Cognitive Enhancement with Transcranial Direct Current Stimulation (tDCS)

http://www.theatlantic.com/magazine/archive/2014/09/prepare-to-be-shocked/375072/

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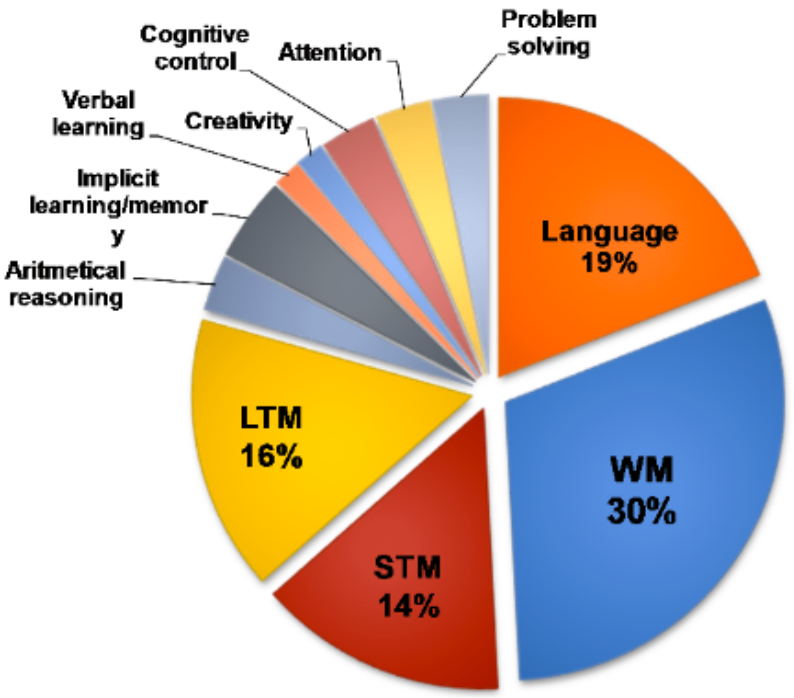
Neuroenhancement

The enhancement of brain processes in healthy individuals

Cognitive Enhancement with tDCS
(Coffman et al., 2014; Horvath et al., 2015)

- Executive functions
  - Set-shifting
  - Stop signal tasks
  - Stroop tasks
- Language
  - Grammatical learning
  - Lexical learning
  - Verbal fluency
  - Naming
- Attention
  - Selective attention
  - Spatial attention
- Learning
  - Motor learning
  - Procedural learning
  - Explicit learning
  - Numerical learning
- Memory
  - Digit-span recall
  - Verbal episodic memory
  - Visual working memory
  - N-back working memory
- Mental arithmetic
- Automaticity
- Picture viewing/rating
- Visual perception
- Multimodal perception
- Social cognition
- Problem-solving
- Mood
- Gambling based risk taking
- Rumination



Santarnecchi et al., *in prep*

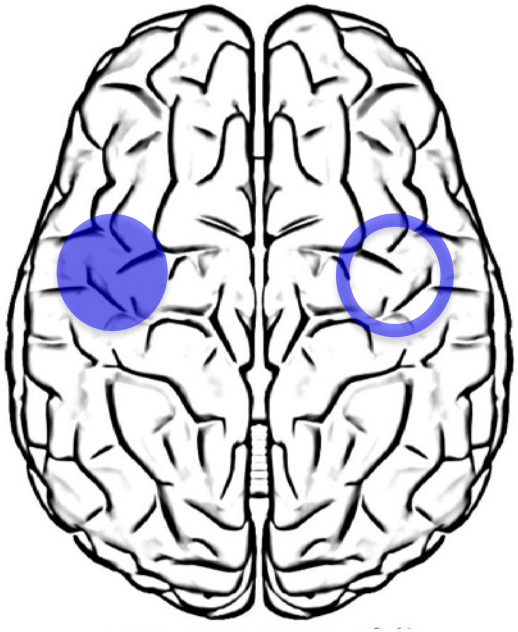
Cognitive Skills

- Learning
  - Implicit
    - Motor/procedural
    - Probabilistic
  - Explicit
- Working Memory
- Attention
- Social Cognition
- Language
- Complex Problem-Solving

Enhancement of Implicit Learning:

Procedural/Motor

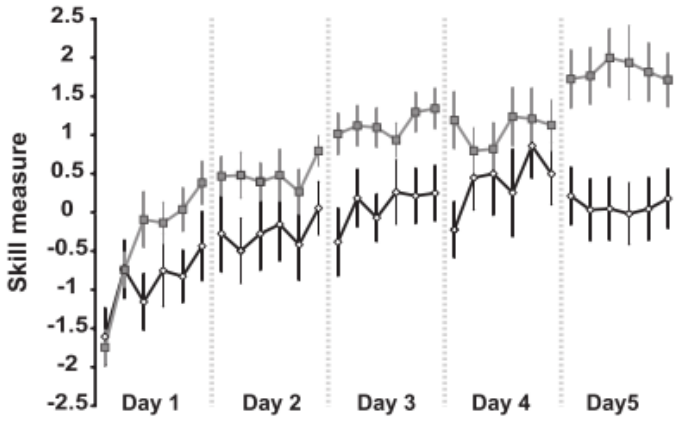
- Anodal tDCS of the left primary motor cortex enhances motor learning of the contralateral hand (Nitsche et al., 2003)

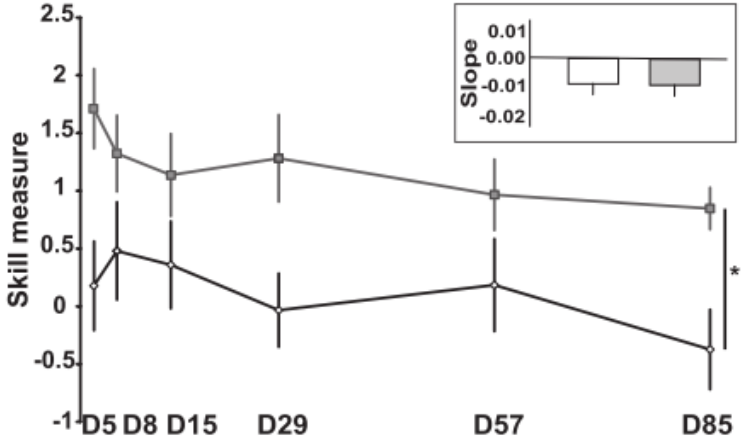


- Cathodal tDCS of the primary motor cortex decreases motor learning of the contralateral hand (Vines et al., 2006)
- Cathodal tDCS enhances motor learning of the ipsilateral hand

Enhancement of Implicit Learning: Procedural/Motor

- Learning occurs in 3 stages
  - Acquisition ➔ Consolidation ➔ Retention
- tDCS improves motor learning by enhancing consolidation (Reis et al., 2009)

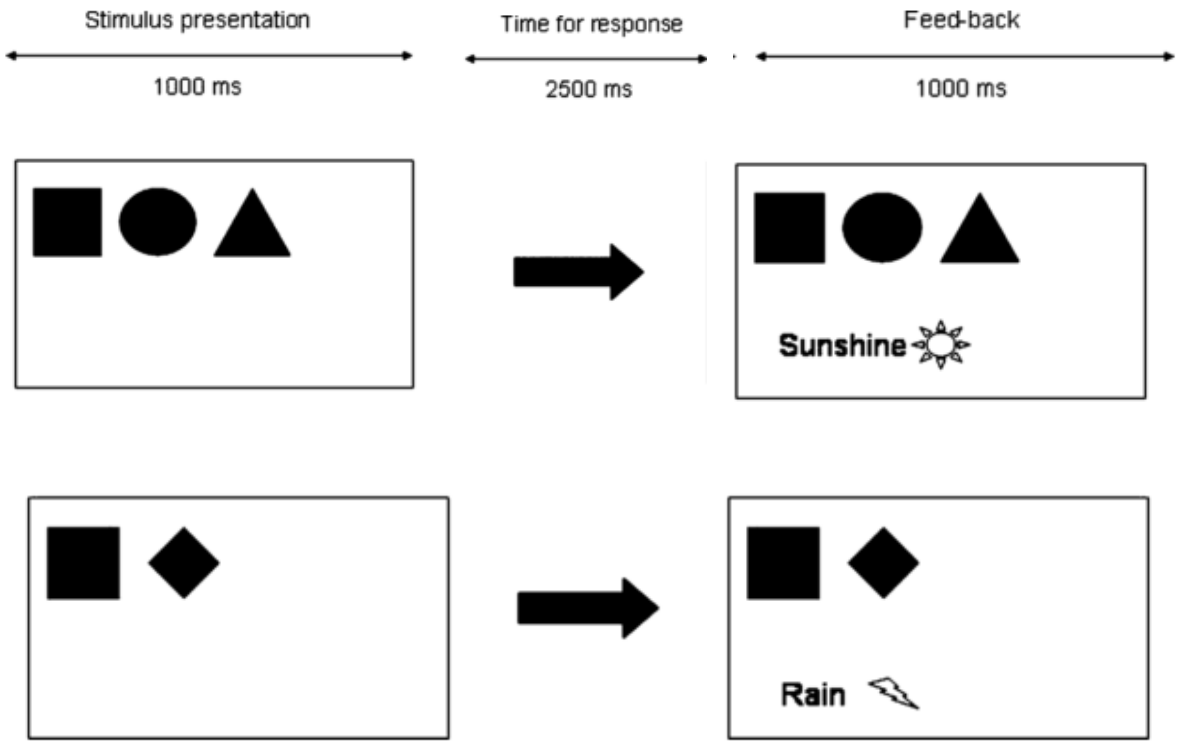




- Others have shown additional improvements in retention (Galea & Celnik, 2009)

