Better Living Through Brain Stimulation:

The Promise and Peril of the TMS and tDCS in the age of cosmetic neurology

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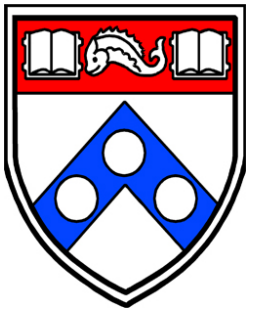
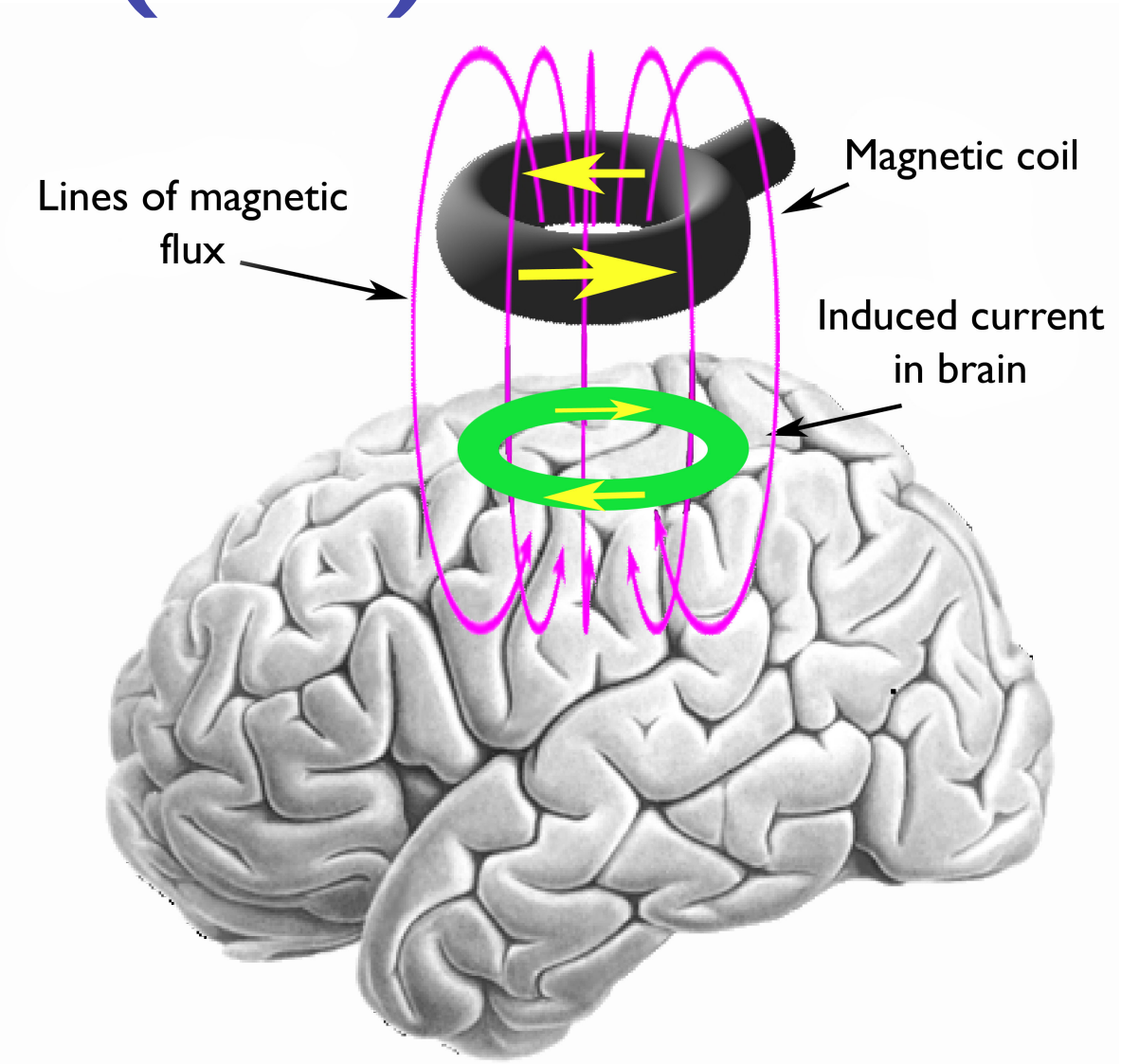


Topics

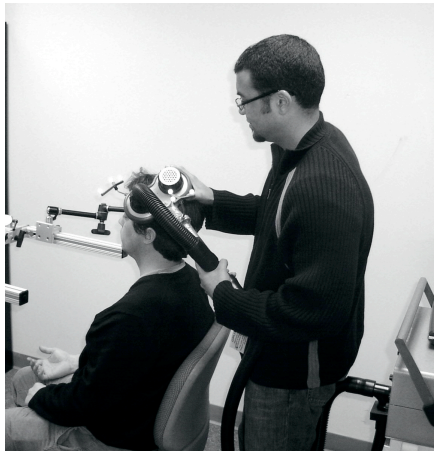
- **The Primer**
  - TMS
  - tDCS
- **The Promise**
  - Cognitive enhancement
  - Mood enhancement
  - Manipulation of social cognition
- **The Peril**
  - Safety
  - Character
  - Justice
  - Autonomy

Transcranial Magnetic Stimulation (TMS)

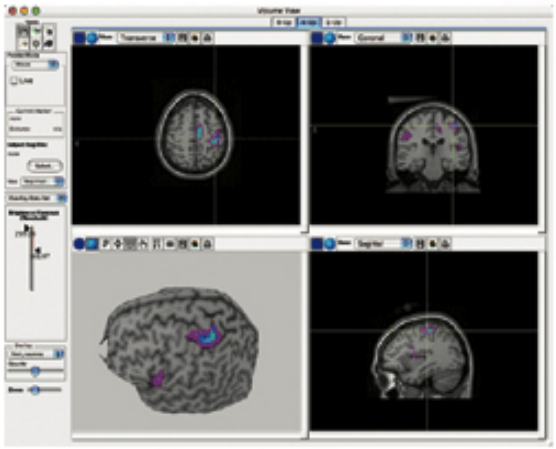
- Based on Faraday Principle
- Rapidly fluxing magnetic field
- Induces current in underlying cortex
- Noninvasive
- Permits focal manipulation of cortical activity



