Some Ongoing tDCS Studies

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Driven to Discover[SM]

Disclosures

None

Outline

- Motivation
- Approach
- Study 1: tDCS Augmentation for Cognitive Remediation in Schizophrenia
- Study 2: Reducing Impulsivity in a Clinical Population

Motivation

- For many psychiatric disorders, our treatments fall short
- Need new treatment approaches
- Can we tap into brain plasticity to change behavior?

Approach

- Use tDCS as tool for inducing brain plasticity
- Primary therapy or augmentation?
- tDCS has coarse spatial targeting
- How to gain greater specificity?
- Hebbian theory – "cells that fire together, wire together"
- Use task related to targeted behavior to gain circuit specificity
- Strengthen that circuit and the associated behavior
- Check generalization by measuring an untrained task

Symptoms of Schizophrenia

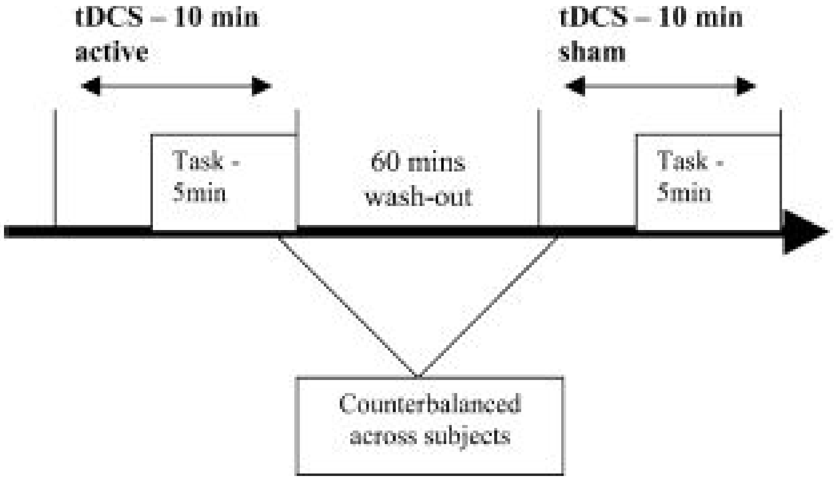
- Positive symptoms
  - Hallucinations
- Negative symptoms
  - Apathy, avolition, flattening of affect, alogia
- Cognitive symptoms
  - Attention
  - Working memory

Working Memory Impairment in Schizophrenia

- Major contributor to functional disability
- Medications not effective
- Cognitive Remediation
  - behavioral training intervention with intensive practice of a cognitive skill
  - Often do many weeks of training
  - Training effect sizes are small to moderate
  - Generalization to untrained tasks inconsistent
- Can we enhance cognitive remediation with tDCS?
  - Improve the learning of the selected task
  - Improve generalization to untrained task