Enhancement of Implicit Learning: Probabilistic

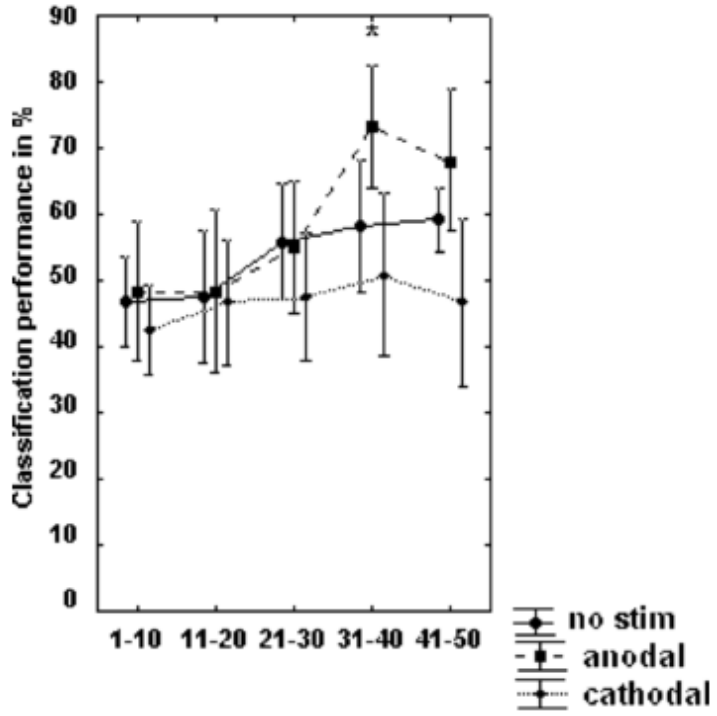
- Probabilistic Classification Learning Task (Kincses et al., 2004)

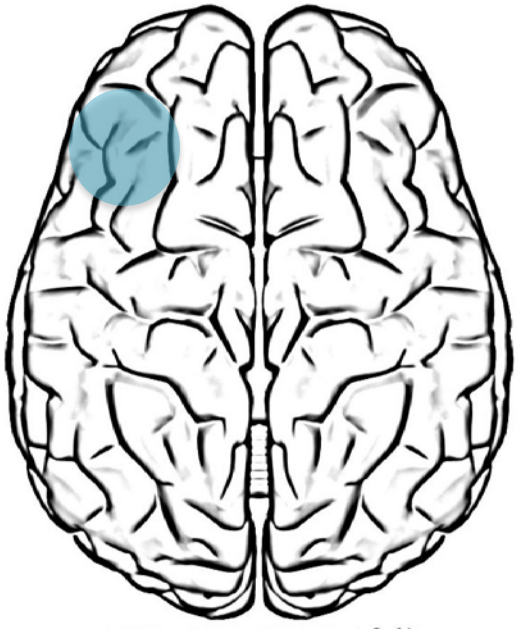


Cue	*P* (Sun)
■, ▲	1.00
■, ▲, ●	1.00
■	0.86
■, ●	0.75
▲	0.60
■, ◆	0.50
▲, ●	0.50
■, ●, ◆	0.50
■, ▲, ◆	0.50
●	0.40
▲, ◆	0.25
◆	0.14
▲, ●, ◆	0.00
●, ◆	0.00

Enhancement of Implicit Learning: Probabilistic

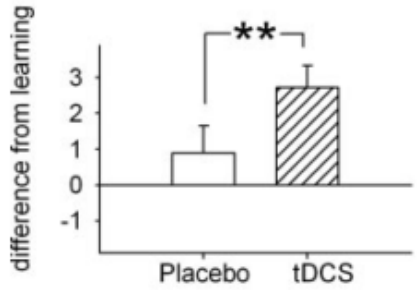
- Anodal tDCS of the left dorsolateral prefrontal cortex (DLPFC) enhances probabilistic learning (Kincses et al., 2004)

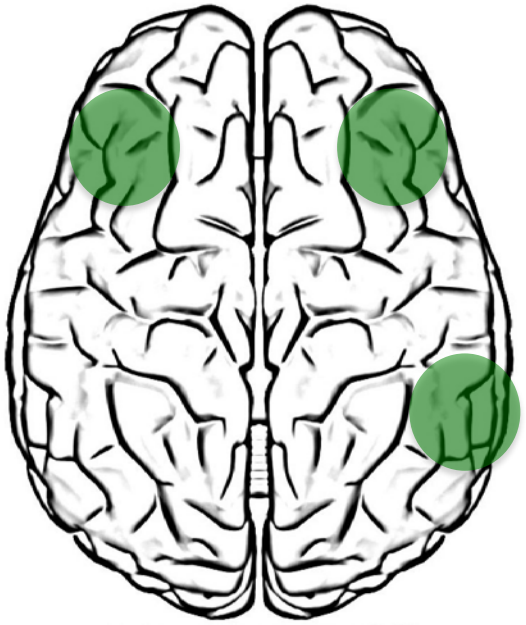




Enhancement of Explicit Learning

- 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

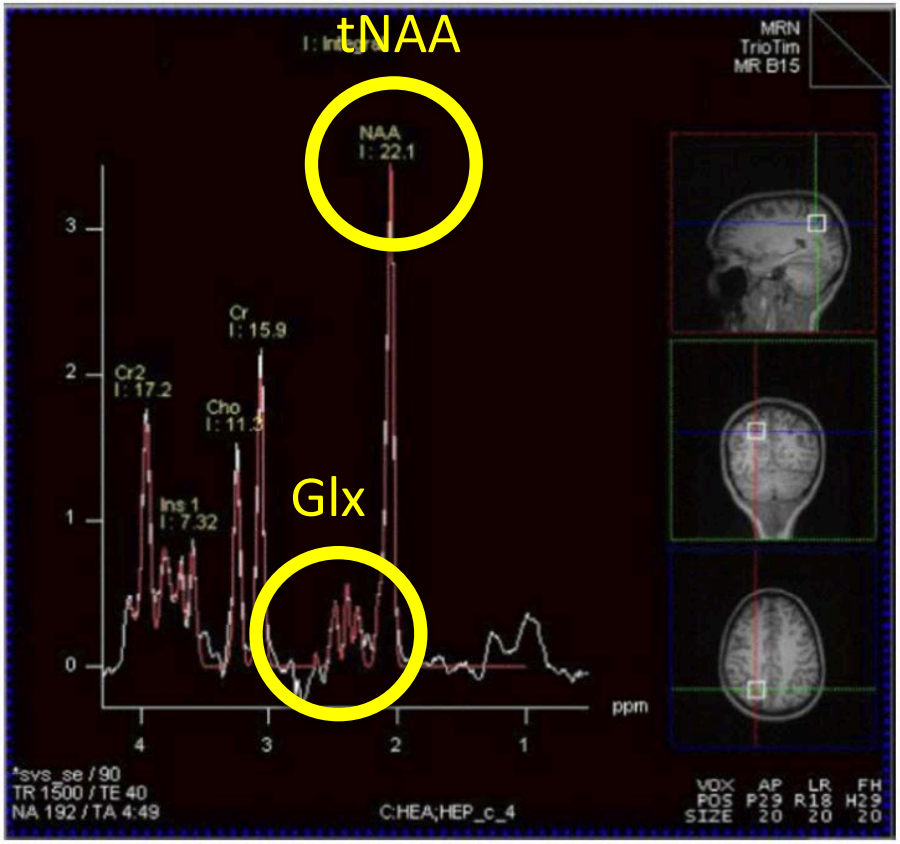




- Anodal tDCS of right temporoparietal area enhances memory of object locations after a 1 week delay (Flöel et al., 2011)
  - However, no difference in immediate acquisition