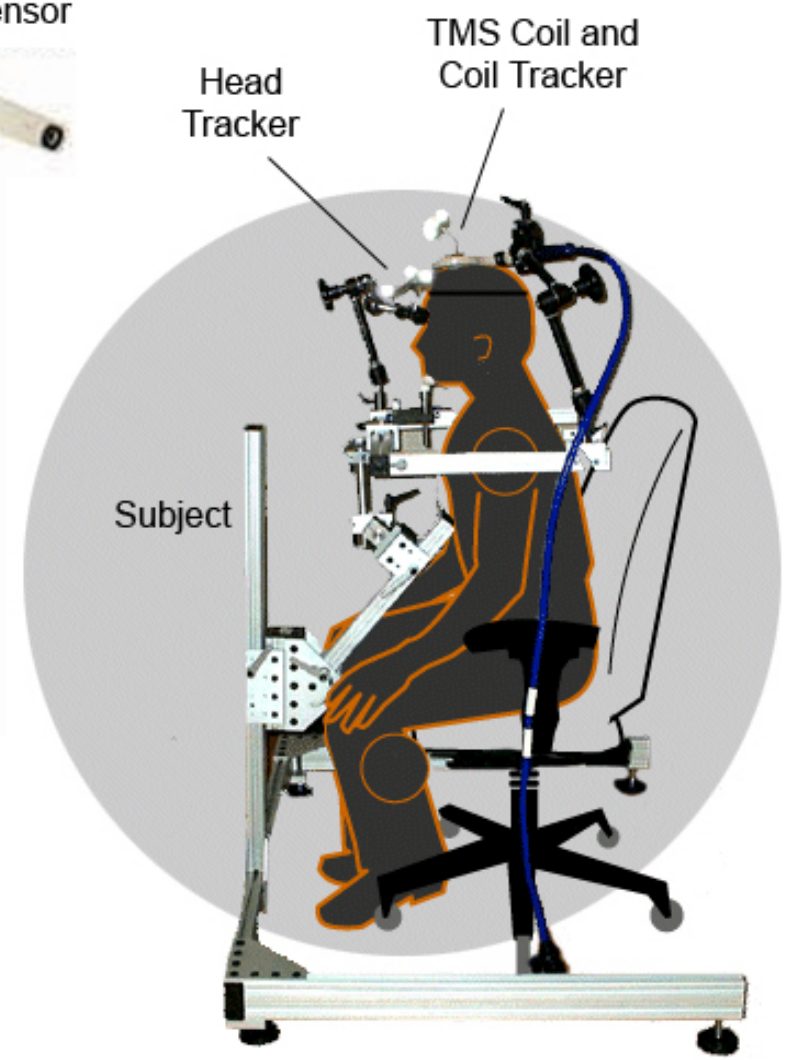
Administration of TMS



Optical
Position Sensor

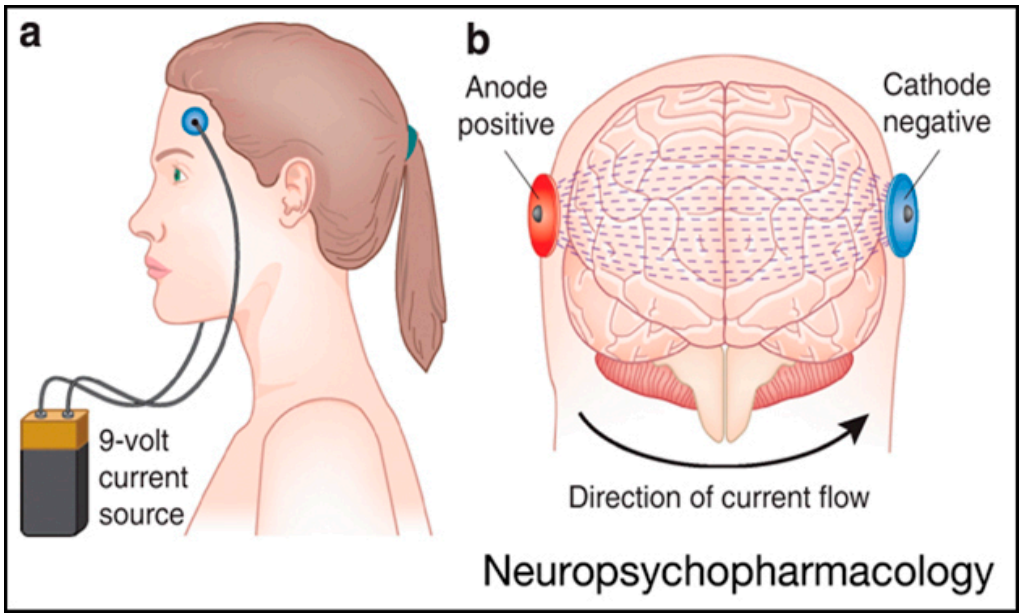


Computer Screen



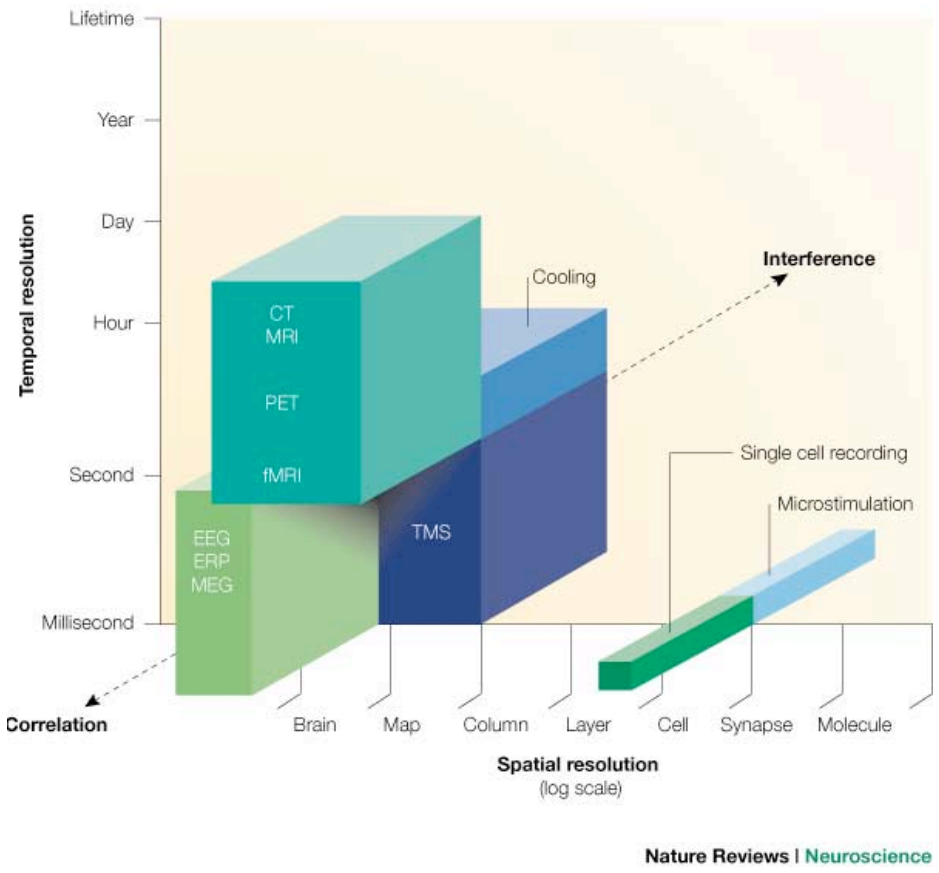
Transcranial Direct Current Stimulation (tDCS)

- Application of weak (1-2 mA) electrical current to cortical neurons
- Neurons respond to static (DC) electrical fields by altering firing rates.
- Anodal or cathodal stimulation have different effects.
- Safe, noninvasive, and painless



George & Aston-Jones, Neuropsychopharmacology, 2010

The 'thoughtspace' of noninvasive brain stimulation



Categories of Manipulation

TMS

- Neurostimulation/depolarization
- Neuromodulation

tDCS

- Neuromodulation

Effects of Manipulation

TMS and tDCS

- Inhibition
- Facilitation

Walsh & Cowey, 2000

Virtual lesions elucidate cortical function

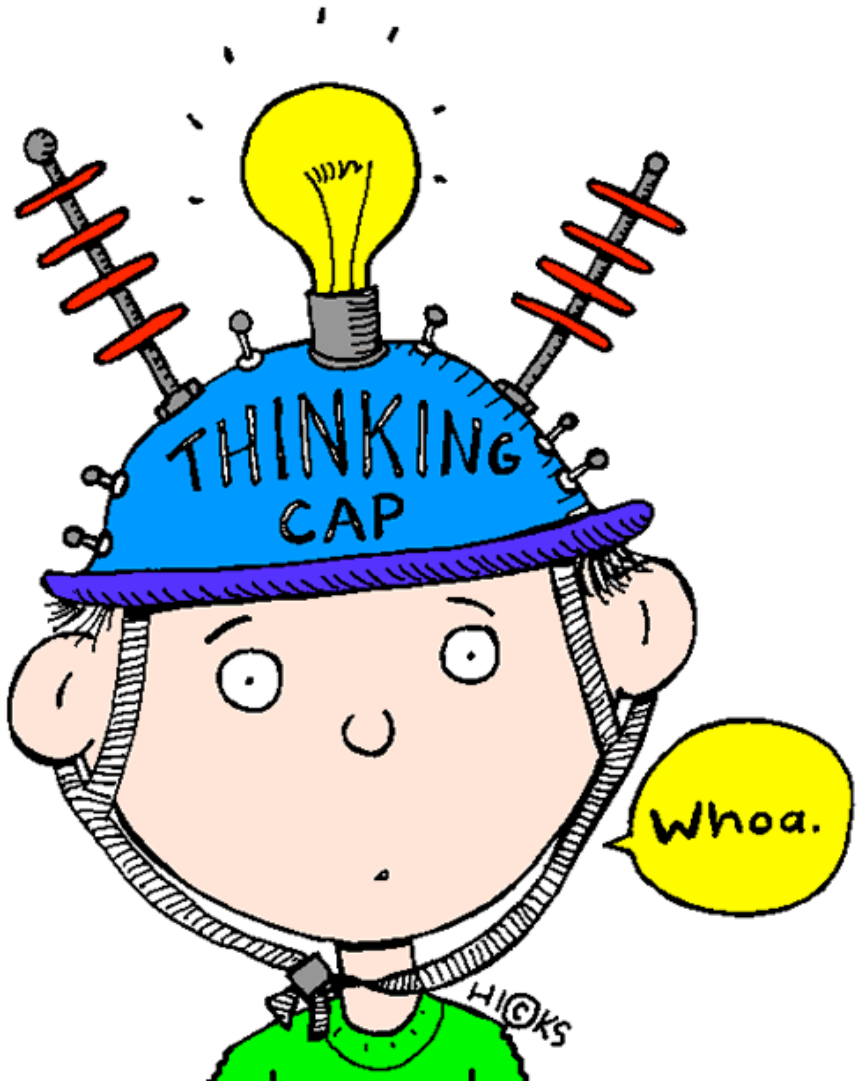
- Avoids confounds from pathological brains
- Acute studies minimize plastic reorganization
- Repeated studies in the same subject
- Multiple subjects with same experimental manipulation; directional hypotheses

	TMS	tDCS
Temporal resolution	Milliseconds	Minutes
Spatial resolution	Millimeters	Centimeters
Duration of effects	Weeks to months after repeated sessions, possibly longer	Not yet well characterized
Ease of localization	High spatial precision requires an MRI-guided stereotactic system. Less precise localization possible using the 10-20 system or other scalp measurements.	Large area of effect allows for localization using 10-20 system or other scalp measurements.
Safety	Safe when applied within established safety guidelines. The additional risk is conferred by prior stroke is not fully known.	No lasting adverse effects reported within currently used stimulation parameters. Additional risk conferred by prior stroke is not fully known.
Patient Discomfort	Mild muscle twitches during stimulation uncomfortable to some subjects. Transient mild headaches reported. Rare cases of dental pain reported.	Itchiness and occasional mild burning sensation has been reported under scalp electrodes. Usually well tolerated.
Ability to Use Sham Control Condition	Sham often readily distinguished from real stimulation. Newer sham coils may simulate stimulation more realistically.	Realistic sham stimulation is easily administered by briefly delivering current.
Portability	Typical setup includes TMS unit, stimulation coils, devices for securing the subject and coil position, and hardware for MRI-guided localization.	Highly portable. Can be used in any traditional experimental or clinical setting.
Cost	Relatively expensive: Approximately $100,000 - $150,000 for TMS unit, coils, and MRI-guided localization system.	Very cost-effective: Approximately $10,000 for tDCS unit.