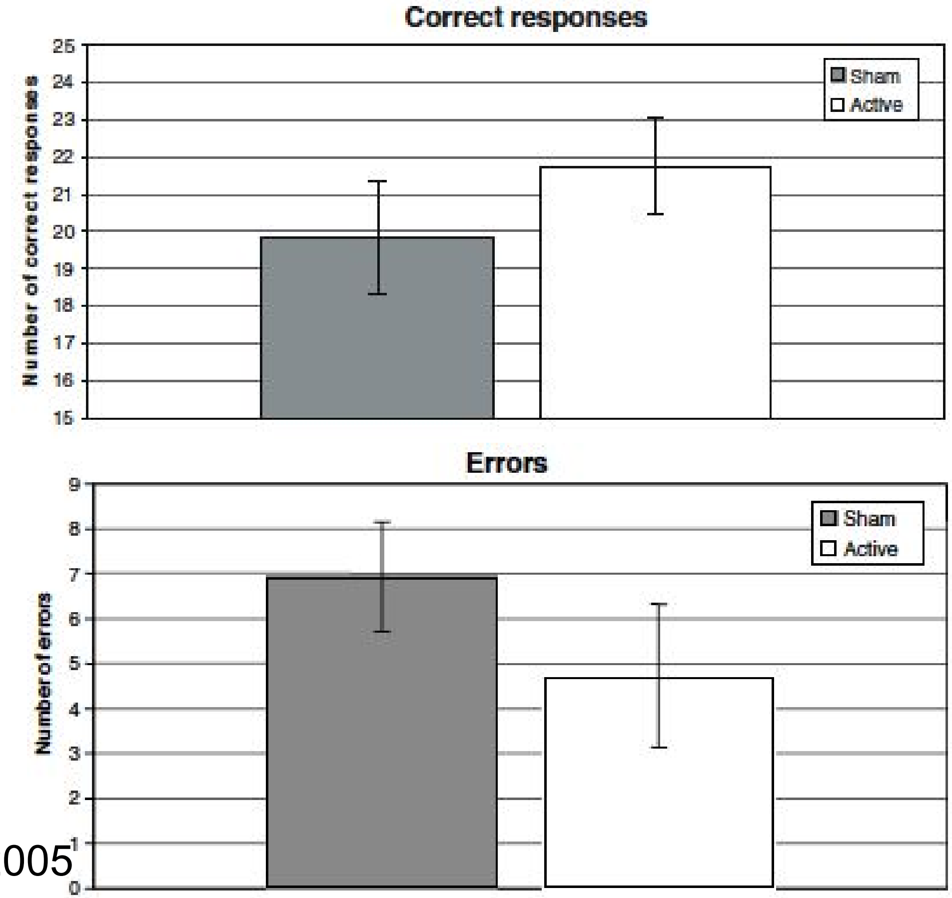
tDCS in Working Memory

- 15 healthy subjects
- 3-back working memory task
- Active (anode left DLPFC) and Sham in same subjects



