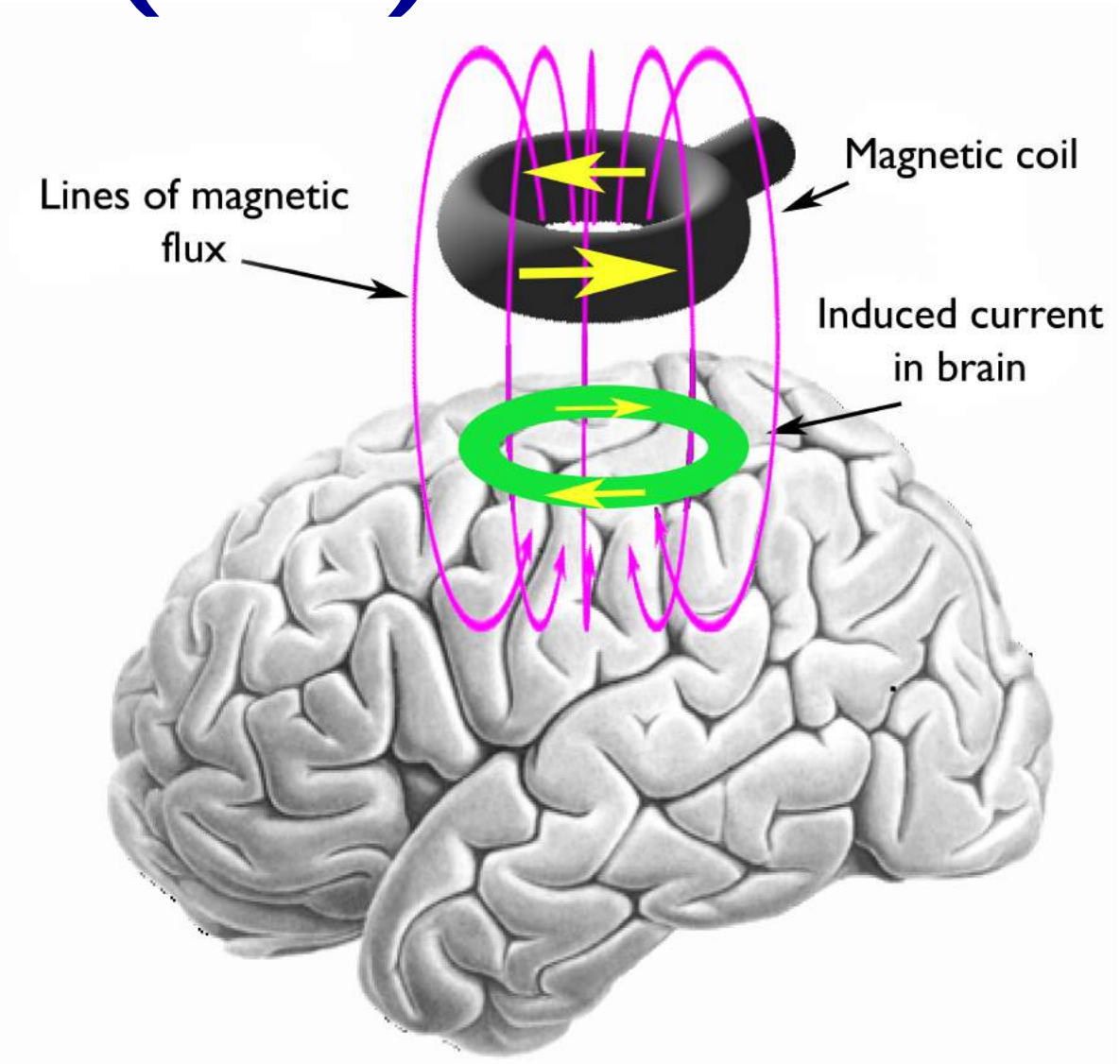
- **The Primer**
  - TMS
  - tDCS
- **The Promise**
  - Cognitive enhancement
  - Manipulation of social cognition
- **The Peril**
  - Safety
  - Character
  - Justice
  - Autonomy





Transcranial Magnetic Stimulation (TMS)

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

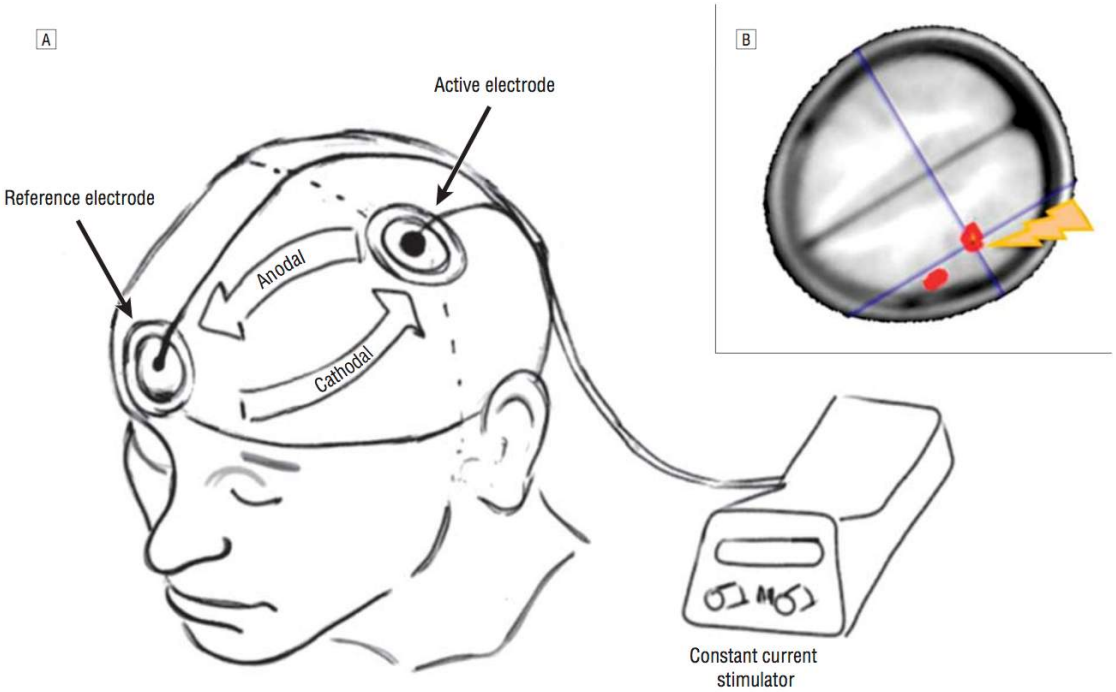


TMS treats depression

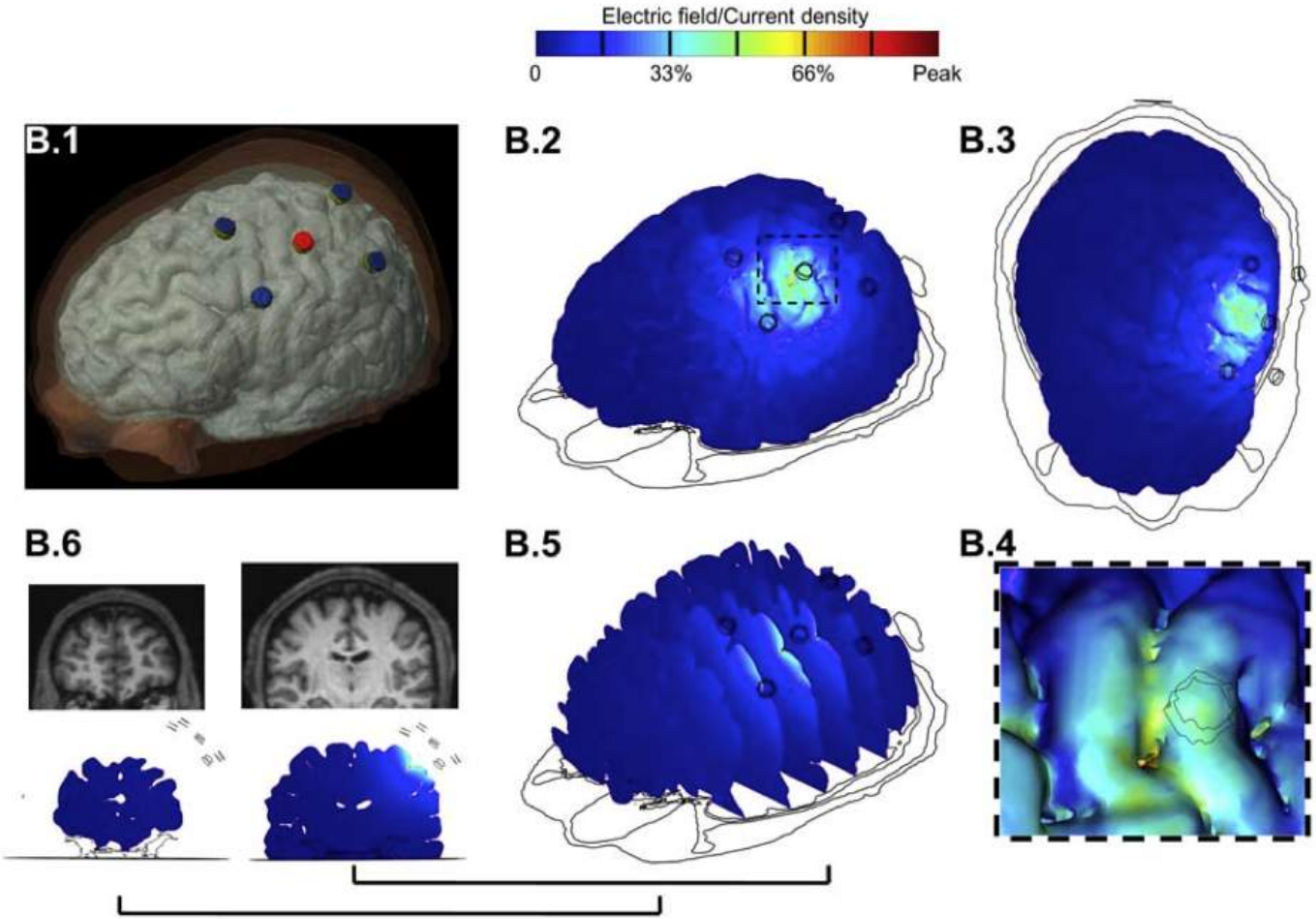
- Approved by FDA in 2008
- Definitive RCT
  - 301 medication-refractory patients in 23 sites
  - 5x/week for 4-6 weeks
  - 14.2% remission (vs. 5.5% sham)
  - 23.9% response rate (12.3% sham)

Transcranial Direct Current Stimulation (tDCS)

- Subthreshold stimulation
- Neurons alter firing rates
- Anodal or cathodal stimulation **may** have different effects.