Cognition

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

- Language
- Learning & Memory
- Spatial Attention
- Problem-solving
- "Savant Skills"



Language

- TMS & tDCS: Faster naming

  (Mottaghy et al., 1999; Sparing et al.,2008)

- tDCS: Improved acquisition of novel names

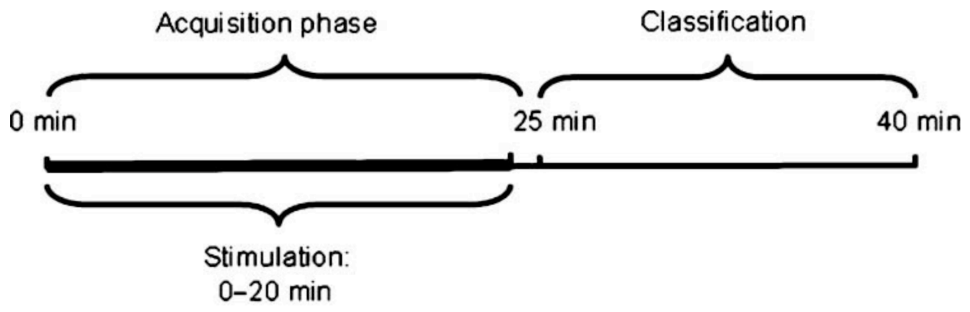
  (Flöel et al., 2009)

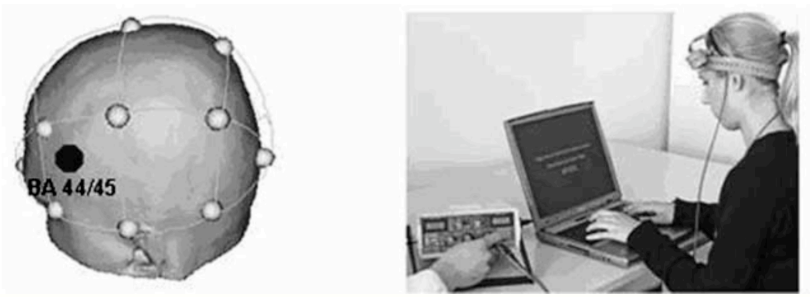
- tDCS: Better acquisition of grammar

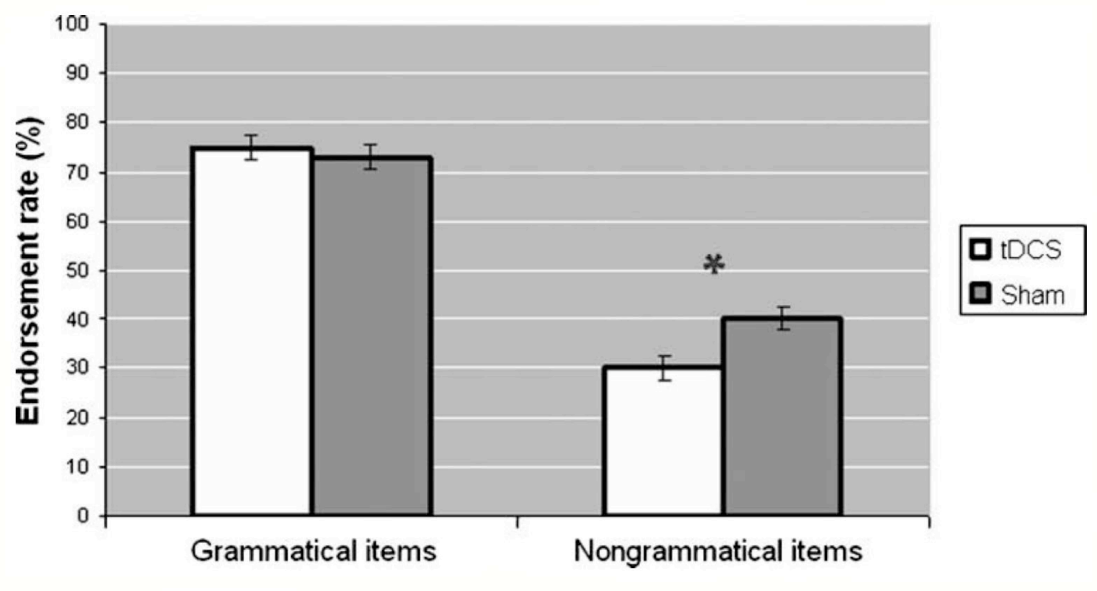
  (de Vries et al, 2009)

- tDCS: Increased verbal fluency

  (Iyer et al 2005)