Pascual-Leone
et al., 2005

tDCS enhancement of working memory



p = .0042

p = .015

Pascual-Leone et al., 2005

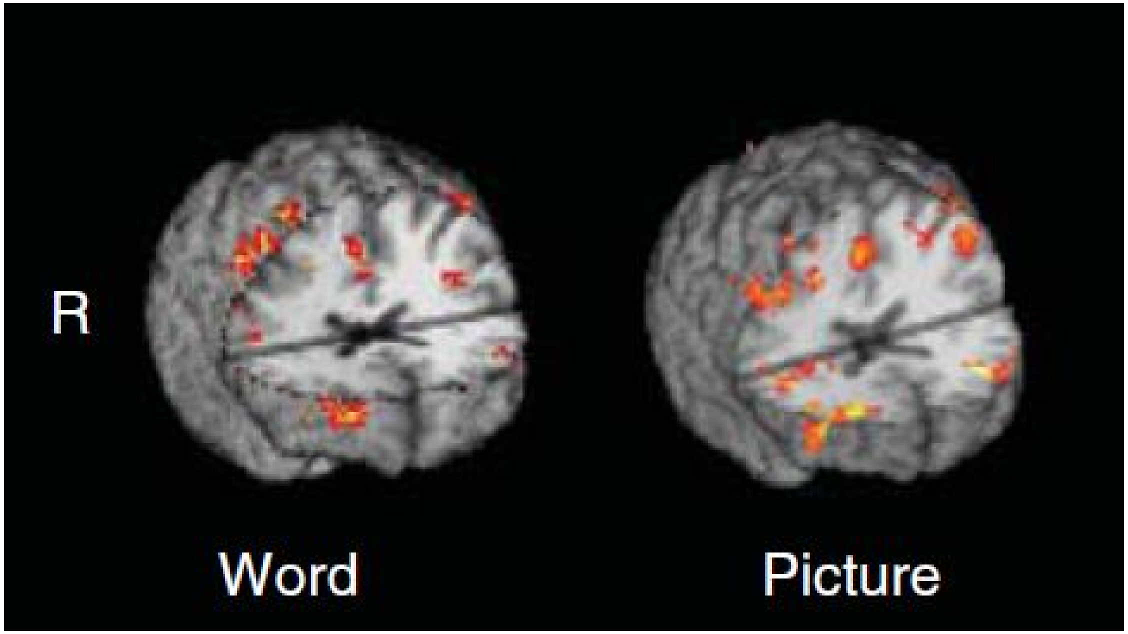
Study Design

- Sample: Outpatients, Schizophrenia/Schizoaffective Disorder
  - Participants were clinically stable at study entry and did not have any hospitalizations or antipsychotic medication changes in the 4 weeks prior to study enrollment
  - Participants were recruited from the Minneapolis VA Health Care System and surrounding community support programs
  - Participants were between the ages of 40-70 and did not have any medical conditions that would make them incompatible with neuromodulation
- Randomization and Blinds
  - Participants randomized to cognitive training with either active transcranial direct current stimulation or sham
  - Participants blind to their assignment
  - Technicians who completed the outcome assessments were blind to group membership