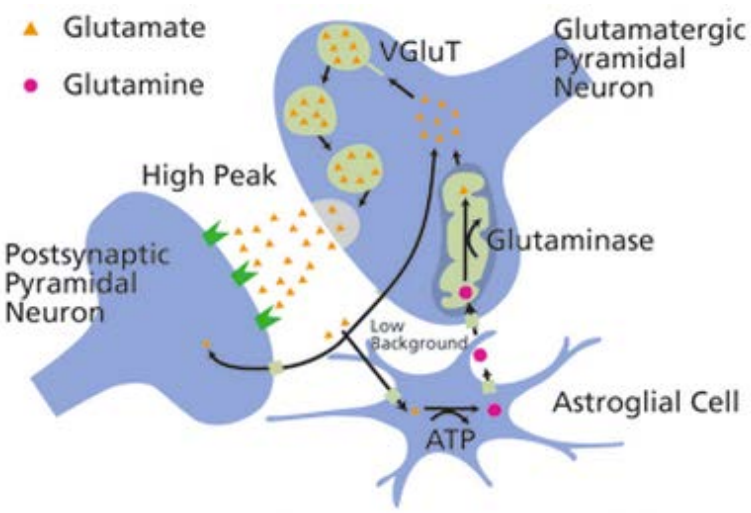
Physiology of Learning Enhancement

- Clark et al. found improvement in spatial learning with anodal tDCS to right parietal cortex (2012)
- They then use magnetic resonance spectroscopy to measure metabolites under anode (2011)
- Elevations in:
  - Glutamine/glutamate (Glx)
  - N-acetylaspartate/N-acetylaspartylglutamate (tNAA)



Physiology of Learning Enhancement

- Glx
  - Glutamate (Glu) is major excitatory neurotransmitter
  - Metabolized to glutamine (Gln)
  - Glutamate binds to NMDA receptor for excitation, long-term potentiation
  - NMDA antagonists suppress tDCS effects, while NMDA agonists enhance tDCS effects (Clark et al., 2011)
- tNAA
  - Thought to be related to neuronal energy status
  - May be due to increased metabolic activity from increased glutamatergic activity



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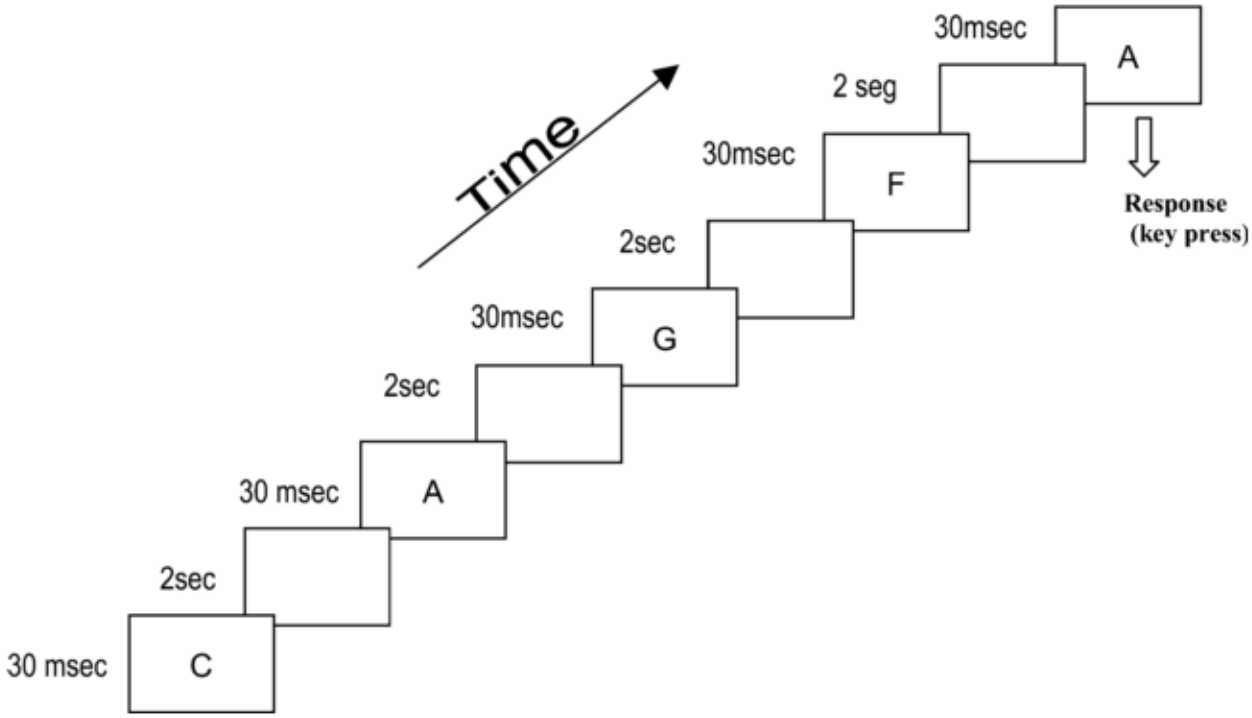
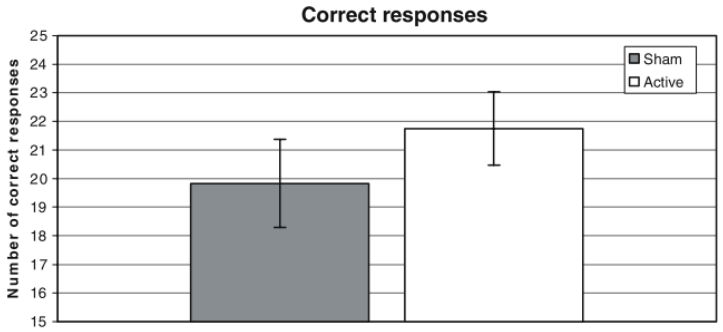
Enhancement of Working Memory

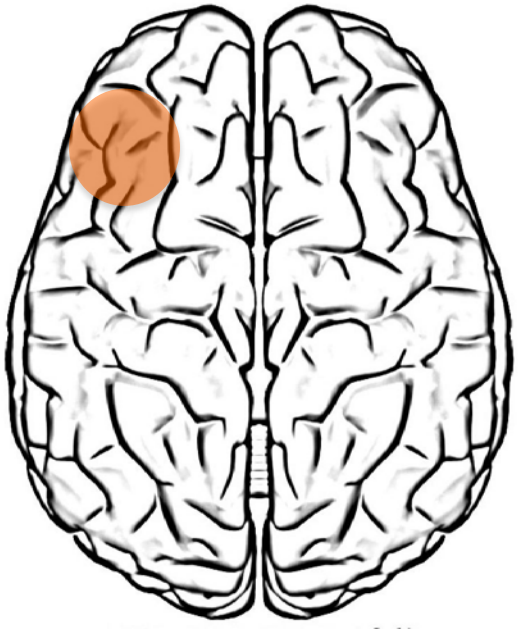
- The N-back working memory task (Fregni et al., 2005)



Enhancement of Working Memory

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





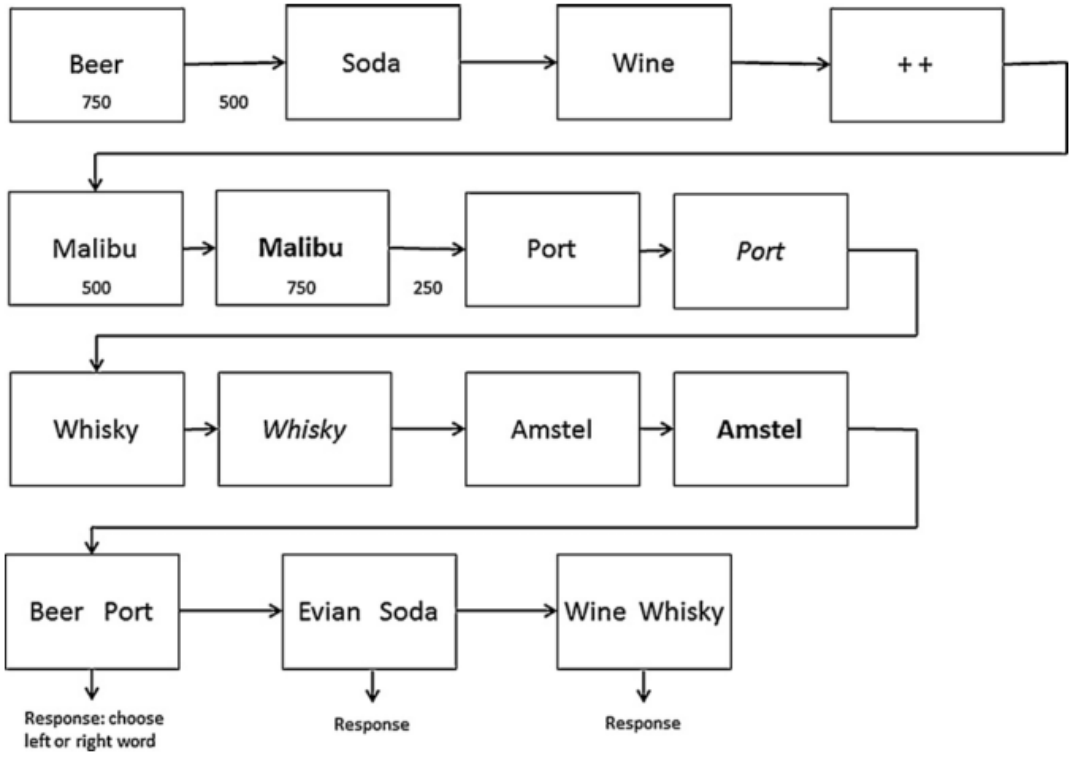
- Anodal tDCS of the left DLPFC, combined with N-back working memory task, enhances digit span (Andrews et al., 2011)
  - Neither tDCS nor N-back testing alone was sufficient