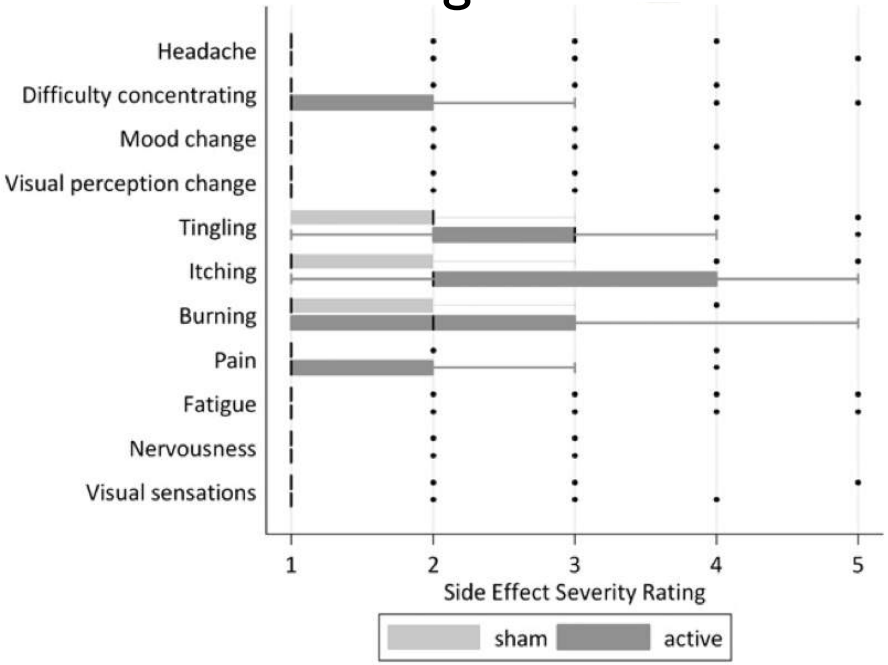
tDCS: Low spatial/temporal resolution



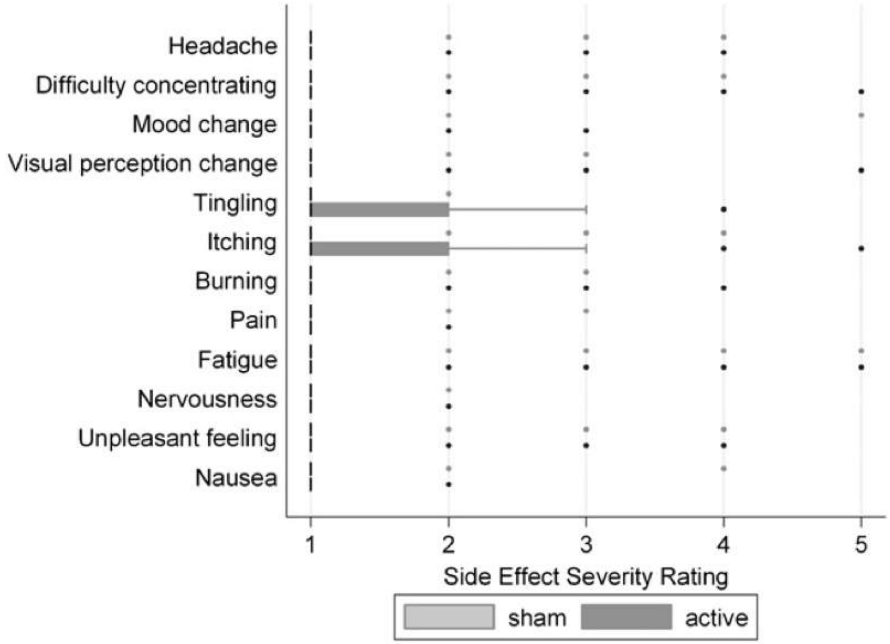
Datta et al., 2009

Safety & tolerability

During Stimulation



After Stimulation

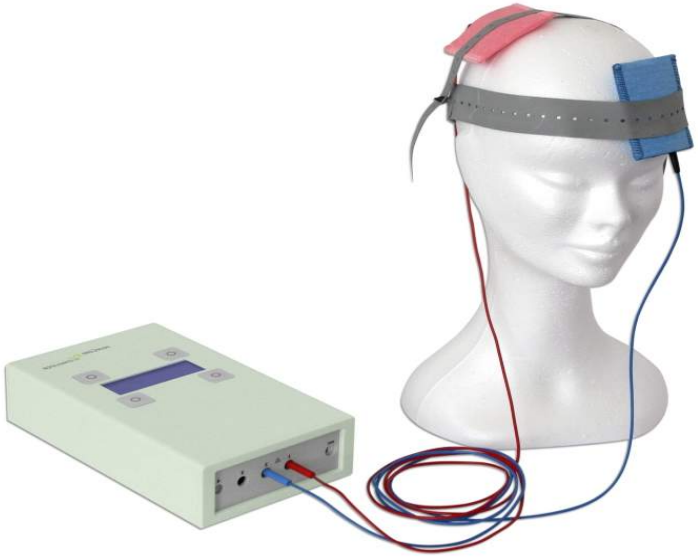


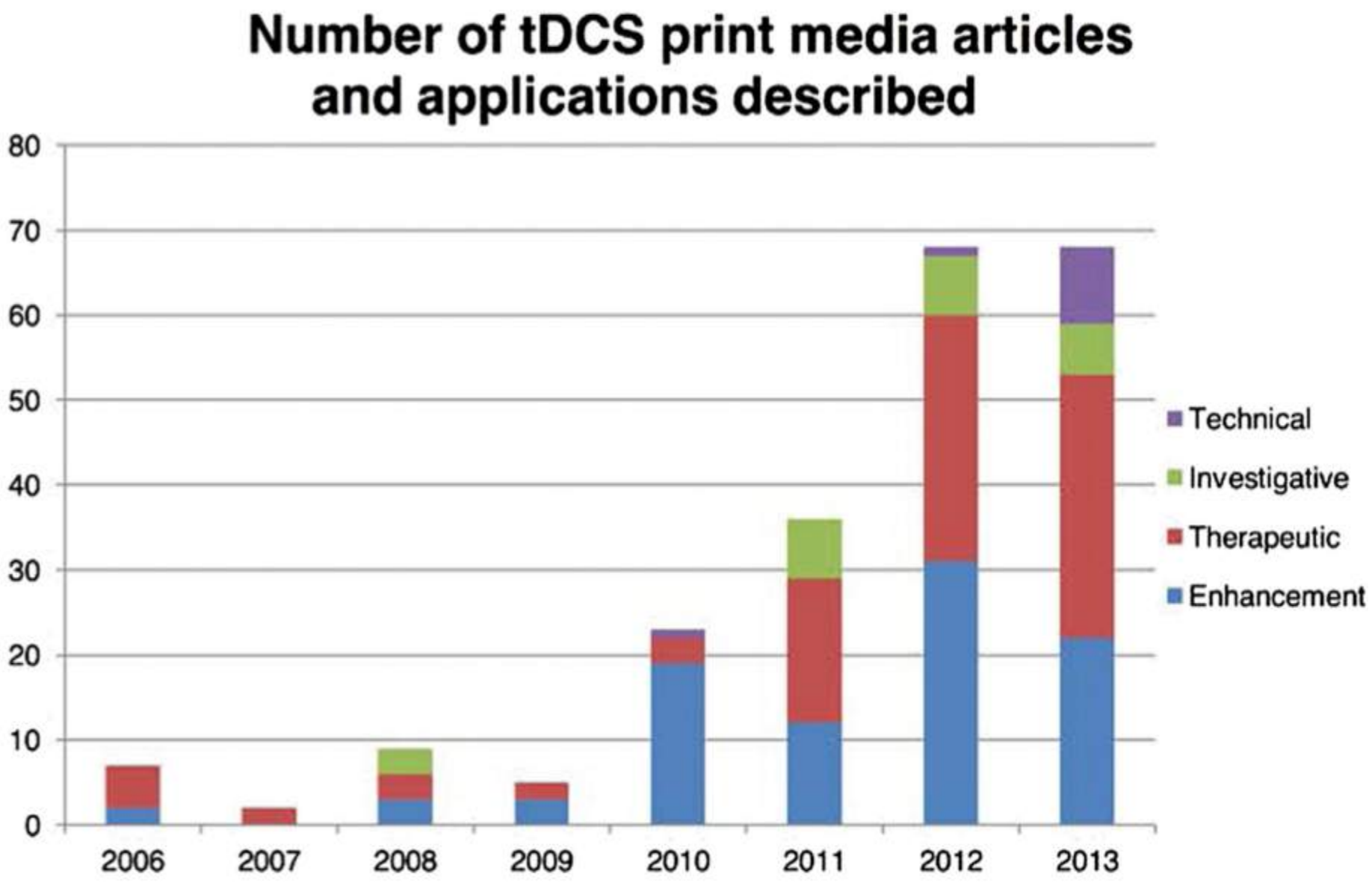
- 137 healthy subjects
- 277 tDCS sessions
- No serious adverse effects occurred.
- Mild side effects: mild tingling (76%), itching (68%), burning (54%), and pain (25%).

Kessler et al., *Brain Stimulation*, *2012*

Convenience & cost

- Portable
- Can be worn during other therapies
- Costs ranging from $100s-$1000s
- Usable without advanced training

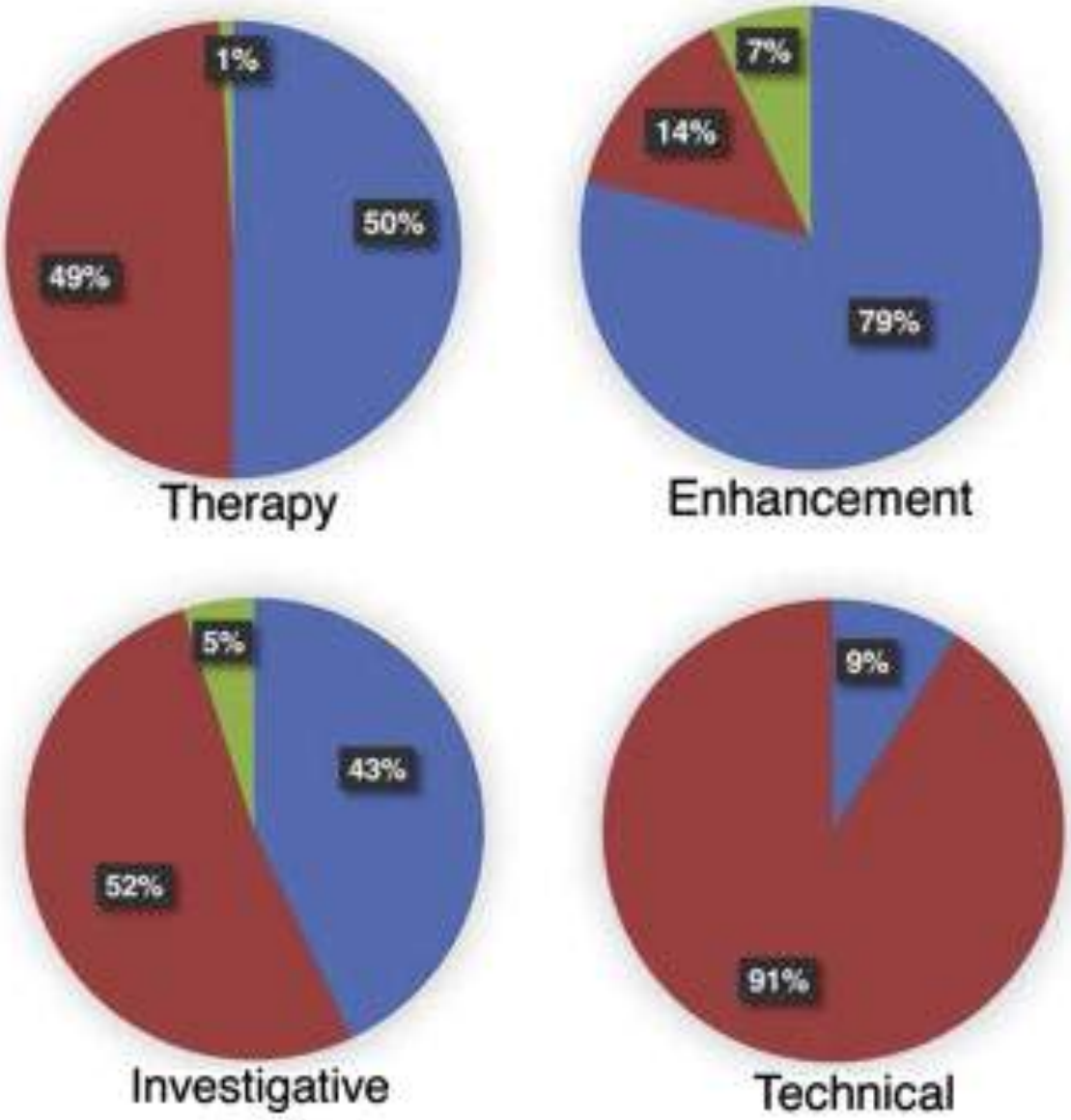




Veljko Dubljević , Victoria Saigle , Eric Racine
Neuron, Volume 82, Issue 4, 2014, 731 - 736

Hope or hype?