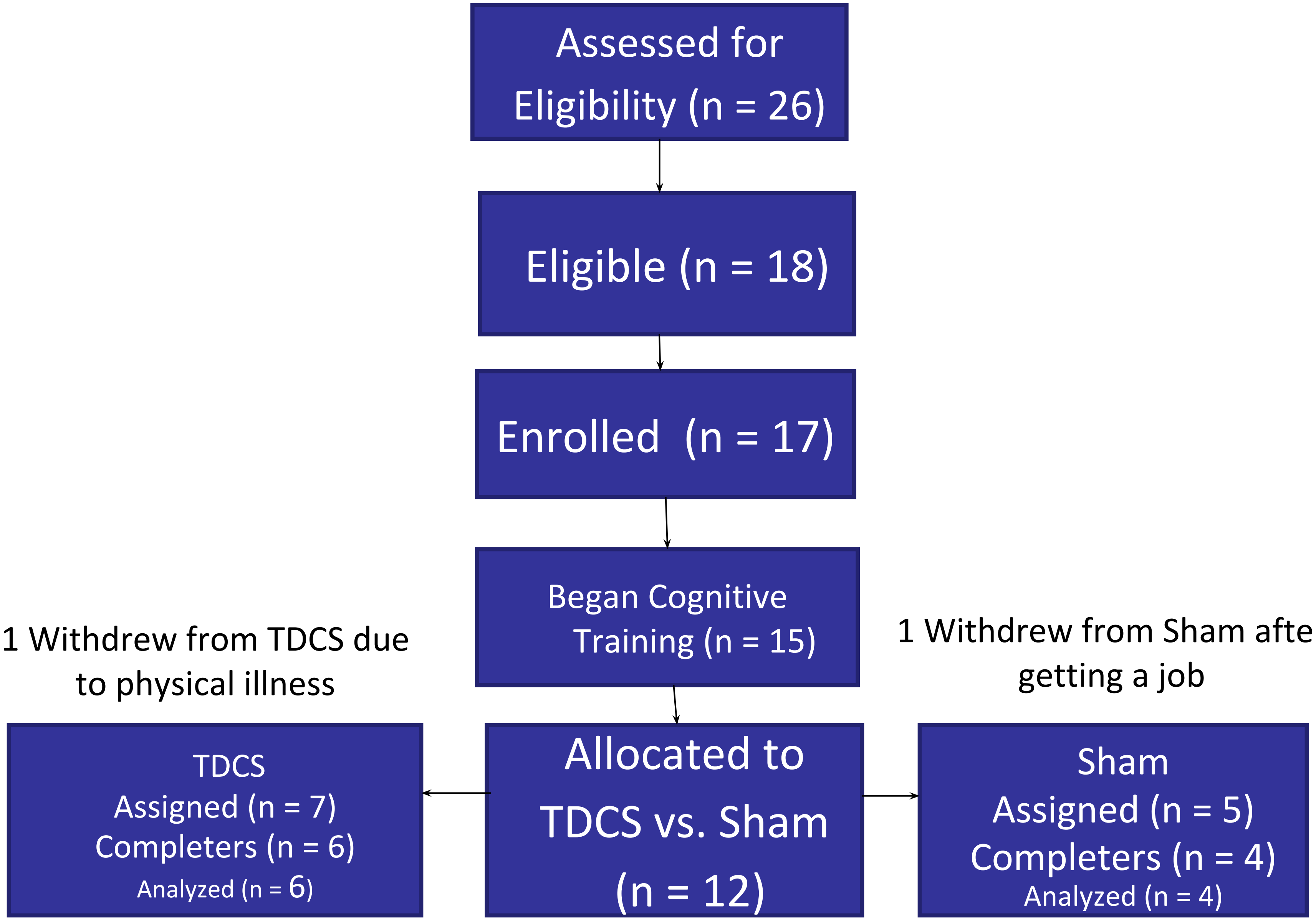
Study Design

- Working Memory Training
  - 16 week program; 3 hours/week; tDCS (active/sham) administered twice a week starting third week
  - Participants completed 5 training activities within a 60-minute session
  - Tasks required attentional control, temporary maintenance of information, manipulation of temporarily stored information, and strategic recall
  - Tasks were adaptive and required use of working memory with verbal, visual, and spatial stimuli
- tDCS Administration
  - Anodal electrode (5x7 cm^2) placed over F3 and cathodal electrode over the contralateral supraorbital position
  - 1 mA of stimulation administered concurrent with first 20 minutes of cognitive training (Soterix)

Increased prefrontal activity for CogRem for 2-back in Subjects with Schizophrenia



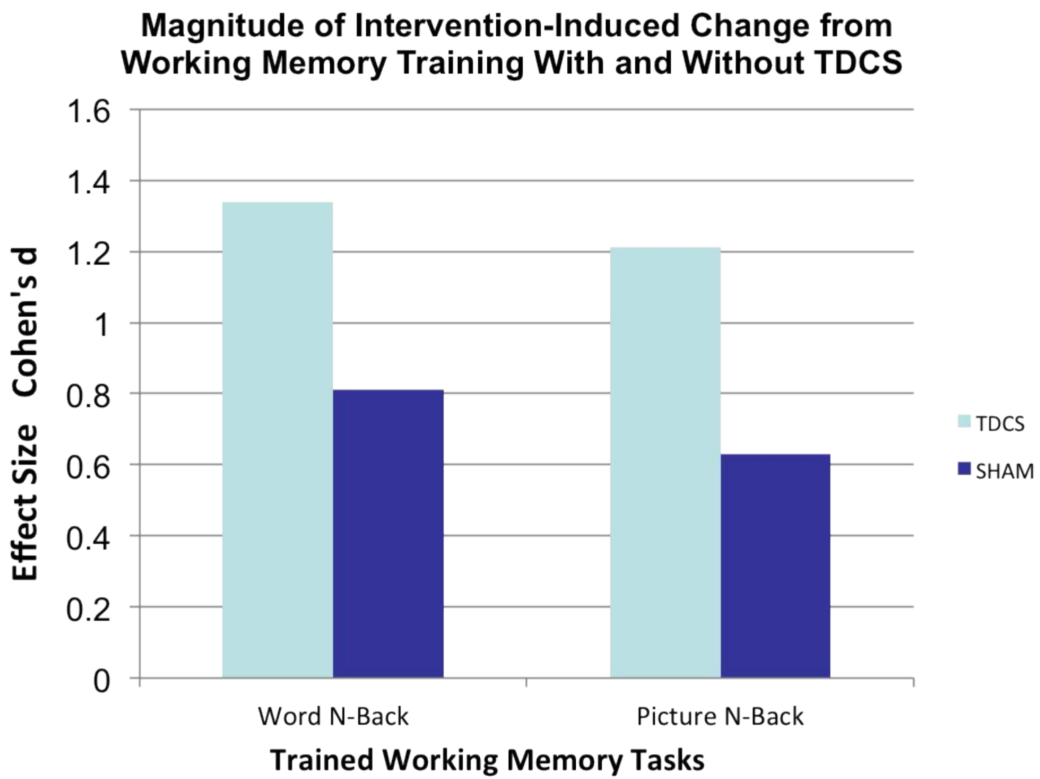
Haut, Lim, MacDonald, Neuropsychpharmacology, 2010