Physiology of Working Memory Enhancement

- Anodal (compared to cathodal) tDCS of the left DLPFC during a 2-back working memory task (Zaehle et al., 2011):
  - Enhanced working memory
  - Increased alpha and theta frequencies
- Alpha and theta frequencies have been linked to working memory (Klimesch et al., 2005)
  - Alpha thought to inhibit non-task relevant areas
  - Theta associated with memory encoding and retrieval

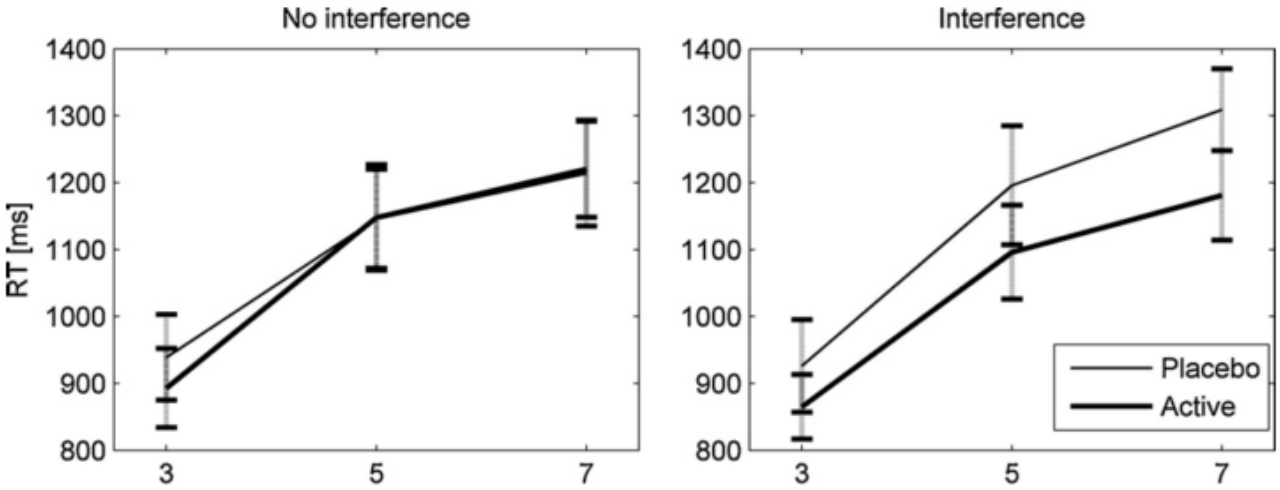
Enhancement of Attention

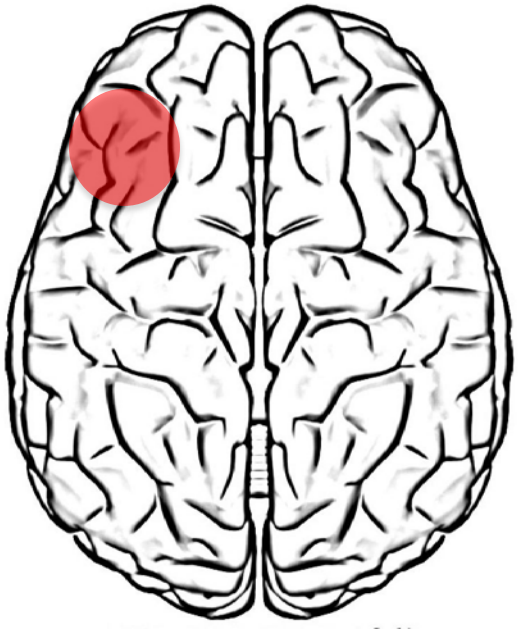
- Executive Attention: Sternberg task (Gladwin et al., 2012)



Enhancement of Attention

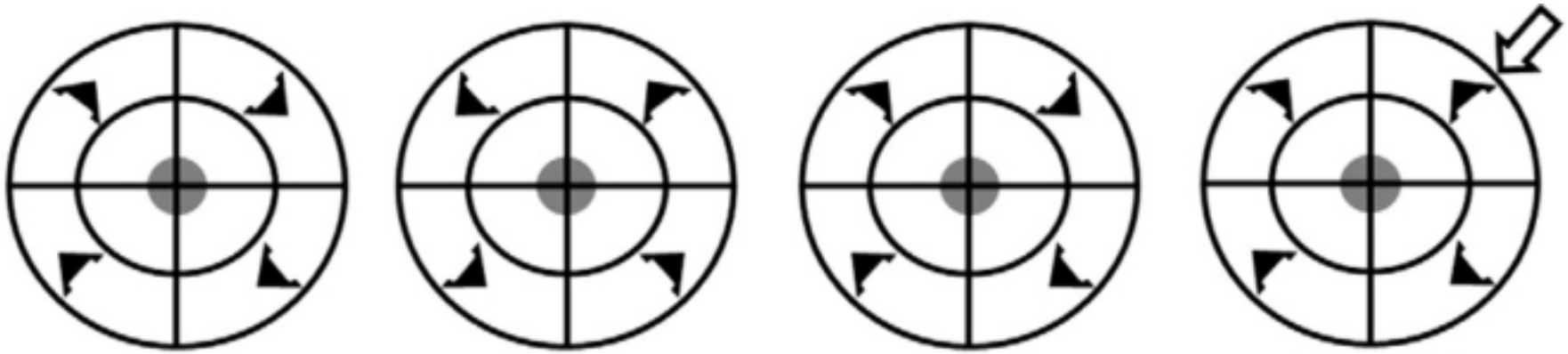
- Anodal tDCS of the left DLPFC improved reaction time on *only on high-interference probes* (Gladwin et al., 2012)