Tone of Print Media Articles Per Area of Application



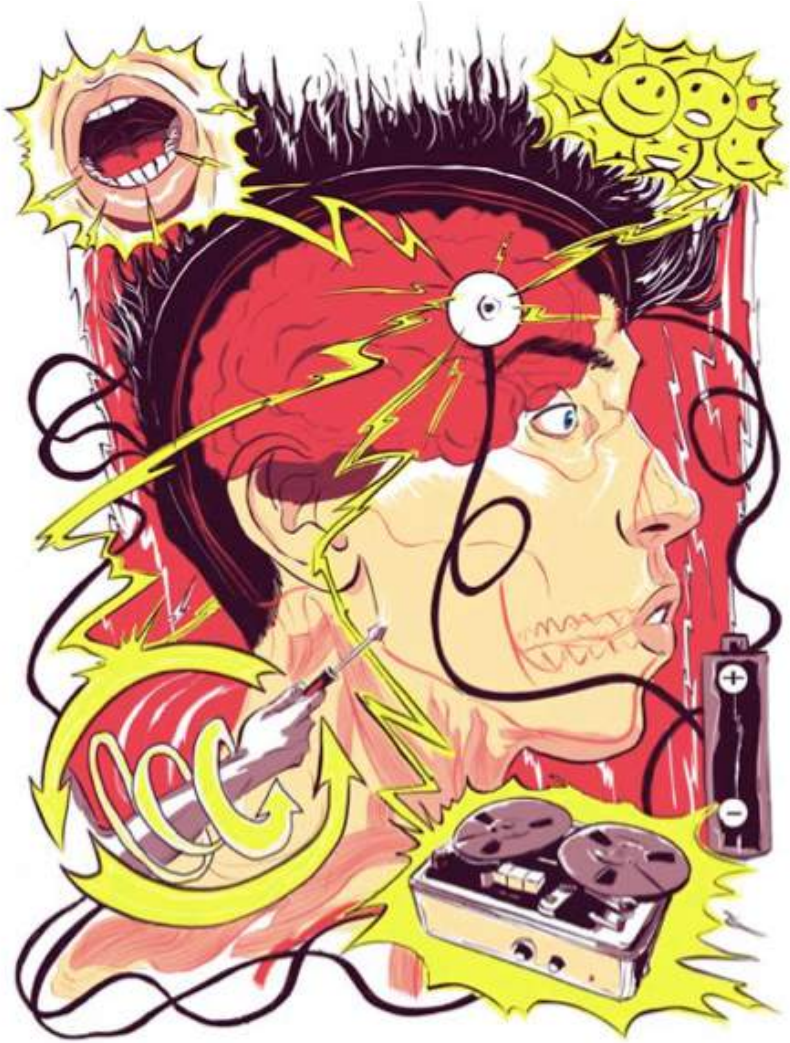
Optimistic
Neutral
Critical

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

NIBS and cognitive enhancement

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

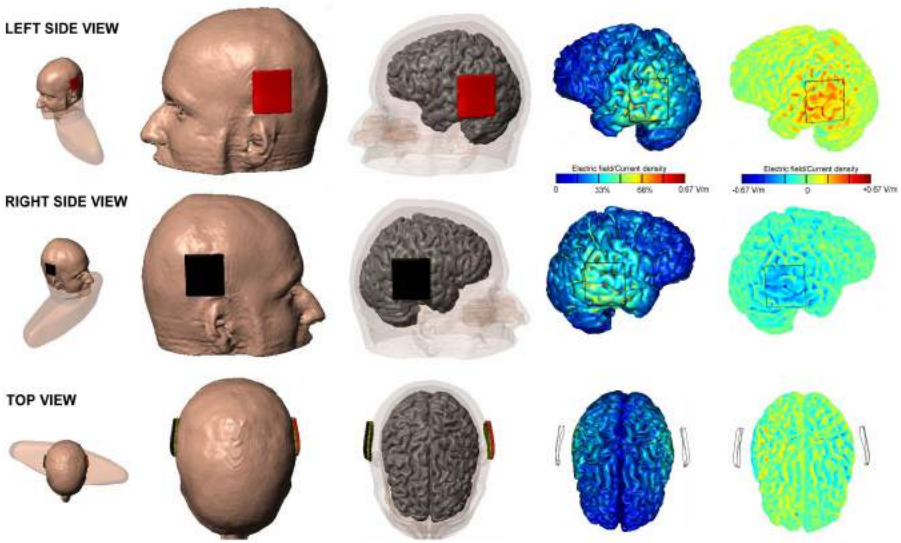
- Language
- Learning & Memory
- Numerical/Mathematical Reasoning
- Visuospatial Processing
- Frontal/Executive Functions
- Social Cognition

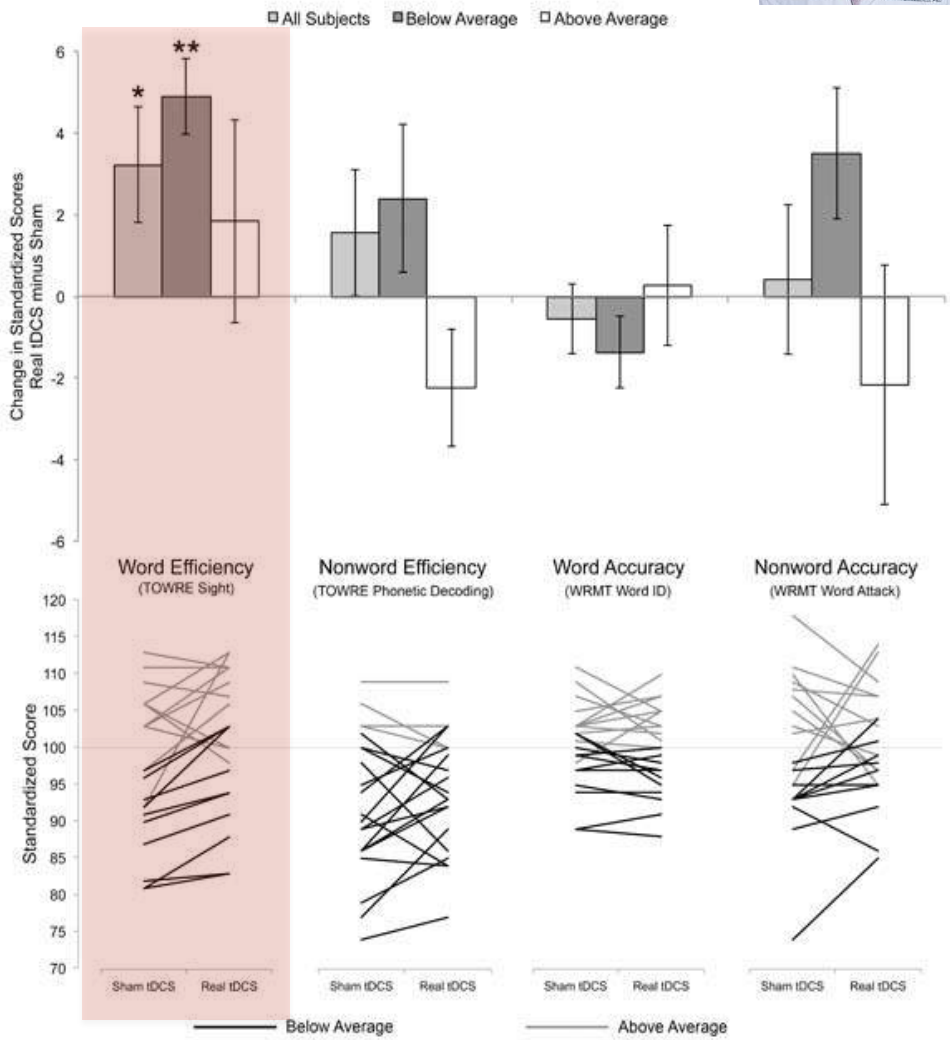


Hamilton & Zreik, *Scientific American*, 2014.