Assessed for Eligibility (n = 26)
Eligible (n = 18)
Enrolled (n = 17)
Began Cognitive Training (n = 15)
1 Withdrew from TDCS due to physical illness
1 Withdrew from Sham after getting a job
Allocated to TDCS vs. Sham (n = 12)
TDCS
Assigned (n = 7)
Completers (n = 6)
Analyzed (n = 6)
Sham
Assigned (n = 5)
Completers (n = 4)
Analyzed (n = 4)

Sample Demographic and Clinical Characteristics

	TDCS (n = 6)		Sham (n = 4)		
Demographic	M	SD	M	SD	p
Gender % Male	50%		75%		
Age	61.50	5.99	61.00	2.83	.88
Education (Yrs)	14.17	3.25	12.5	3.42	.46
Parental Ed (Yrs)	12.67	3.08	12.63	.95	.98
Baseline Word N-Back	1.57	1.16	1.34	1.15	.77
BPRS Total	38.33	8.17	48.5	15.59	.21
Age of Illness Onset	25.67	7.17	28.25	7.5	.60
Length of Illness (Yrs)	36.83	9.97	32.75	6.13	.50
CPZ Total	741.50	549.26	756.25	575.32	.97

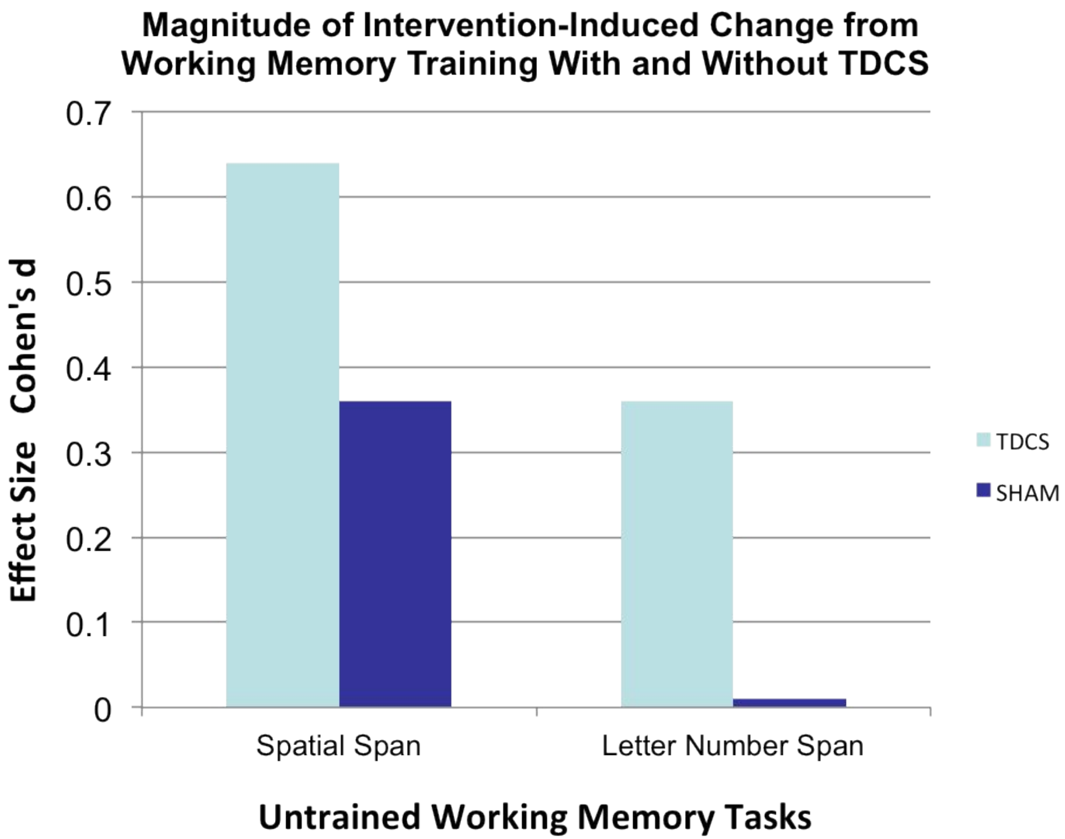
Outcomes: Training Tasks



Patients (n = 6) receiving TDCS showed greater change on training tasks compared to those receiving sham (n = 4).

Nienow, MacDonald, & Lim, Schiz Res, 2016

Outcomes: Untrained Tasks



Patients (n = 6) receiving TDCS demonstrated greater change on untrained tasks compared to those receiving sham (n = 4).

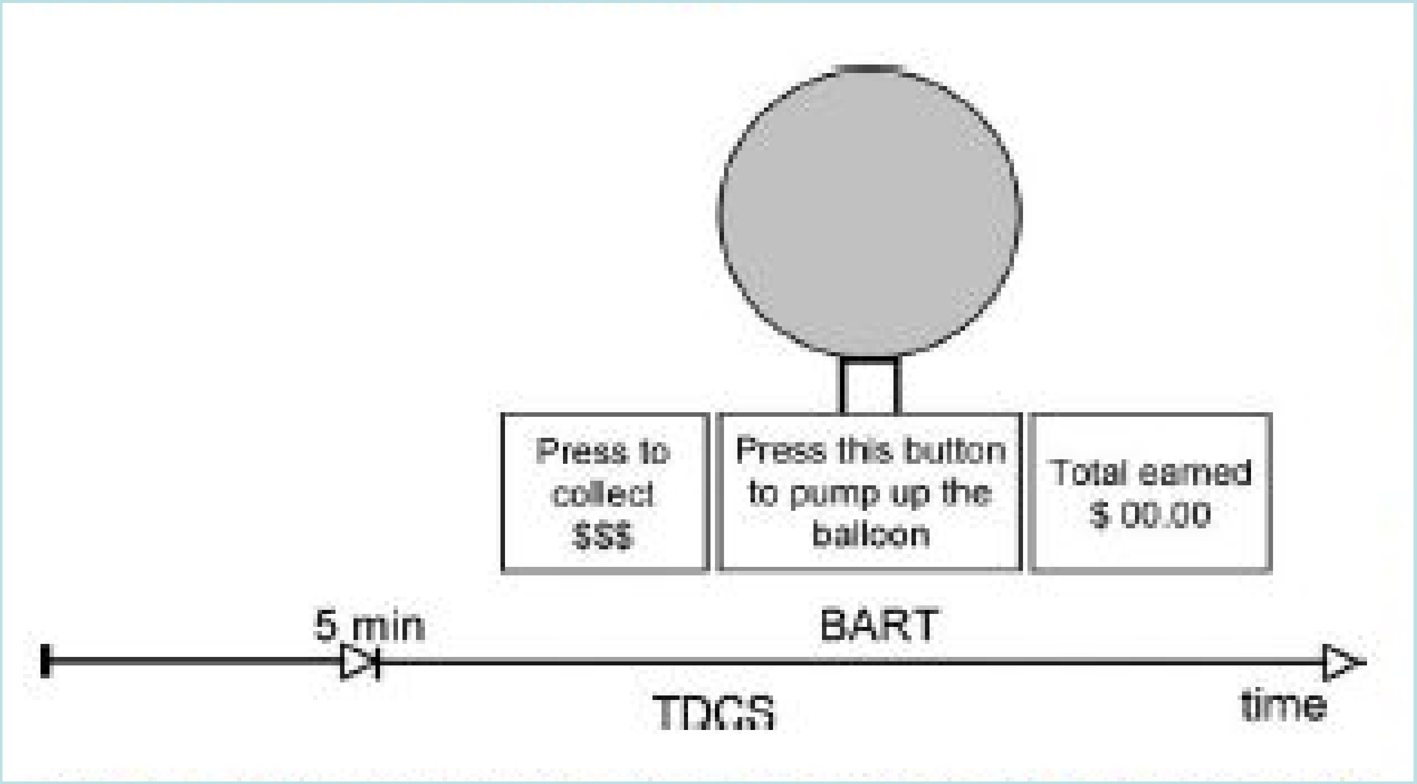
Nienow, MacDonald, & Lim, Schiz Res, 2016