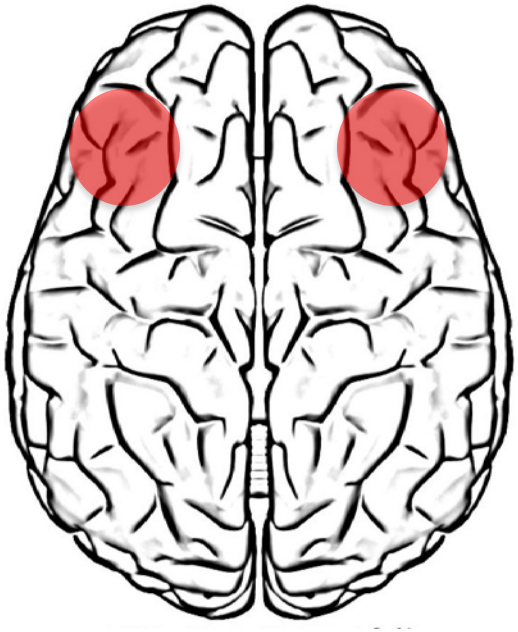
Enhancement of Attention

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



Enhancement of Attention

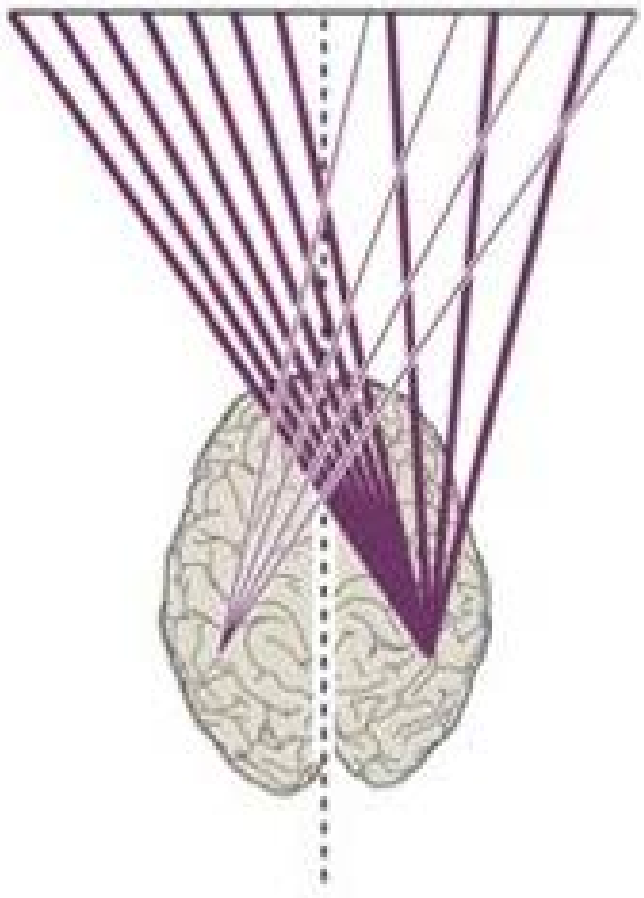
- With sham tDCS, attention decreases over time (Nelson et al., 2014)
  - Lower target detection rate
  - Slower reaction times
  - Reduction in cerebral blood flow velocity
- Anodal tDCS of the DLPFC (left or right) enhances attention
  - Higher target detection rate
  - Maintained blood flow velocity
  - Increased cerebral oxygenation



Enhancement of Attention

- Spatially-Specific Attention Task (Sparing et al., 2009)

Enhancement of Attention



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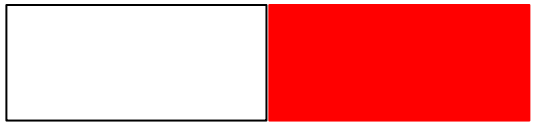
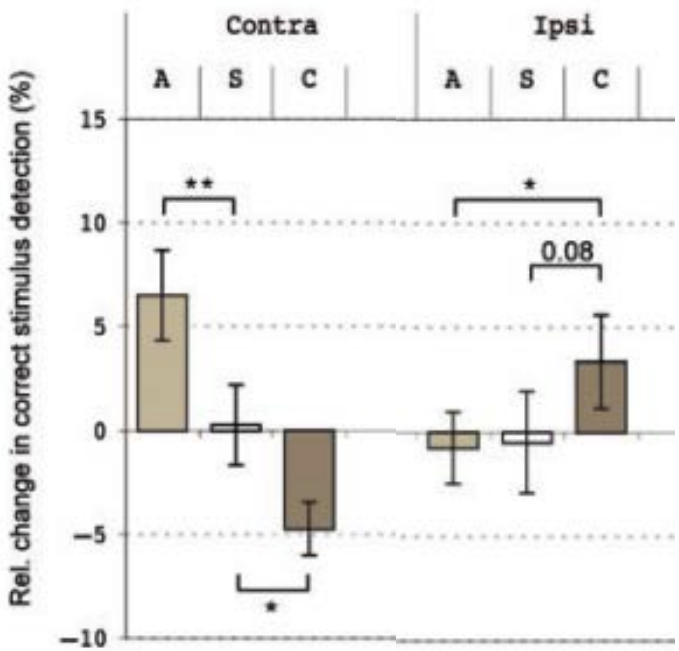
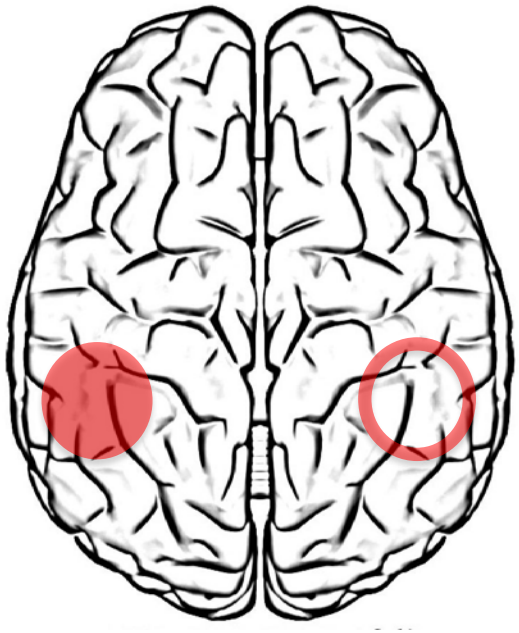
Enhancement of Attention

- Anodal tDCS of parietal cortex enhances visual detection in the contralateral visual field (Sparing et al., 2009)

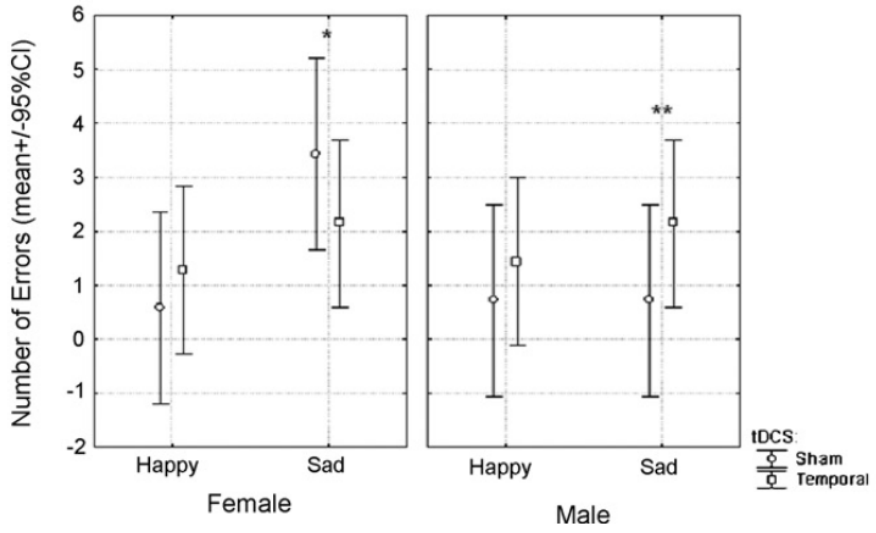


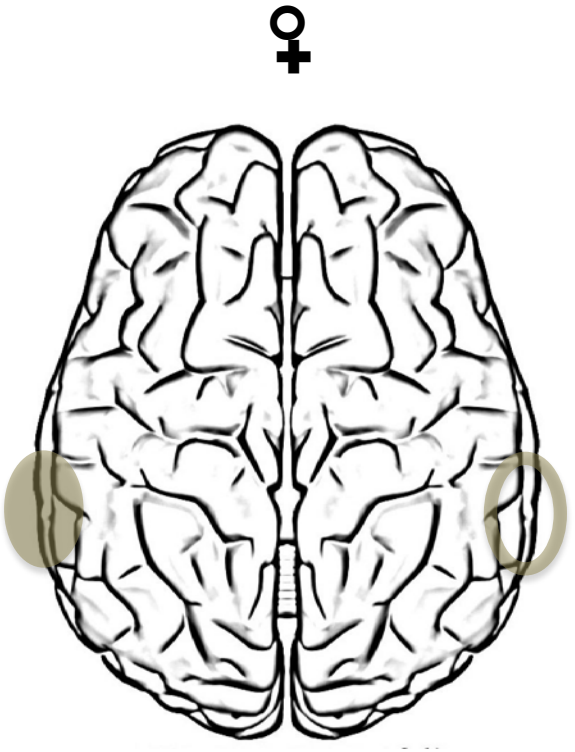




Enhancement of Social Cognition

- Subjects quickly shown a series of happy, sad, or neutral faces
- Asked to identify either happy or sad faces
- Anodal tDCS of the left temporal cortex & cathodal tDCS of the right temporal cortex enhances recognition of sad faces
  - … only in women
  - Impairs recognition of sad faces in men

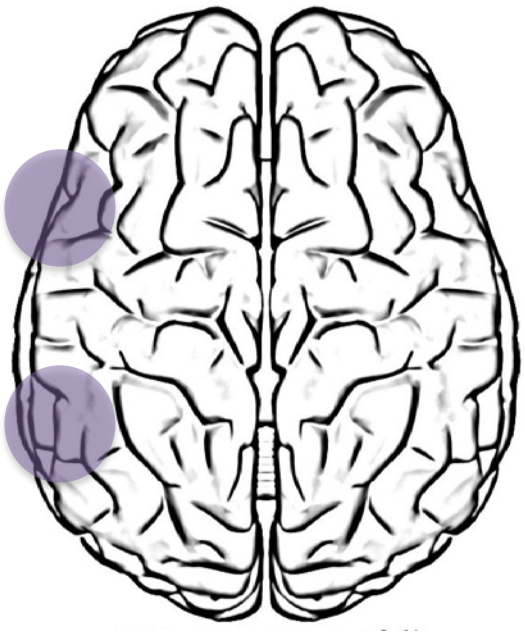




Enhancement of Language

- Anodal tDCS of Broca's area enhances grammatical learning (de Vries et al., 2009)