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





Turkeltaub et al. *Brain Stimulation*, 2011

Motor learning

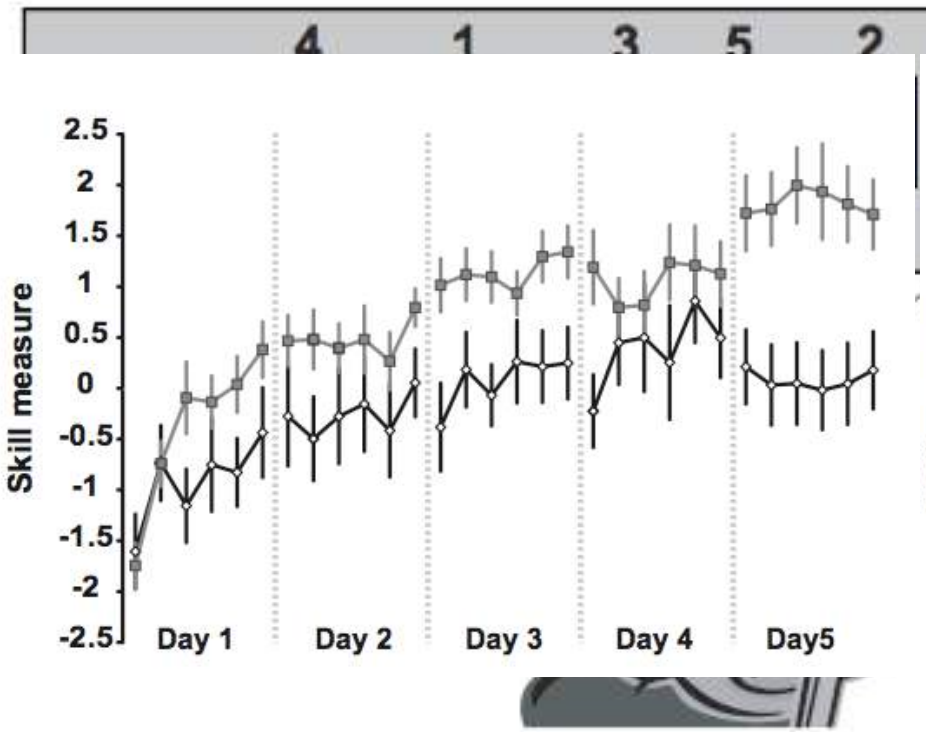
PNAS

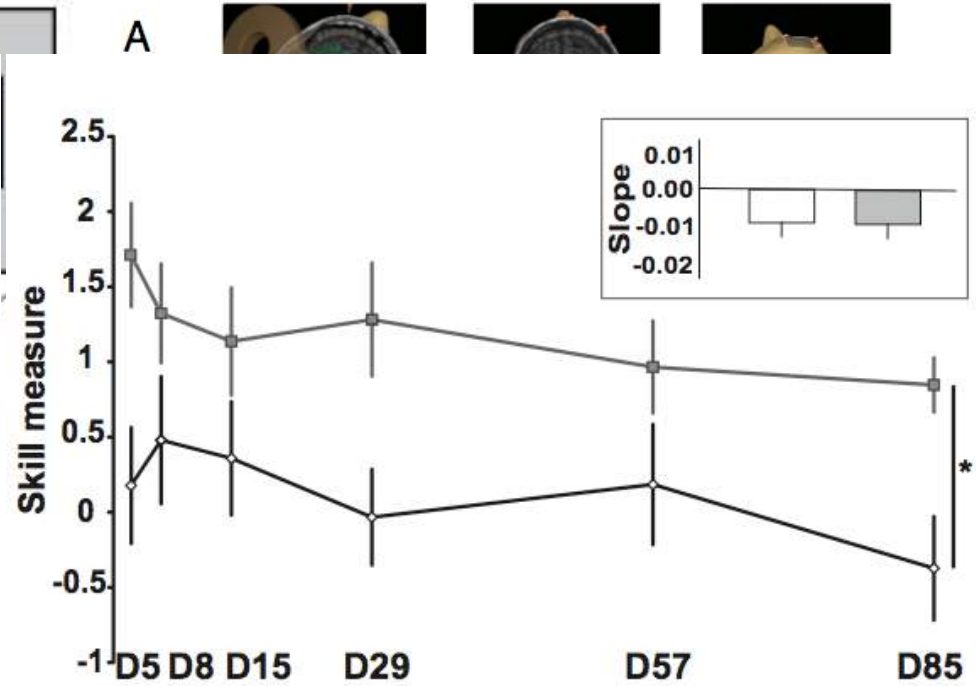
Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation

Janine Reis[a,b], Heidi M. Schambra[a], Leonardo G. Cohen[a,1], Ethan R. Buch[a], Brita Fritsch[a,b], Eric Zarahn[c], Pablo A. Celnik[d,1,2], and John W. Krakauer[c,2]

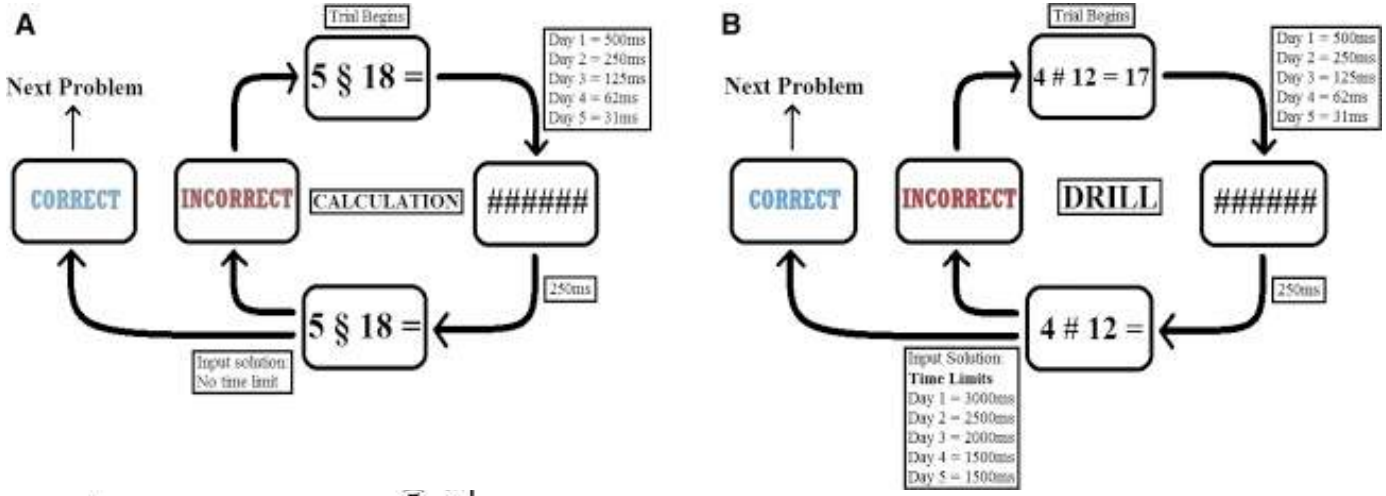
[a]Human Cortical Physiology Section and Stroke Neurorehabilitation Clinic, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892; [b]Department of Neurology, Albert-Ludwigs-University, Freiburg 79106, Germany; [c]Motor Performance Laboratory, Department of Neurology, Columbia University College of Physicians and Surgeons, New York, NY 10032; and [d]Department of Physical Medicine and Rehabilitation, Johns Hopkins University, Baltimore, MD 21287

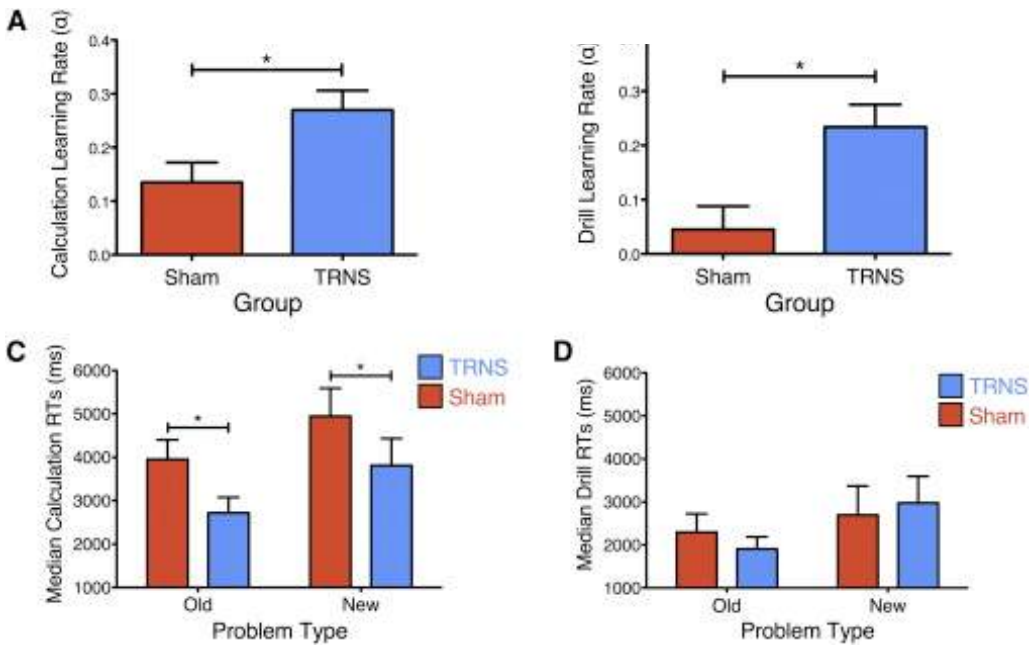
Edited by Emilio Bizzi, Massachusetts Institute of Technology, Cambridge, MA, and approved November 25, 2008 (received for review June 5, 2008)





Numerical competence

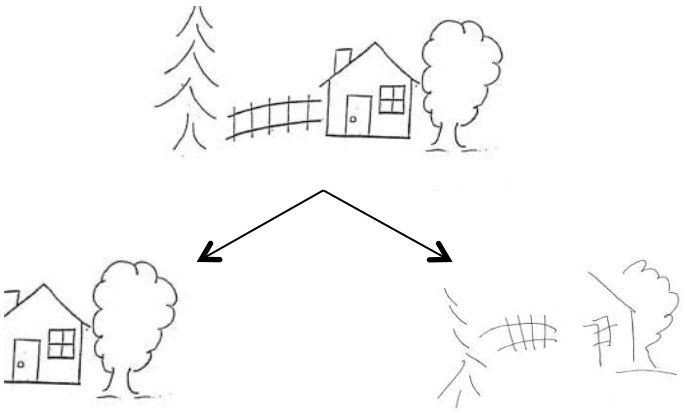




- TRNS of bilateral DLPFC with arithmetic training
- Short- and long-term improvements in calculation
- NIRS changes: Enhanced neurovascular coupling efficiency