Nienow, MacDonald, & Kim, unpublished

Impulsivity

- Major clinical challenge that crosses many diagnoses including substance use, TBI, etc.
- No effective treatments available
- Can we reduce instrumented measures of impulsivity by combining tDCS with a task?

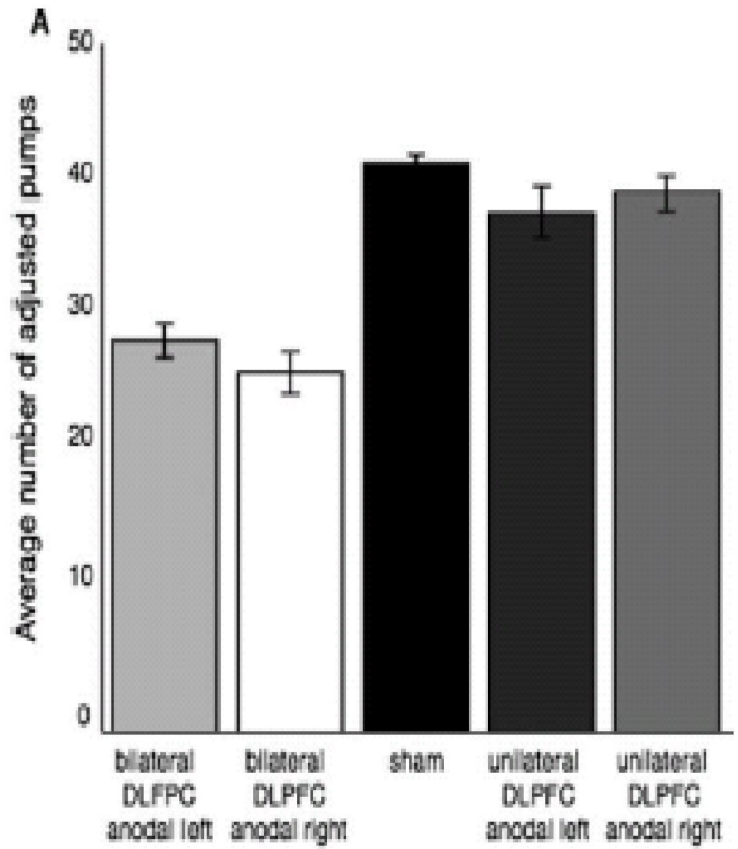
Ambiguous Risk Task (BART) with tDCS



Fecteau et al., JNeurosci, 2007

Ambiguous Risk

32%



Fecteau et al., JNeurosci, 2007

Subjects

- Subjects with impulsivity clinically referred
- N=16 (8 active tDCS: 1 female; 8 sham tDCS: 1 female)
- Mean age:
  – Active = 57.9 (5.2) years,
  – Sham = 59.1 (7.5) years
  – $t(14)=.39$, $p>.05$