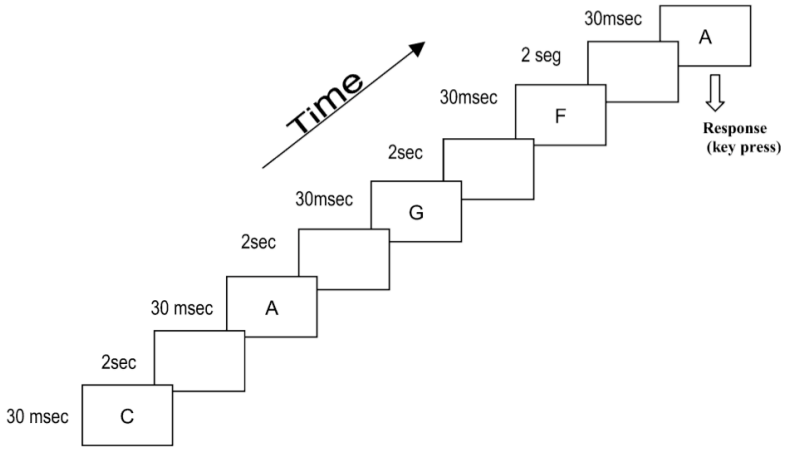


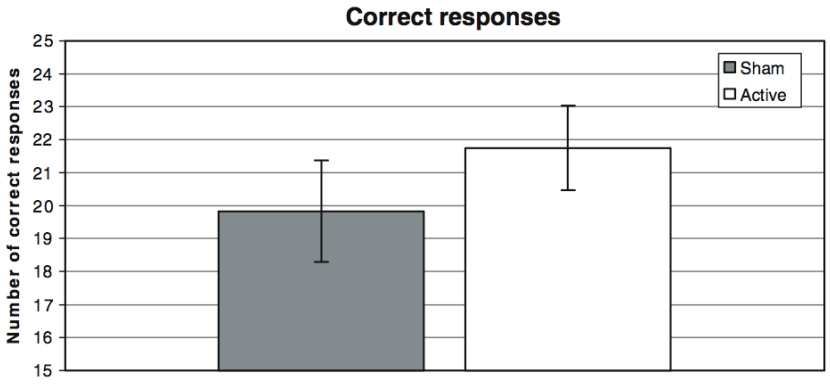


De Vries et al., JOCN, 2009

Learning and Memory

- TMS: Enhances phonological memory
  (Kirschen et al., 2006)
- TMS & tDCS: Motor skill learning
  (e.g. Nitsche et al., 203; Kobayahi et al., 2009; Kim et al, 2004; Vines et al., 2006)
- tDCS: Improves verbal working memory
  (Fregni et al., 2005)

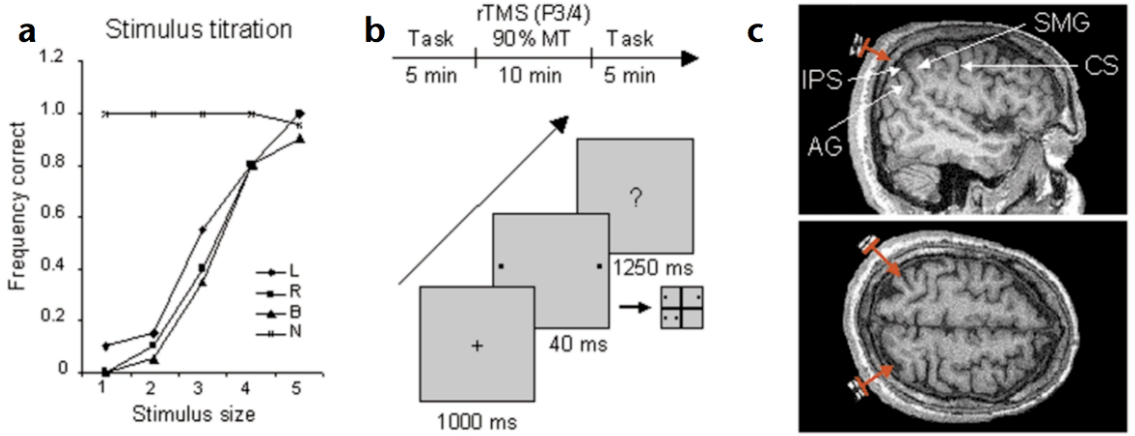


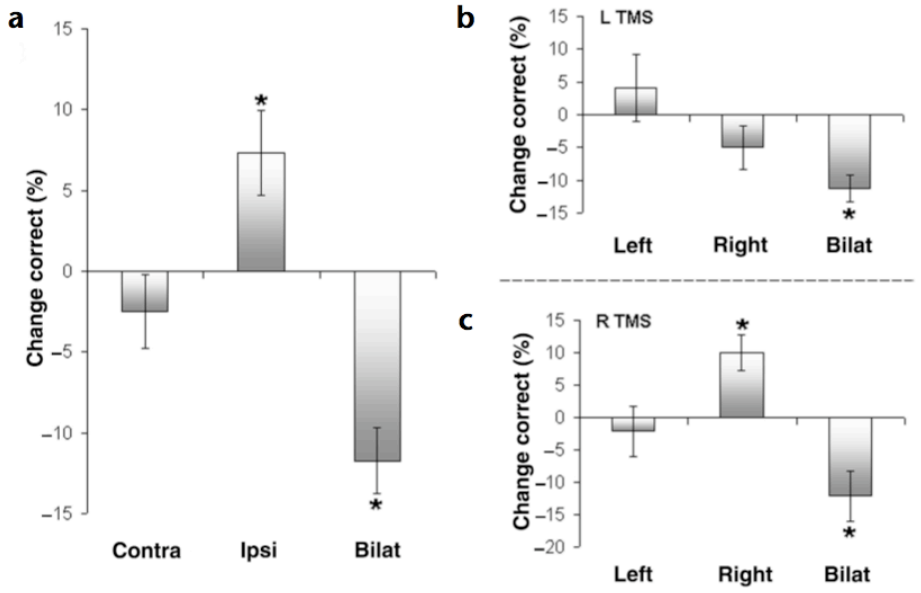


Fregni et al., 2005

Spatial Attention

- 600 pulses of 1 Hz rTMS for over right and left parietal cortex
- Induced extinction for contralateral targets
- Improvement in ipsilateral target detection.
- Supports model of interhemispheric competition in visuospatial processing.