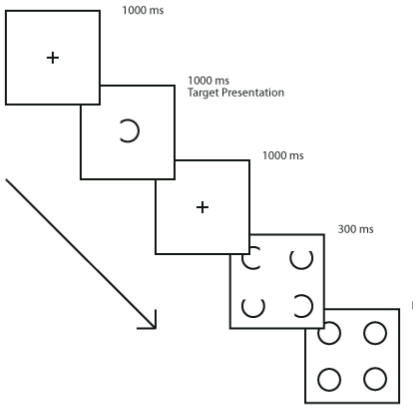
Snowball et al., 2013

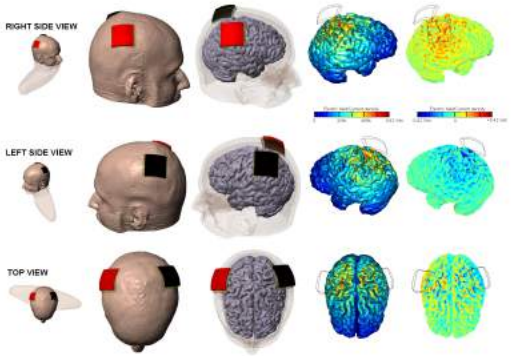
Visuospatial processing

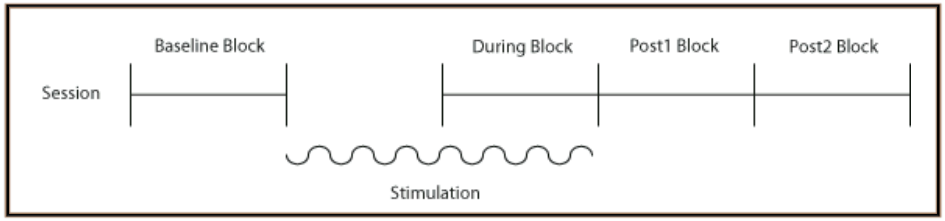


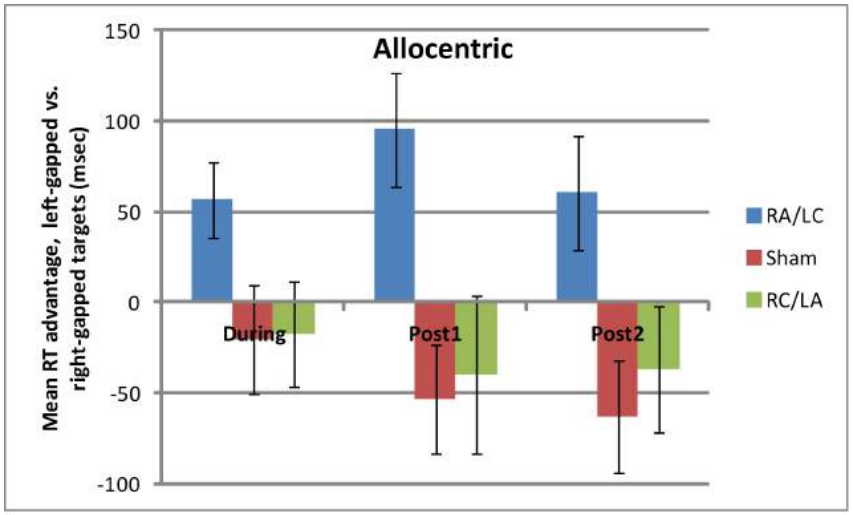
Egocentric Neglect

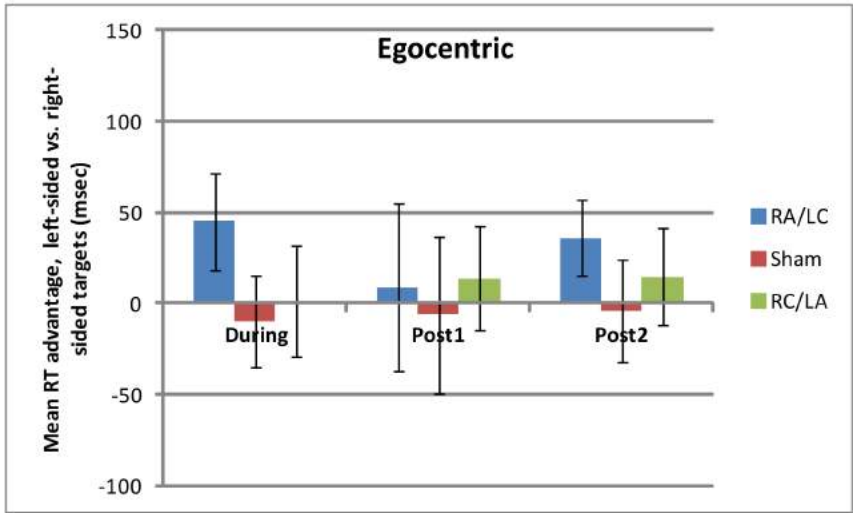
Allocentric Neglect





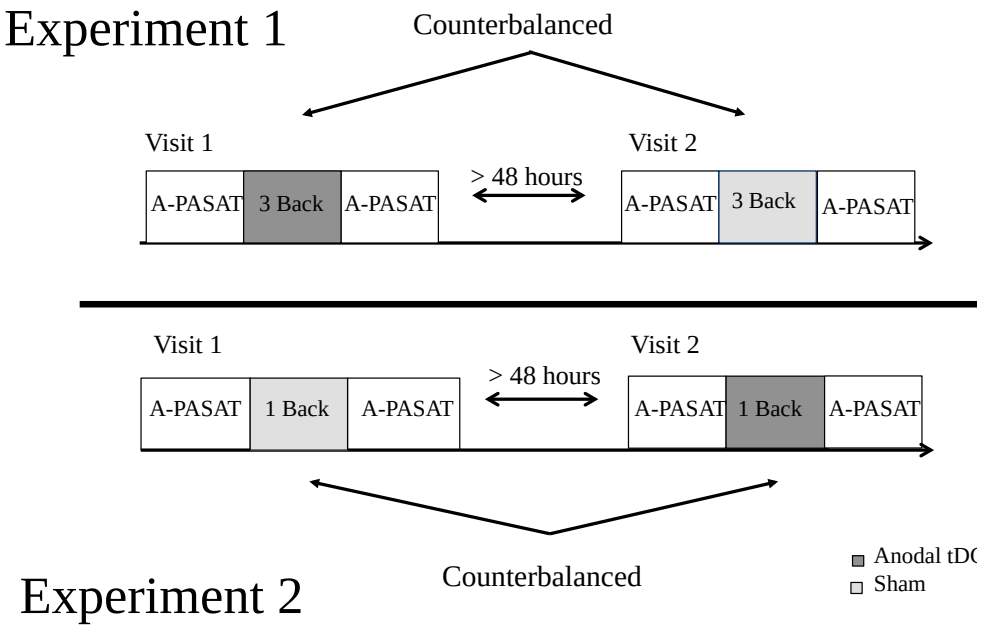


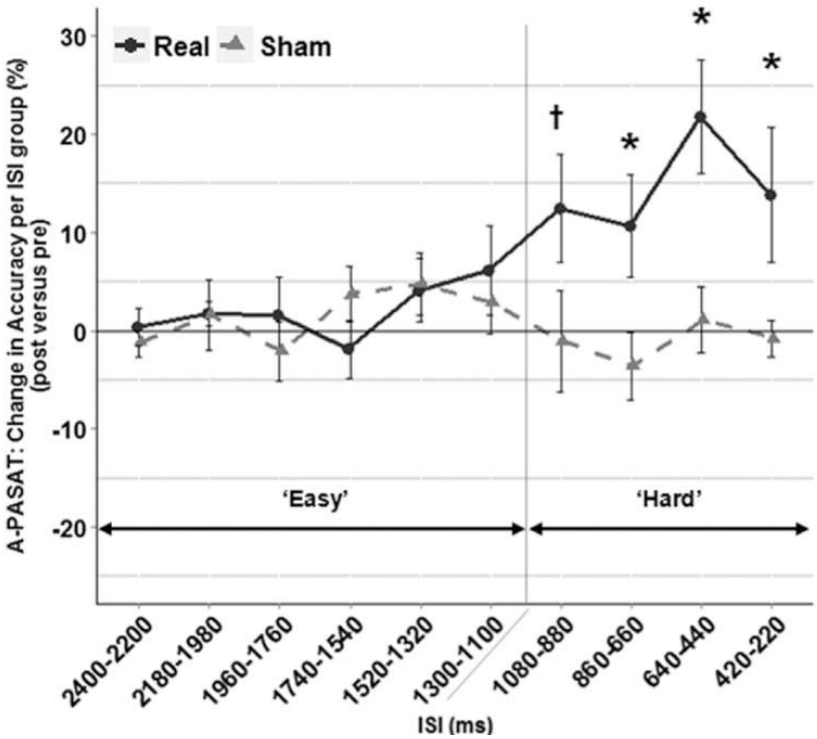




Medina et al., 2012

Task-dependent working memory enhancement





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

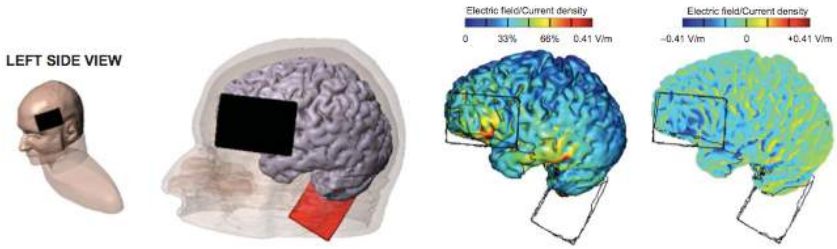
Gill et al., *Brain Stimulation. 2015*

Frontal lobe functions

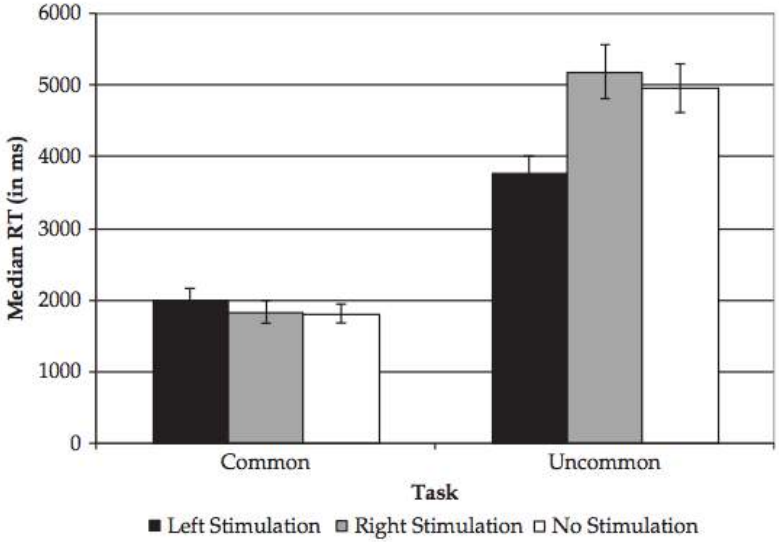
Impulse Control, Cognitive Control & Creativity

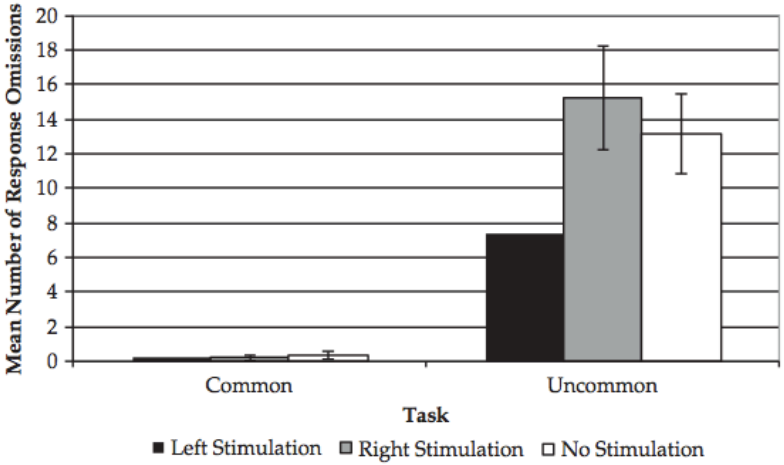
Novel Uses

"Use it to hammer nails?"