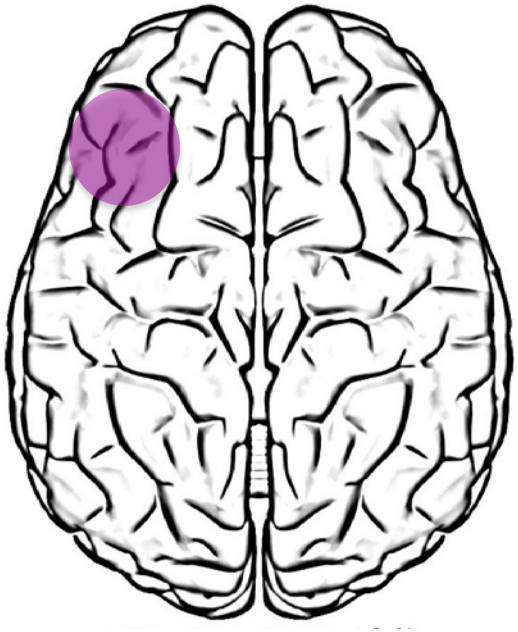
- Anodal tDCS of Wernicke's area enhances lexical learning (Flöel et al., 2008)

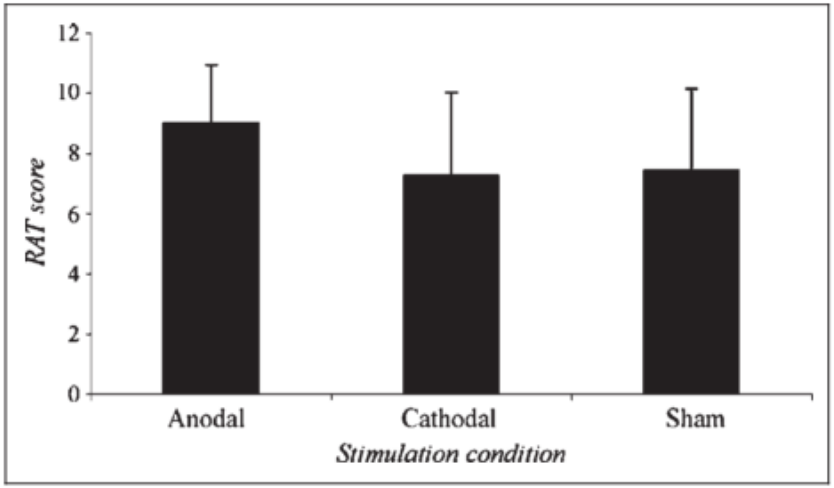


Enhancment of Complex Cognition

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

- Anodal tDCS of the left DLPFC enhances performance





Mood enhancement

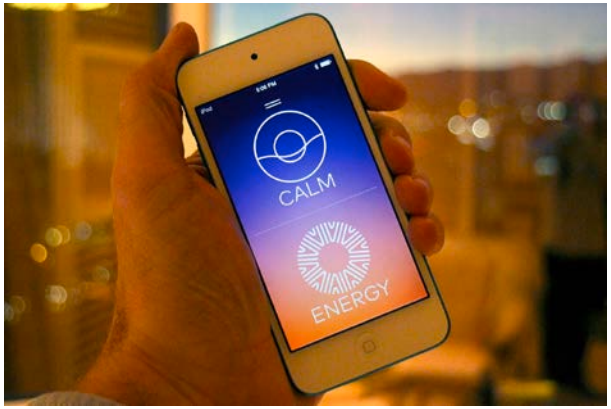
- Observed that tDCS can induce mood changes in healthy subjects
- Marshall et al., (2004) found improvement in mood with anodal tDCS of bilateral DLPFC
- tDCS investigated as treatment for depression
- However, recent placebo-controlled studies have found no mood changes with tDCS, with various positions and polarity (Plazier et al., 2012)

Brit. J. Psychiat. (1964), 110, 768–772

Mental Changes Resulting from the Passage of Small Direct Currents Through the Human Brain

By O. C. J. LIPPOLD and J. W. T. REDFEARN*

http://www.thync.com/



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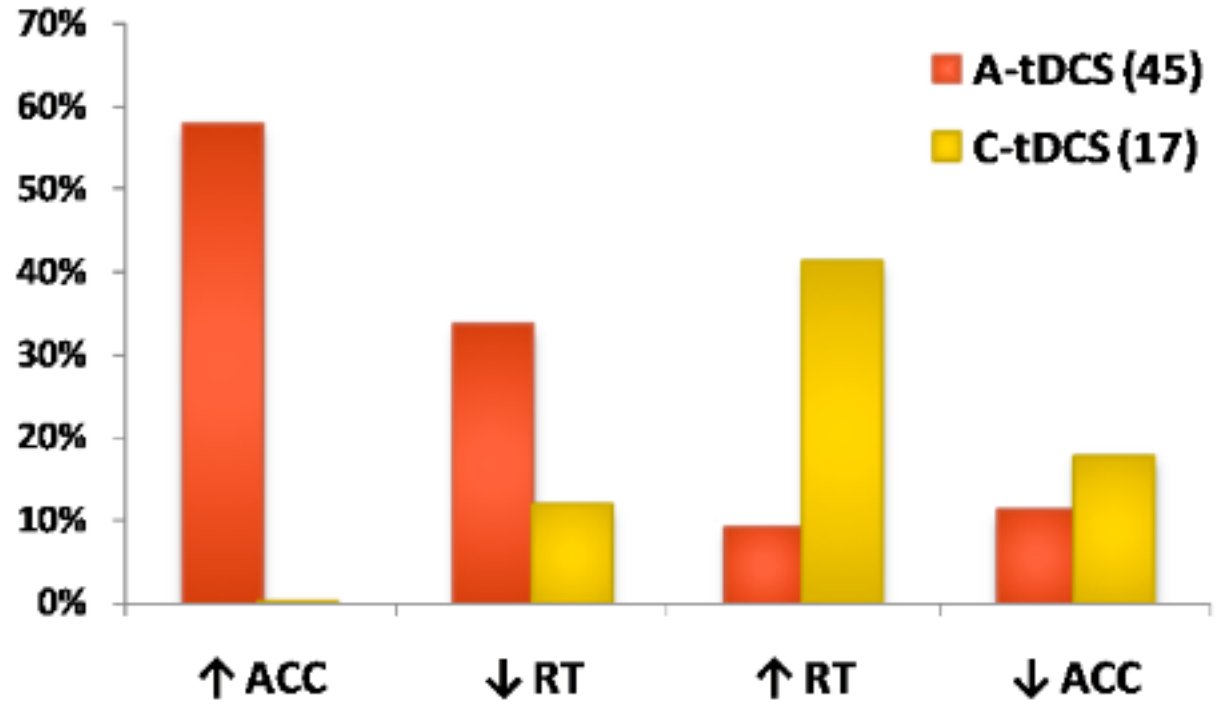
Cognitive Enhancement with tDCS



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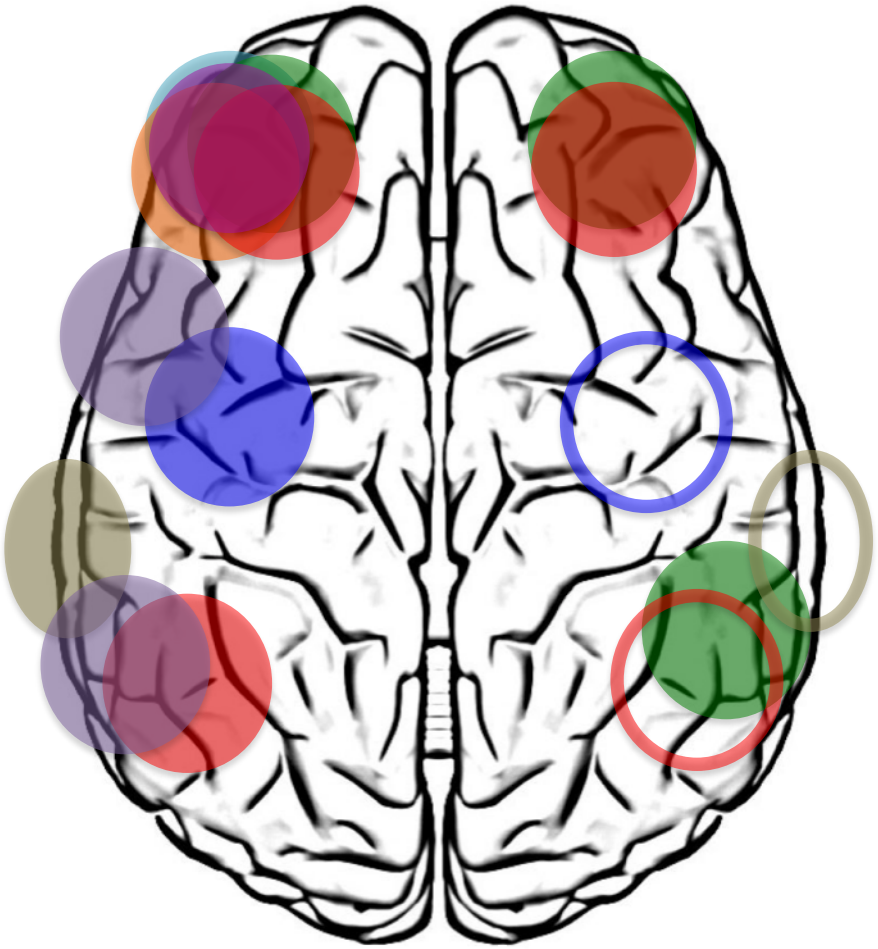
Cognitive Enhancement with tDCS: Stimulation Sites