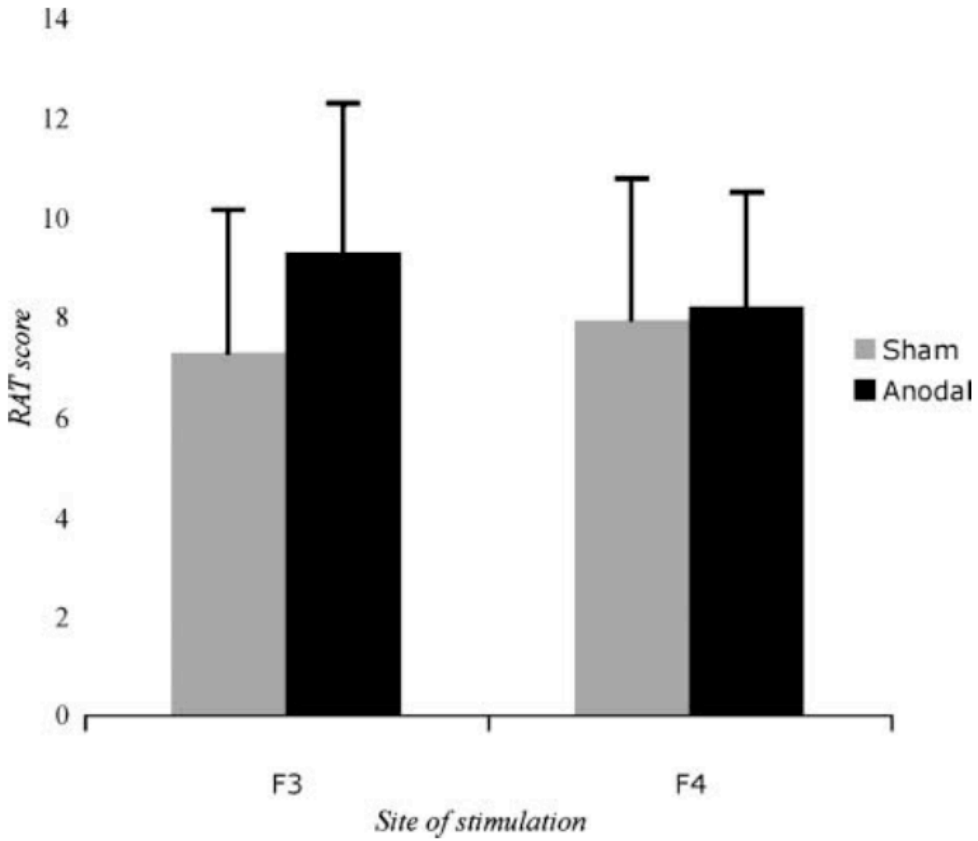


Hildetag et al., 2001

Problem Solving

Remote association test (RAT)

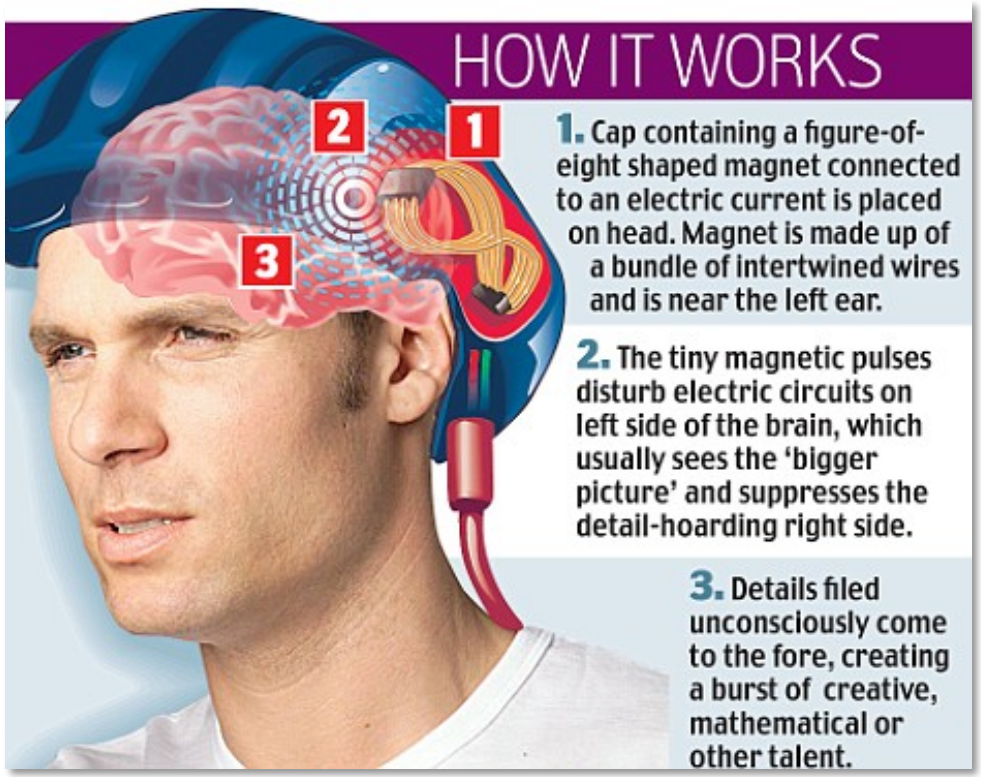
- Identify common linguistic association between three words: e.g. scan, wash, child
- Associations to creative thought, executive function and general intelligence.
- "Aha" moment
- Anodal tDCS of left DLPFC associated with improved performance