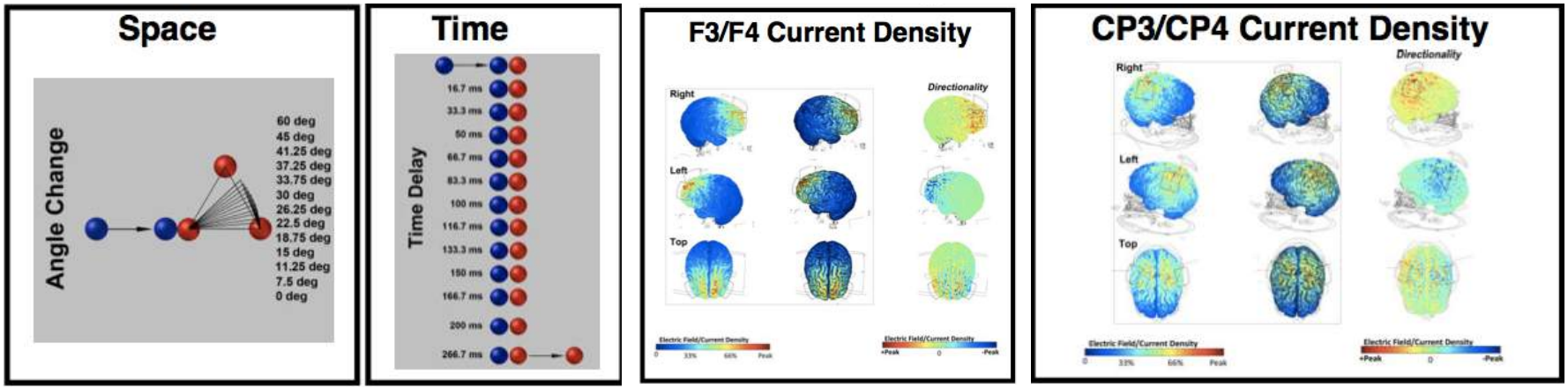


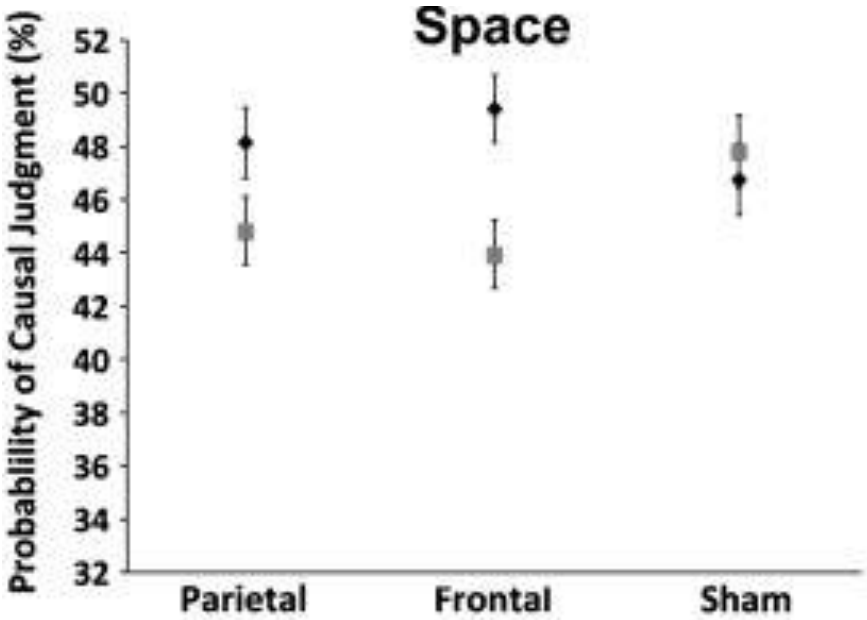
Chrysikou et al., *Cognition*, 2013

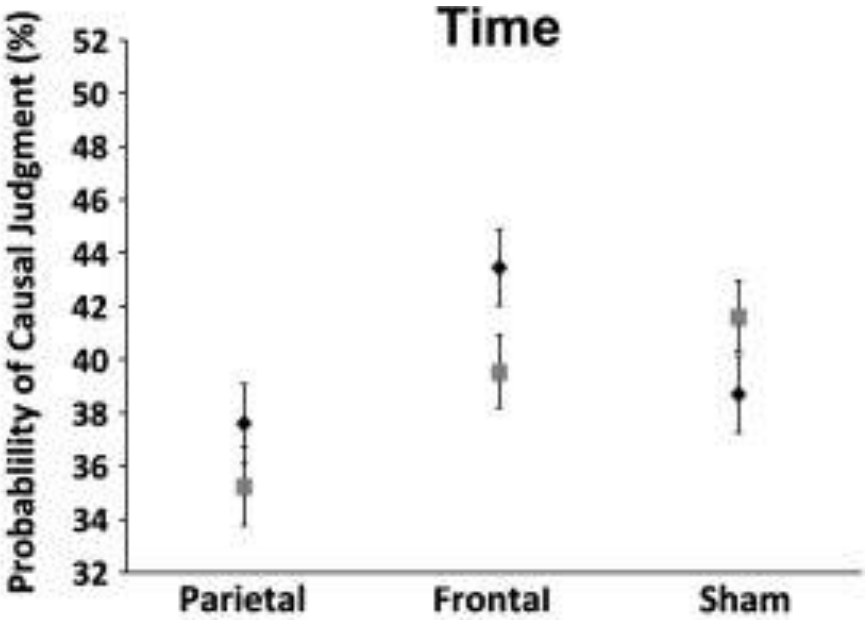




tDCS and causal reasoning







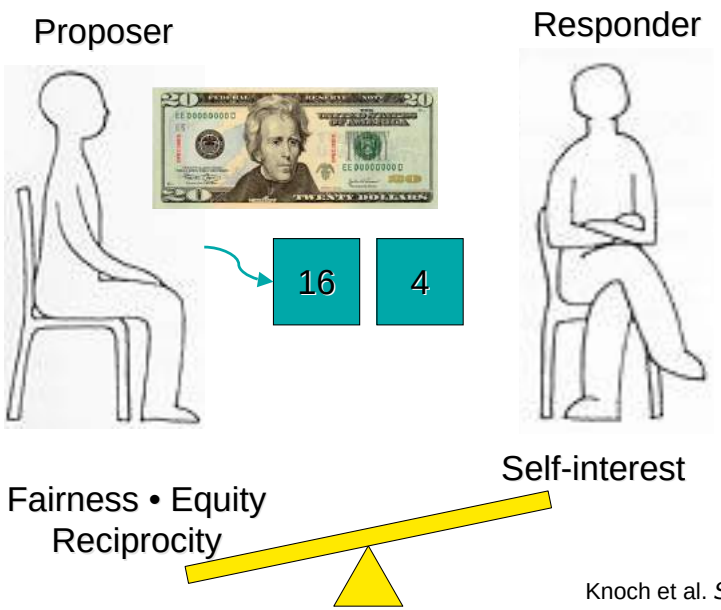
◆ Pre ■ Stimulation

Woods et al., *Neuroimage, 2014*

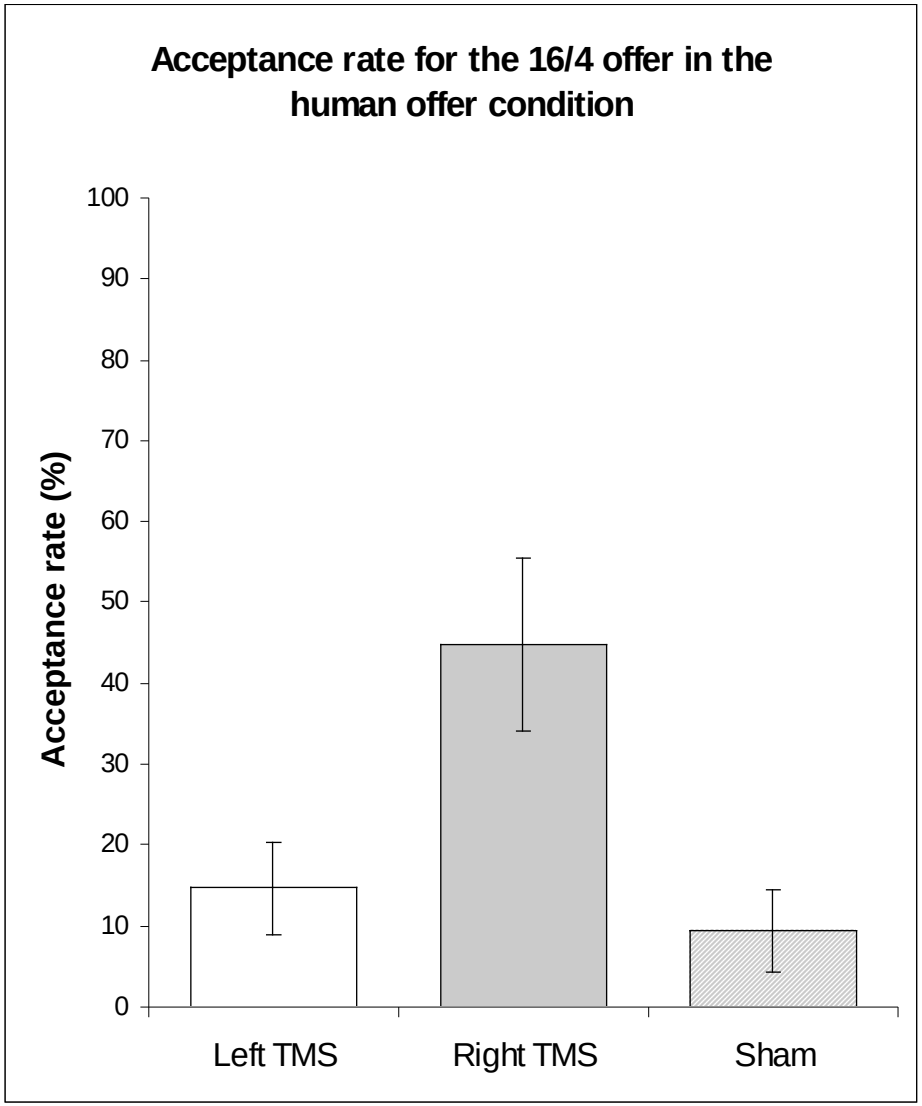
Social Cognition

Altruistic punishment

Ultimatum Game



Knoch et al. *Science* 2006



Stimulation of rDLPFC facilitates acceptance of unfair offer

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?

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How good feels

MY ACCOUNT

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2 6 Would you let someone zap your brain? Why electronic brain stimulation is trending | LA Times
(latimes.com)
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3 5 Noob cable question (foc.us v2 to amrex) (self.tDCS)
submitted 2 days ago * by Gawgba
4 comments share

4 0 Can somebody sell me a tDCS that goes to 4mA (self.tDCS)
submitted 2 days ago by forgottenemporium
8 comments share

5 5 Any montage suggestions for improving focus and attention? (self.tDCS)
submitted 2 days ago by 167elizabethstreet
9 comments share

6 3 Making sponge electrodes (self.tDCS)
submitted 2 days ago by conorohiggins

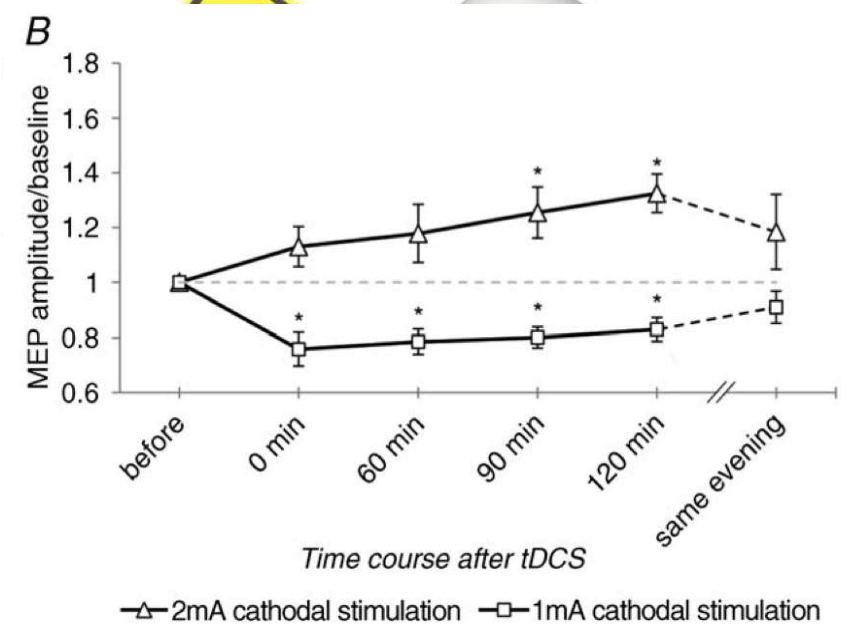
Neuroethical concerns of enhancement with NBS