Motor Learning

Probabalistic Learning

Explicit Learning

Working Memory



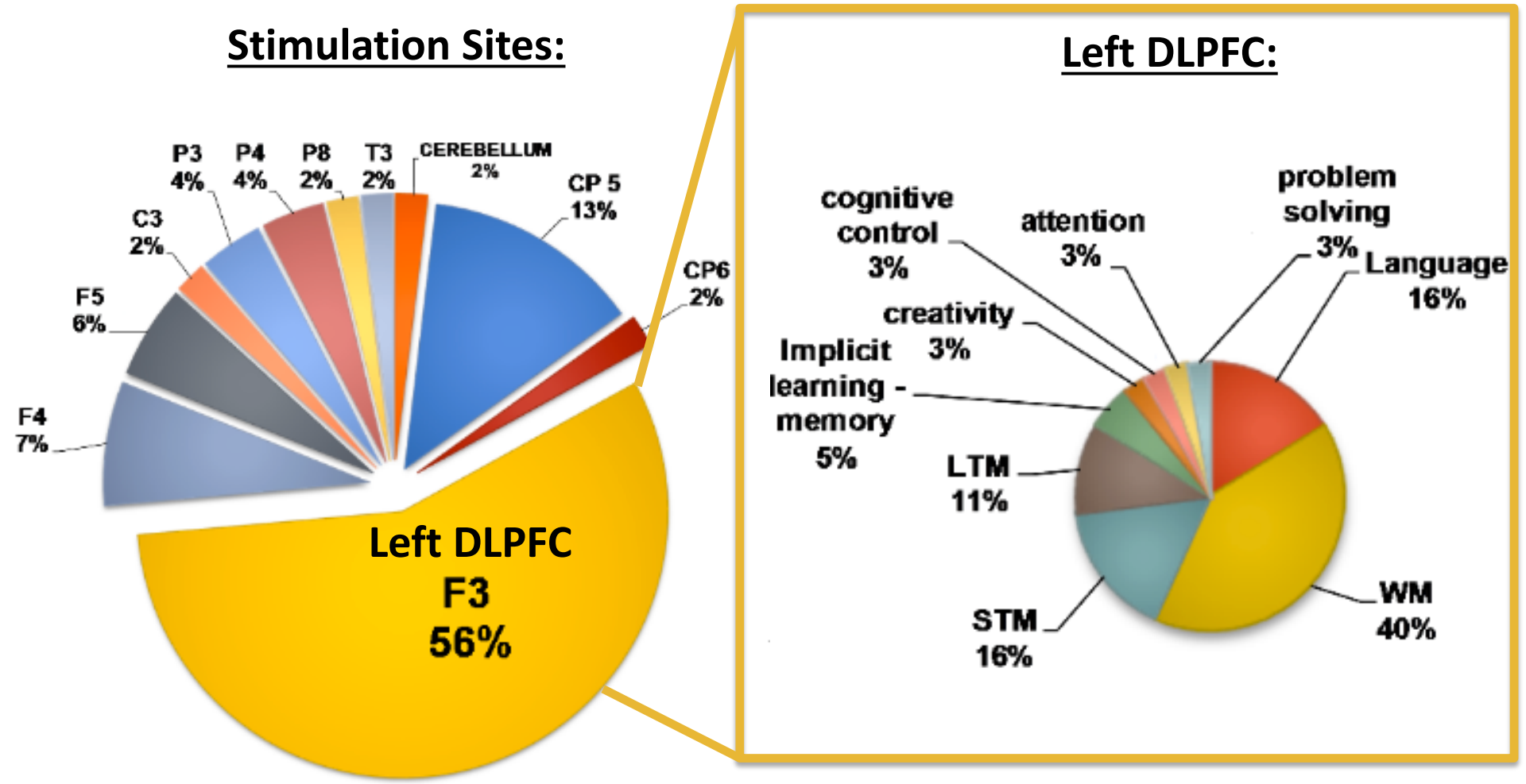
Attention

Social Cognition

Language

Complex Cognition

Cognitive Enhancement with tDCS: Stimulation Sites



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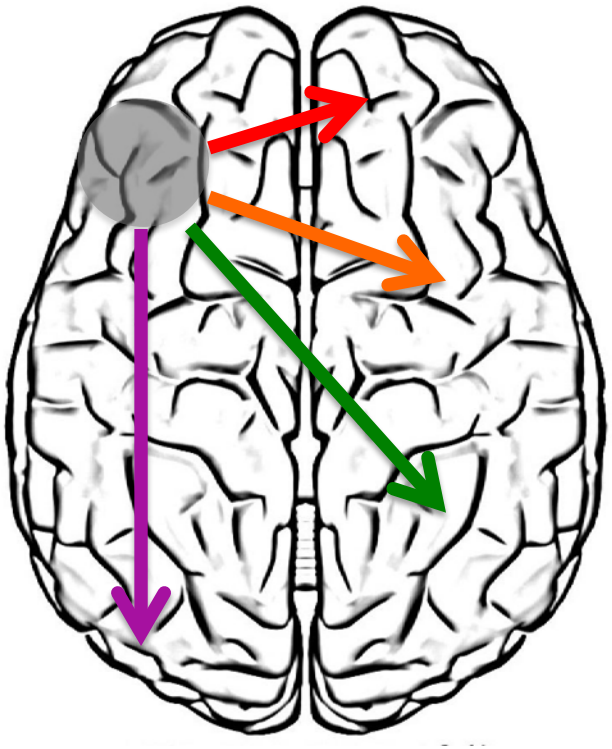
Different Networks?

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



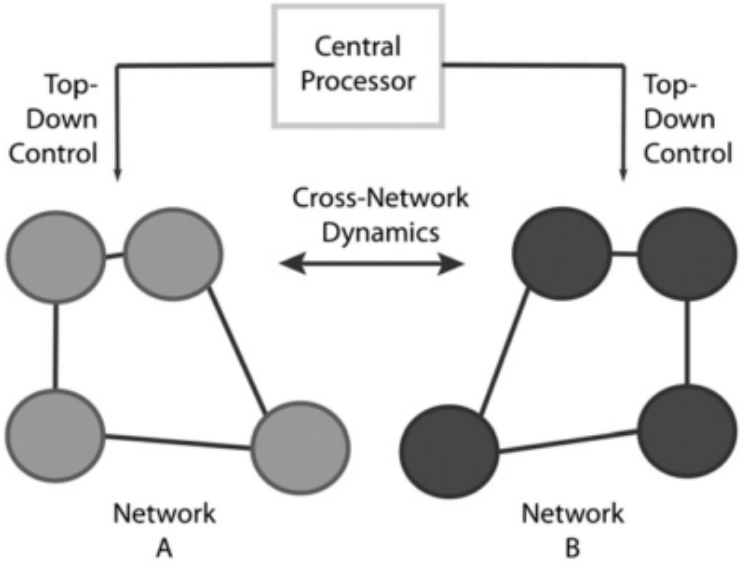
Overlapping Cognitive Skills?

- 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)

Net zero-sum?