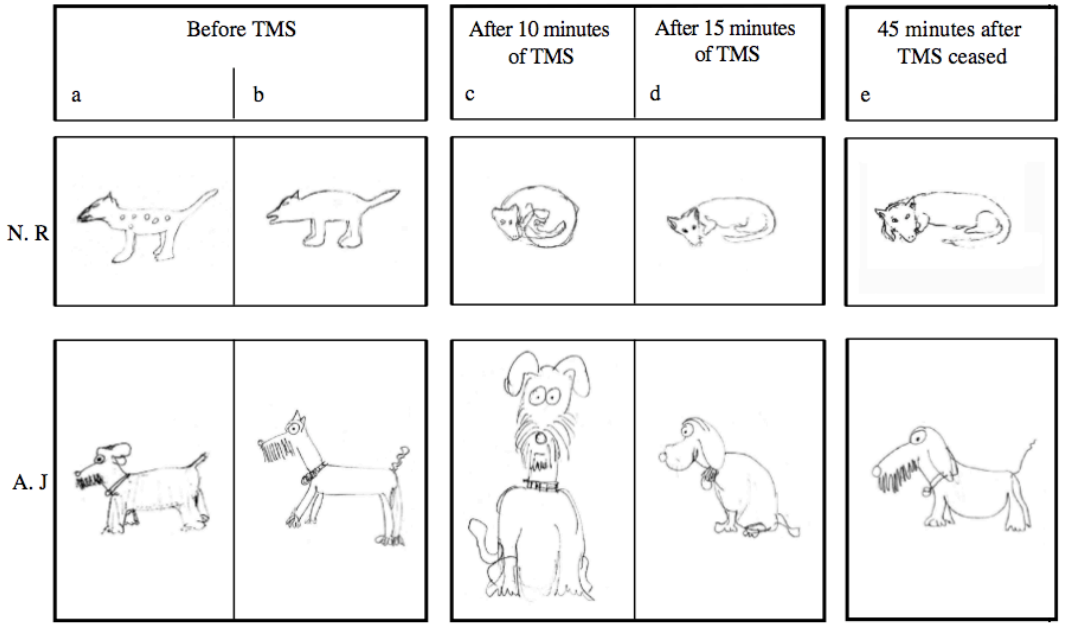


Cerruti et al., 2009

"Savant Skills"

- **Left anterior temporal lobe low-frequency TMS**
  - Improved drawing skills (4/11 subjects)
  - Improved self-reporting of visual details
  - Improved proofreading (2/11)
  - Numerousity judgment (10/12)
- **Hypothesis:** All persons possess masked "savant skills": art, music, calendar calculating mathematics, mechanical/ spatial skills
- Access to lower-level "less-processed" information





Snyder, 2003

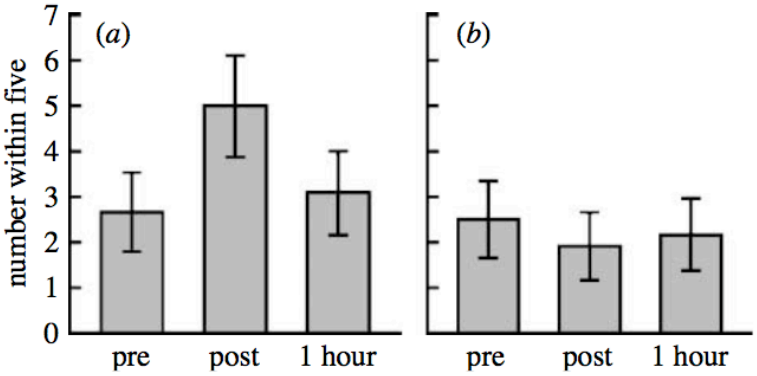
"Savant Skills"

- Diminished LATL "hypothesis/ concept formation" about incoming information.
  - Inhibitory TMS of LATL shown to reduce false memory formation.
    (Gallate et. al., 2005)
  - Diminished ability to interpret opaque idioms (Oliveri et al., 2004)

Drawn Right Side Up

Drawn Upside Down

Figure 1. TMS set-up for the numerosity experiment.



Mood enhancement

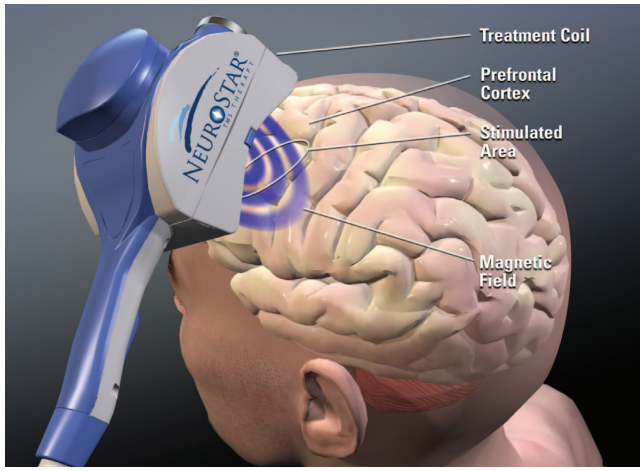
- Now considerable evidence that TMS is effective in treating depression

- Largest RCT conducted in 23 sites in US, Canada, and Australia
  - 301 medication-refractory patients
  - 10 Hz, 4sec trains 120% MT
  - 3000 pulses/session
  - 5x/week for 4-6 weeks
  - 3x remission rate (14.2% vs 5.5% sham) compared to placebo
  - 23.9% response rate (12.3% sham)

- Approved by FDA for treatment of major depression in July 2008

Mood enhancement

- TMS currently being studied for OCD, PTSD, & schizophrenia
- Promising recent studies in the use of tDCS for depression
  (Fregni et al., 2006; Boggio et al., 2006)
- Mood effects noted in healthy individuals after stimulation