- 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



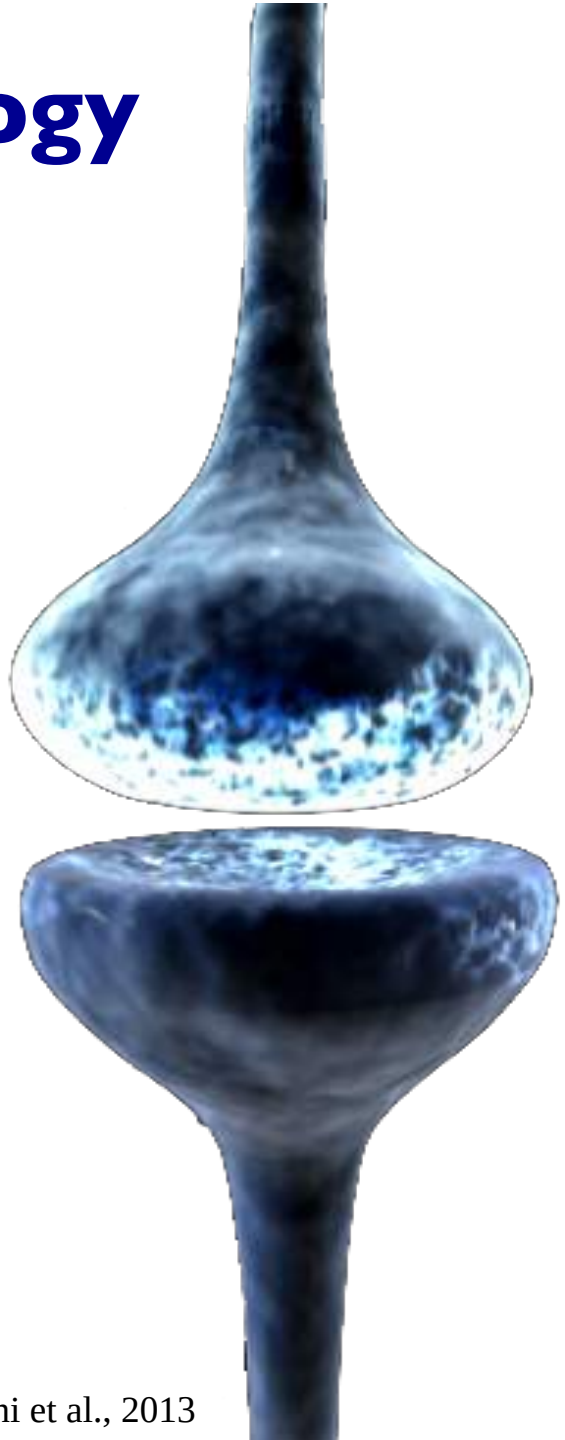
Cathode: DLPFC; Anode: Mastoid (Chrysikou et al., 2013)

Batsikadze et al., 2013

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

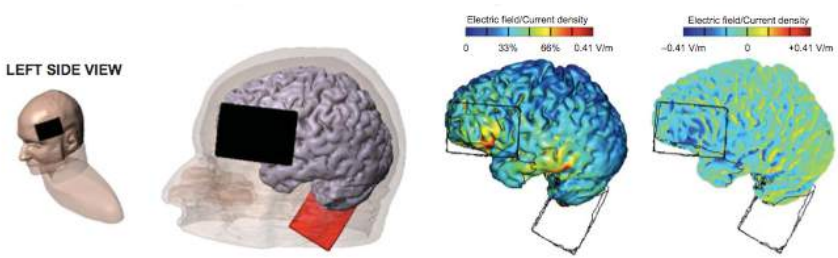


Brunoni et al., 2013

Gains in some performance measures may have a cost…

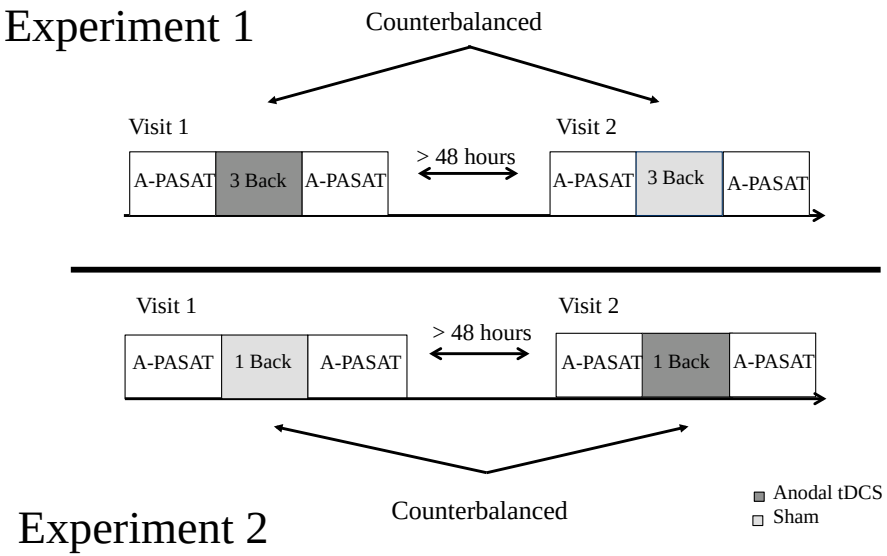
Novel Uses: Left PFC cathodal

"Use it to hammer nails?"



Chrysikou et al. 2013

Working memory: Left PFC anodal



Gill et al., 2014

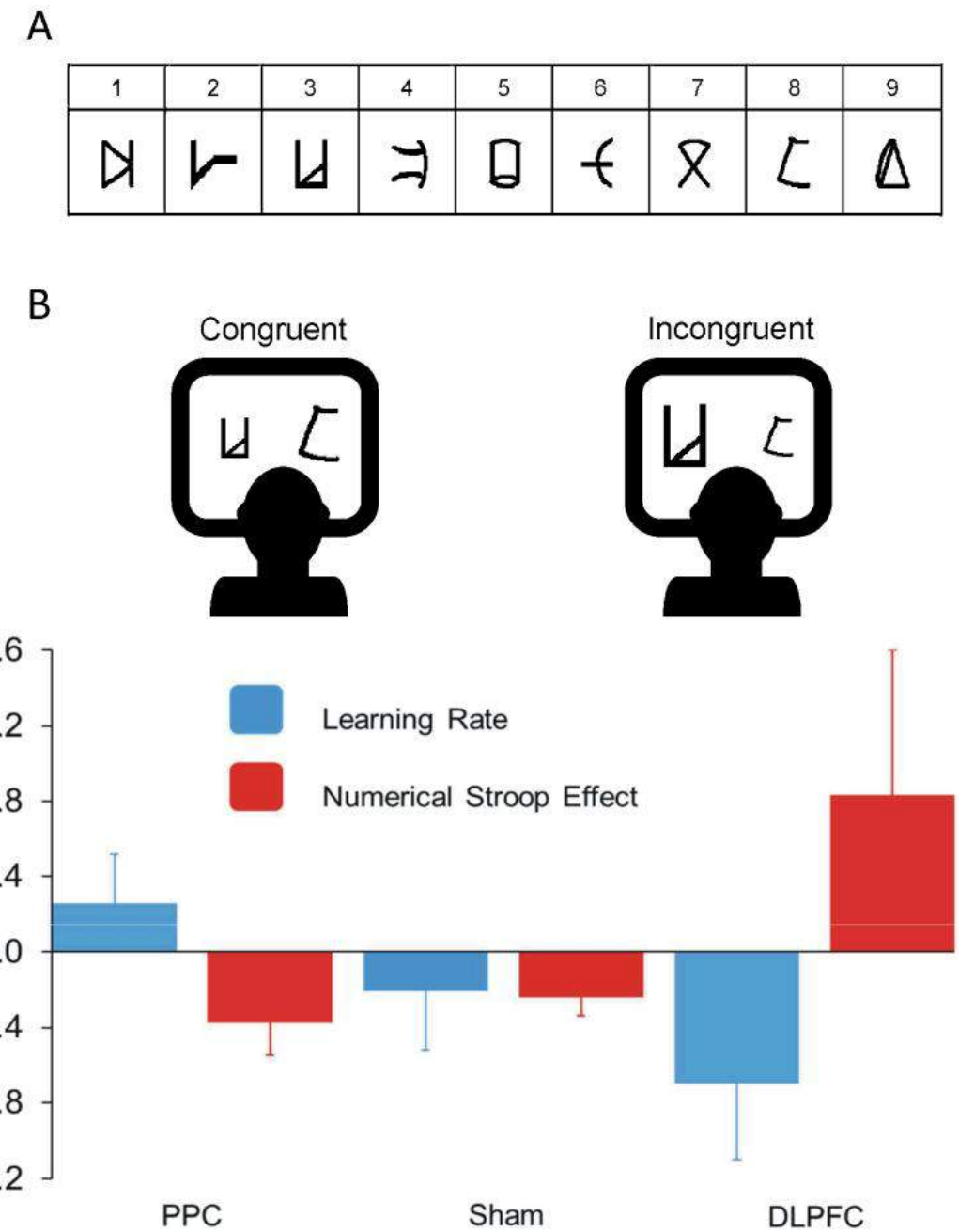
Unintended tradeoffs…

Iuculano & Cohen Kadosh, 2013

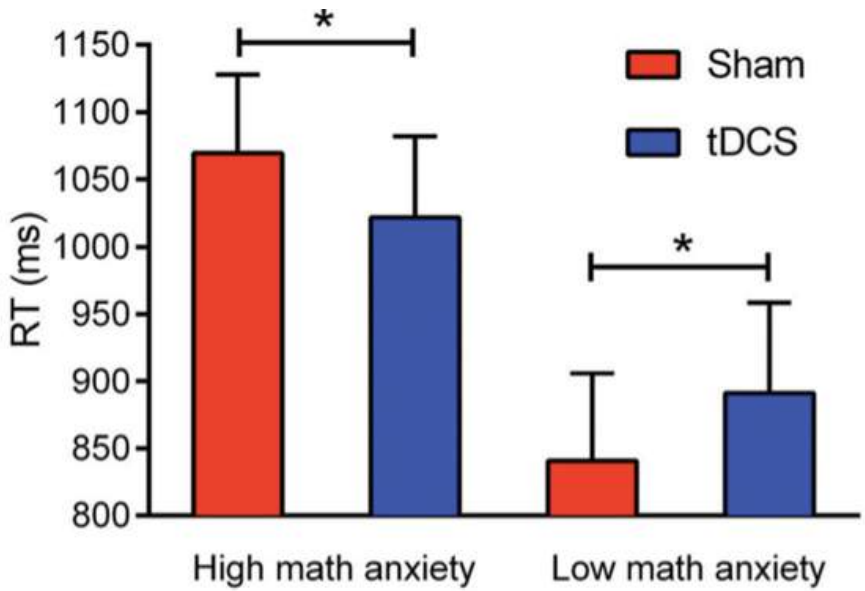
6 days of training + TES

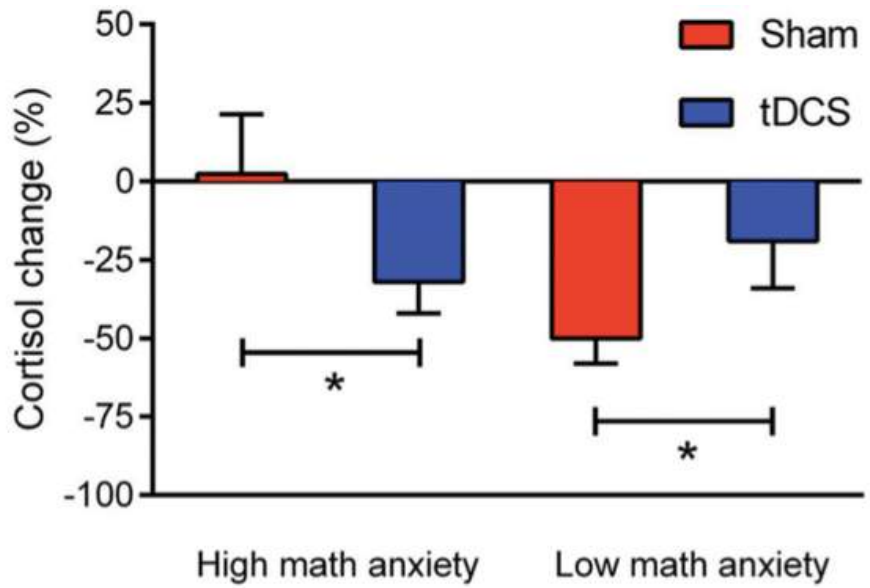
- Posterior parietal cortex
- Dorsolateral prefrontal cortex