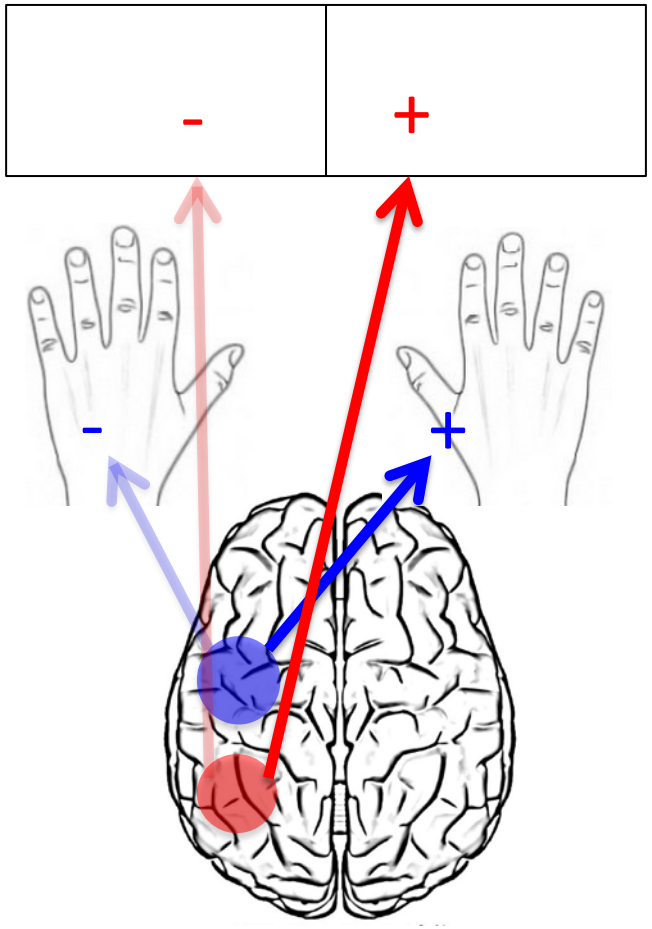
- Net zero-sum derived from notion of conservation of energy
- A gain in function is accompanied by an equal loss of function

- Is brain enhancement a zero-sum game? (Brem et al., 2014)
  - Distribution of processing power
  - Trade-offs



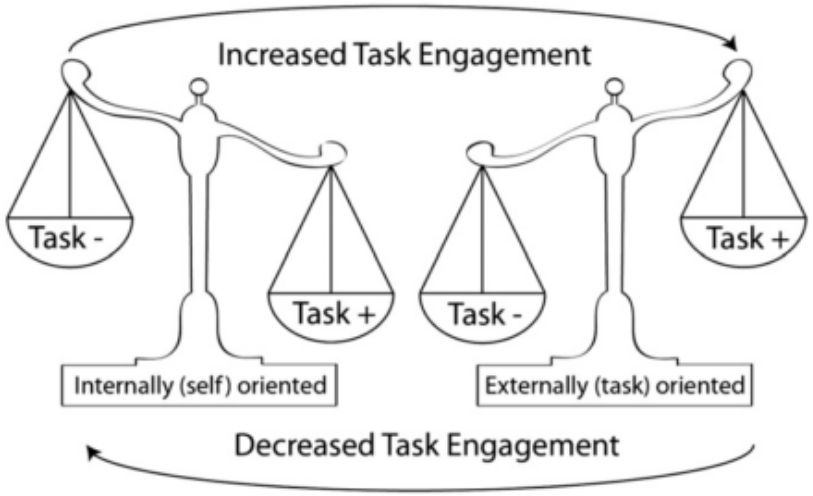
Evidence for Zero-Sum

- Inter-hemispheric inhibition
  - Motor Learning
  - Attention
- Anodal tDCS increases tNAA locally, but decreases tNAA in the opposite hemisphere (Clark et al., 2011)



Evidence for Zero-Sum

- Enhancement of social cognition in women, but impairment in men
- In a study of numerical learning (Iuculano & Cohen Kadosh, 2013):
  - tDCS of the DLPFC enhanced automaticity, but impaired numerical learning
  - tDCS of the posterior parietal cortex enhances numerical learning, but impairs automaticity
- Negatively correlated networks (Brem et al., 2014; Fox et al., 2005)



Controversy about efficacy

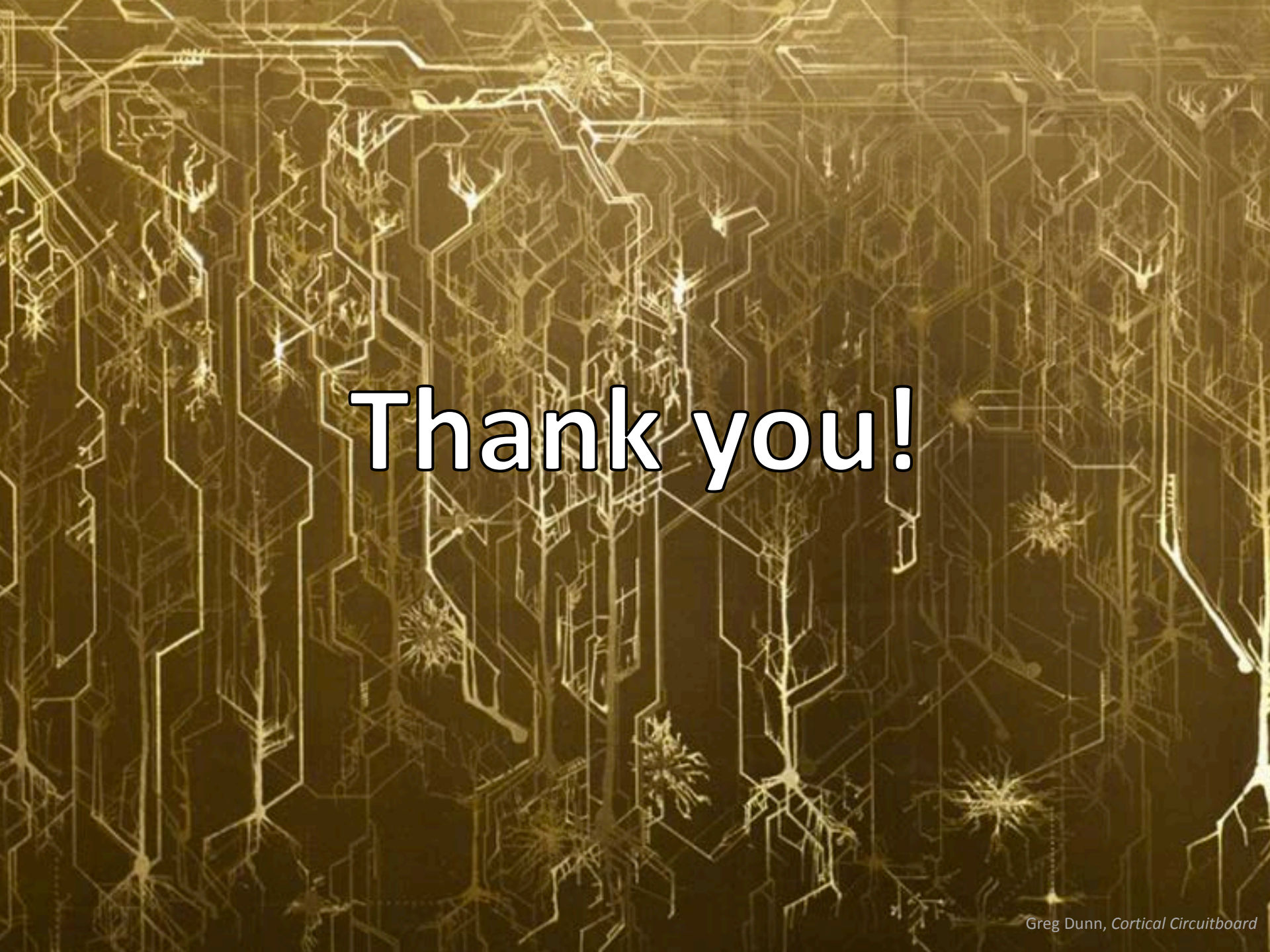
- Meta-analysis of cognitive effects of tDCS (Horvath et al., 2015)
  - Included every study of the cognitive effects of tDCS among healthy adults
  - Cognitive tasks must be used by 2 or more groups
  - Included only studies of single session tDCS
  - Spanned executive function, memory, language, and other
  - No significant effects of any

Controversy about efficacy

- Of the 50 cognitive tasks replicated by 2 or more research groups, 35 include 2-3 papers
- Significant effects may exist for multiple-day tDCS regimens
  - E.g., overnight consolidation
- State-dependency?

Overview

- Evidence that tDCS can enhance:
  - Learning
  - Working memory
  - Attention
  - Language
  - Social Cognition
  - Complex problem-solving
- Enhancing consolidation of memories
- Mechanisms may involve glutamatergic signaling, and EEG frequencies
- State dependency of enhancement
- Involvement of diverse networks vs. overlapping cognitive functions
- Net zero-sum
  - Inter-hemispheric inhibition
  - Different populations
- Conflicting findings
- Ethical considerations


Thank you!
Greg Dunn, *Cortical Circuitboard*

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