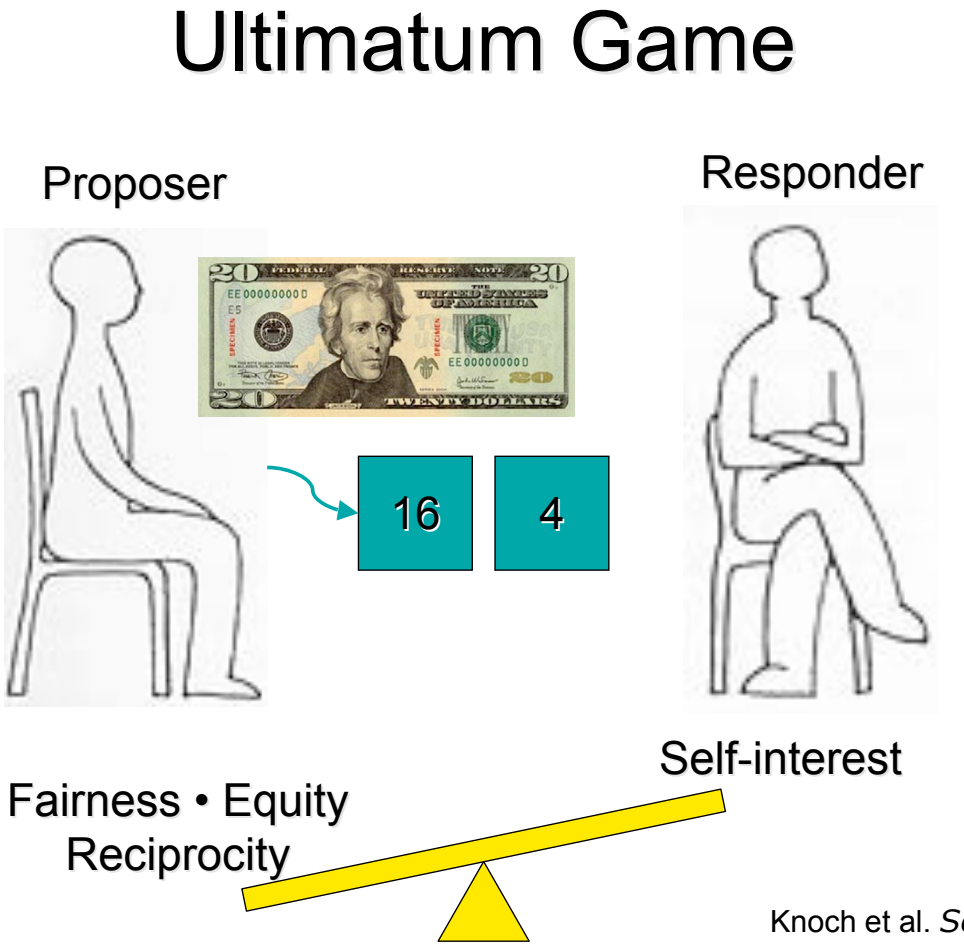
Social Cognition

- Noninvasive brain stimulation can elucidate neural mechanisms of social cognition that inform our understanding of ethical behavior:
  - Bias and prejudice*
  - Altruism and self-interest
  - Deception
- The ability to manipulate these cognitive constructs introduces ethical questions

Social Cognition

Altruistic punishment

- High rejection rates when offers are below 25%
- Responders reject low offers as high as 3 months income
- Balance of self interest and fairness/reciprocity
- fMRI data indicates that DLPFC activated when offer is unfair (Sanfey et al., 2003)



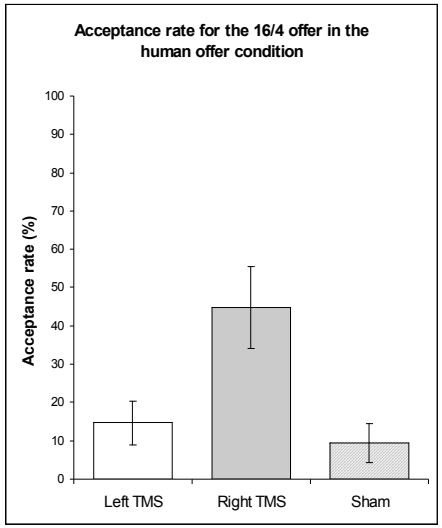
Knoch et al. *Science* 2006

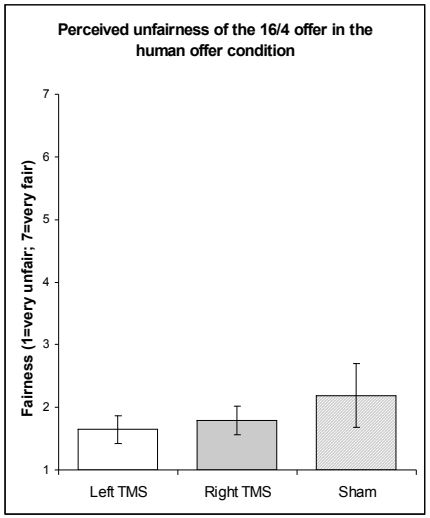
Social Cognition

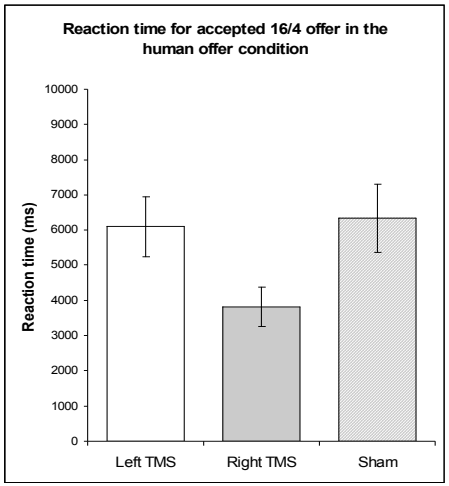
Manipulation of self-interest using brain stimulation

- Increased acceptance rates of unfair offers after inhibitory TMS of right DLPFC
- Shown in large groups of subjects using tDCS.

  (Knoch et al., 2007)
- TMS/tDCS of DLPFC manipulates performance on a variety of other tasks involving risk-taking and addiction cravings.







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?

Acknowledgement

Special thanks to Anjan Chatterjee, MD for consultation and feedback regarding the ethical implications of neurologic self-enhancement.

The perils of brain enhancement

- Safety
- Character
- Justice
- Autonomy

Safety

Risks associated with TMS

Known Risks

- **Seizure induction**
- Effects on Cognition
- Effects on Mood
- Endocrine effects
- Transient effects on lymphocytes
- Transient auditory threshold shift
- Local pain and headache
- Burns from scalp electrodes

Theoretical Risks

- Histotoxicity
- Kindling
- Long-term Potentiation
- Long-term Depression
- Social and psychological consequences of a seizure

To date, there are no known or theoretical or serious risks associated with tDCS.

Safety

- Important but familiar problem
- Ubiquitous to any therapeutic or cosmetic intervention
- Good risk/benefit ratio
- No conflict of interest

Justice

- Equitable distribution of resources
- Boutique cognitive enhancement regimens for the wealthy
- Problematic but mirrors existing problems
- Brain stimulation may be less problematic than pharmacologic agents

"The future is here. It's just not evenly distributed yet."
-*William Gibson*

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

Autonomy

"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

"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

Next steps?

- Awareness of issues and their plausibility
- Learning from other examples of elective self-enhancement:
  - Cosmetic surgery
  - Cosmetic neurology
- Monolithic policies unlikely to be useful.