- PPC: Increased learning but reduced automaticity
- DLPFC: Increased automaticity but decreased learning



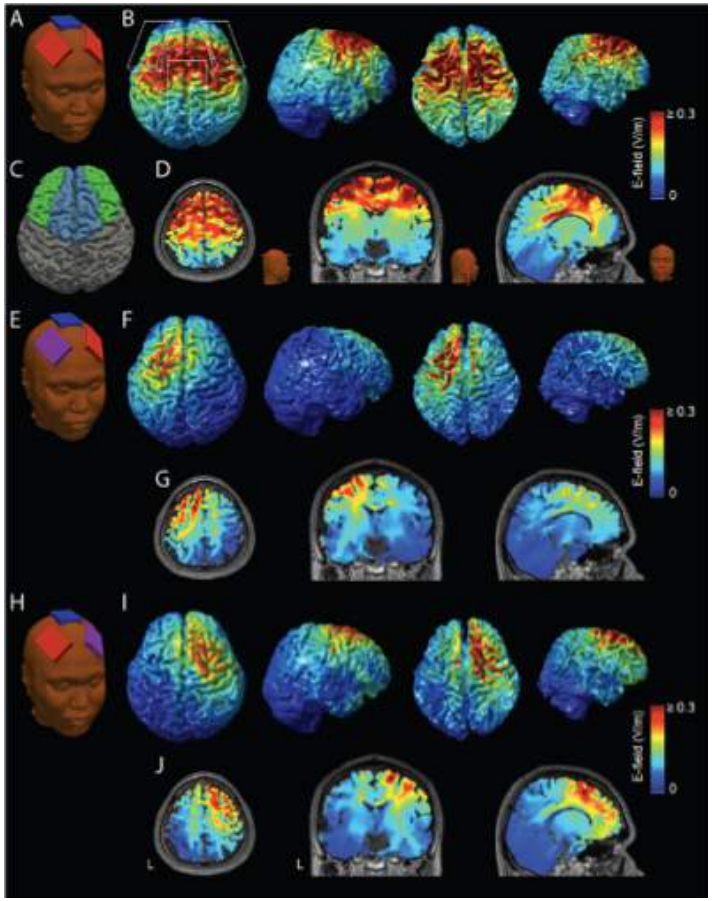
Trait and individual-specific outcomes…

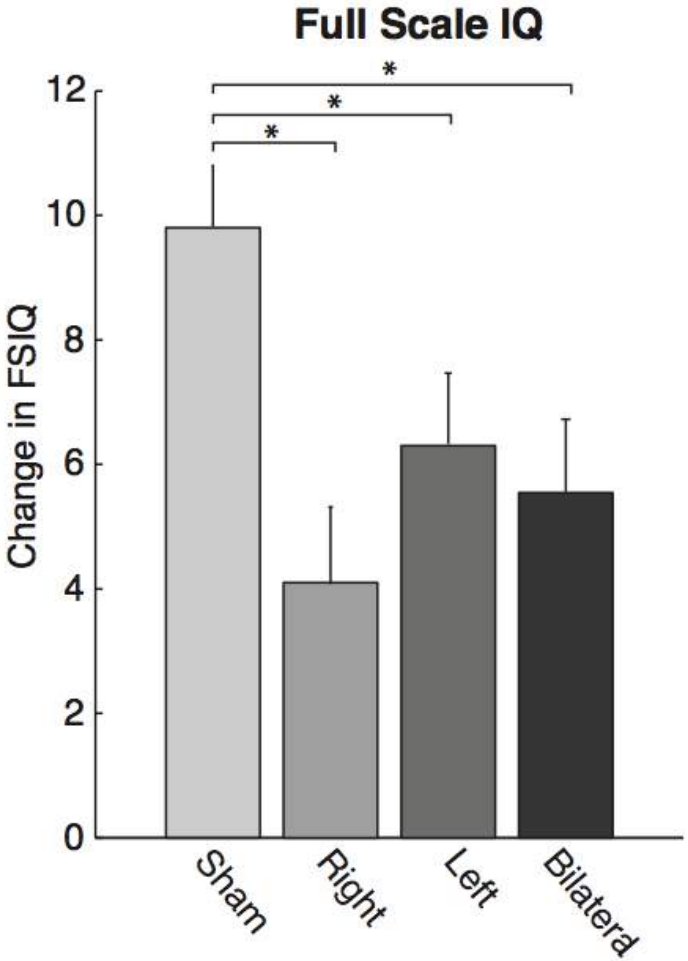




Sarkar et al., 2014

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

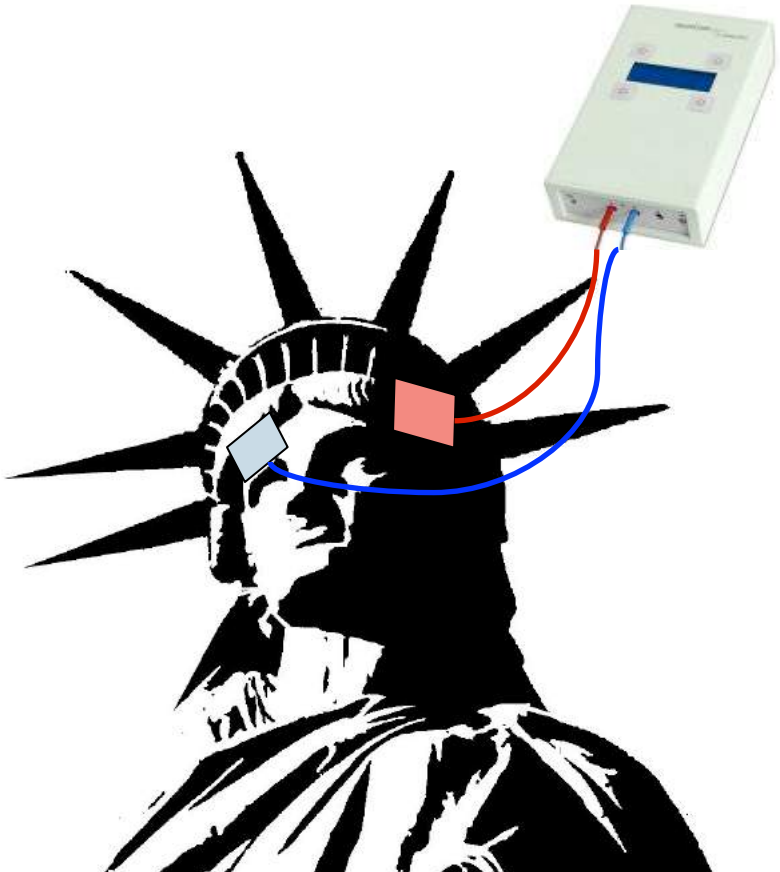
"Hard" & "soft" coercion

- 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

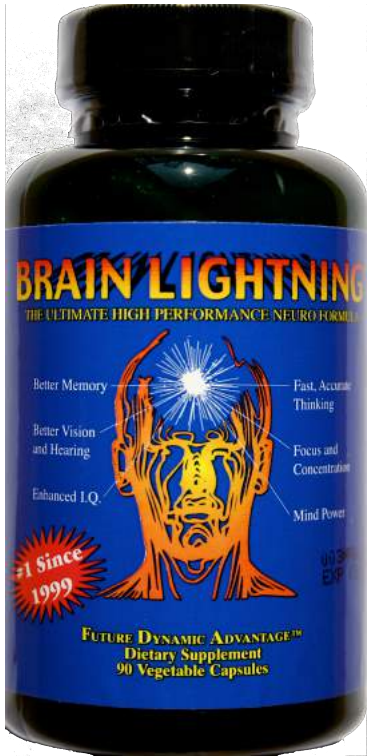
- Liberty to do what one thinks is best for oneself
- Impossible/impractical to ban
  - Communication and education
  - Gain insight into self-enhancement community
  - Promote ethos of responsible use



Fitz & Reiner, 2013

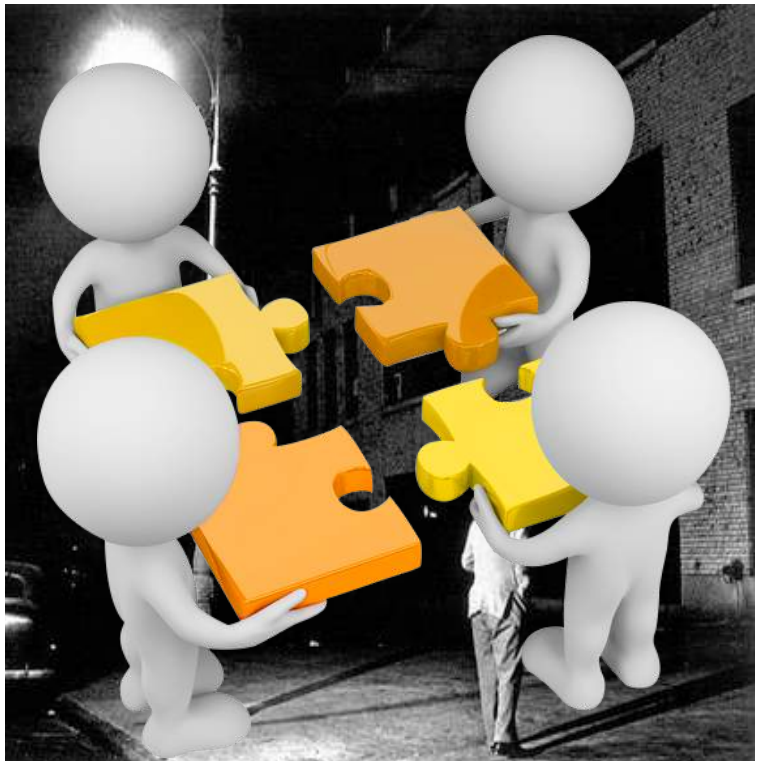
Next steps?

- 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

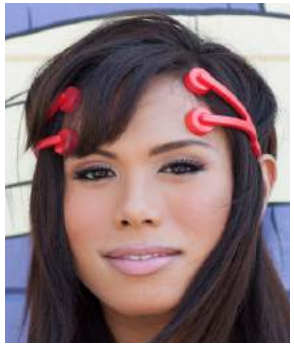
*Wexler, 2014

Supplements for cognitive	Consumer EEG devices	Consumer tDCS devices

"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."

OptiMind	Melon	TCT Technologies
"unleash your mind" "clear brain fog" "focus longer"	"improve your focus"	"when only the best in tDCS therapy will do"

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

Fitz & Reiner, 2013