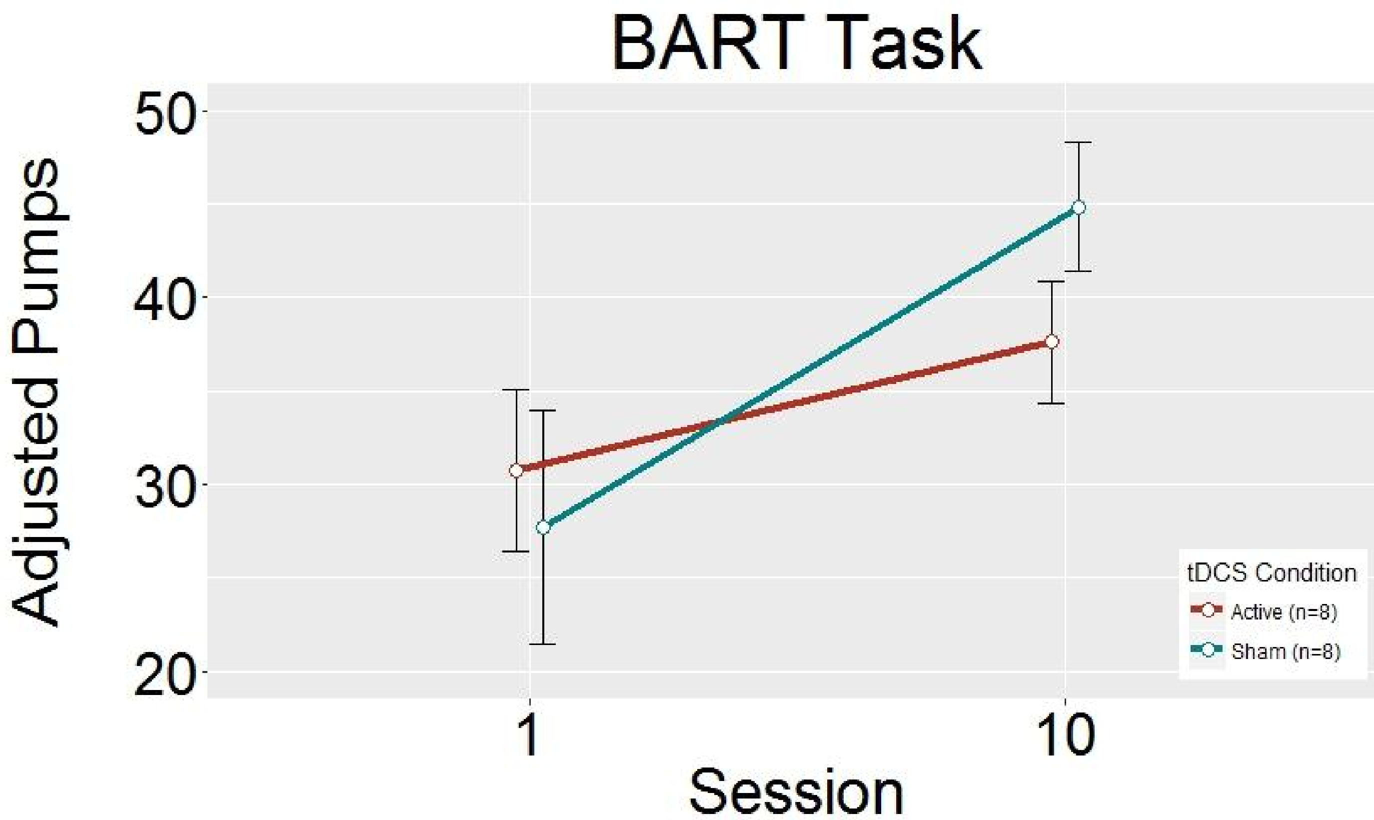
Procedures

- Subjects randomly assigned to receive either active tDCS or sham stimulation Only subject blinded
- Two 20 minute sessions per day (2 hour separation) for 5 days
- Subjects perform the BART task during stimulation period (training)
- Risk task used to assess generalization

tDCS Parameters

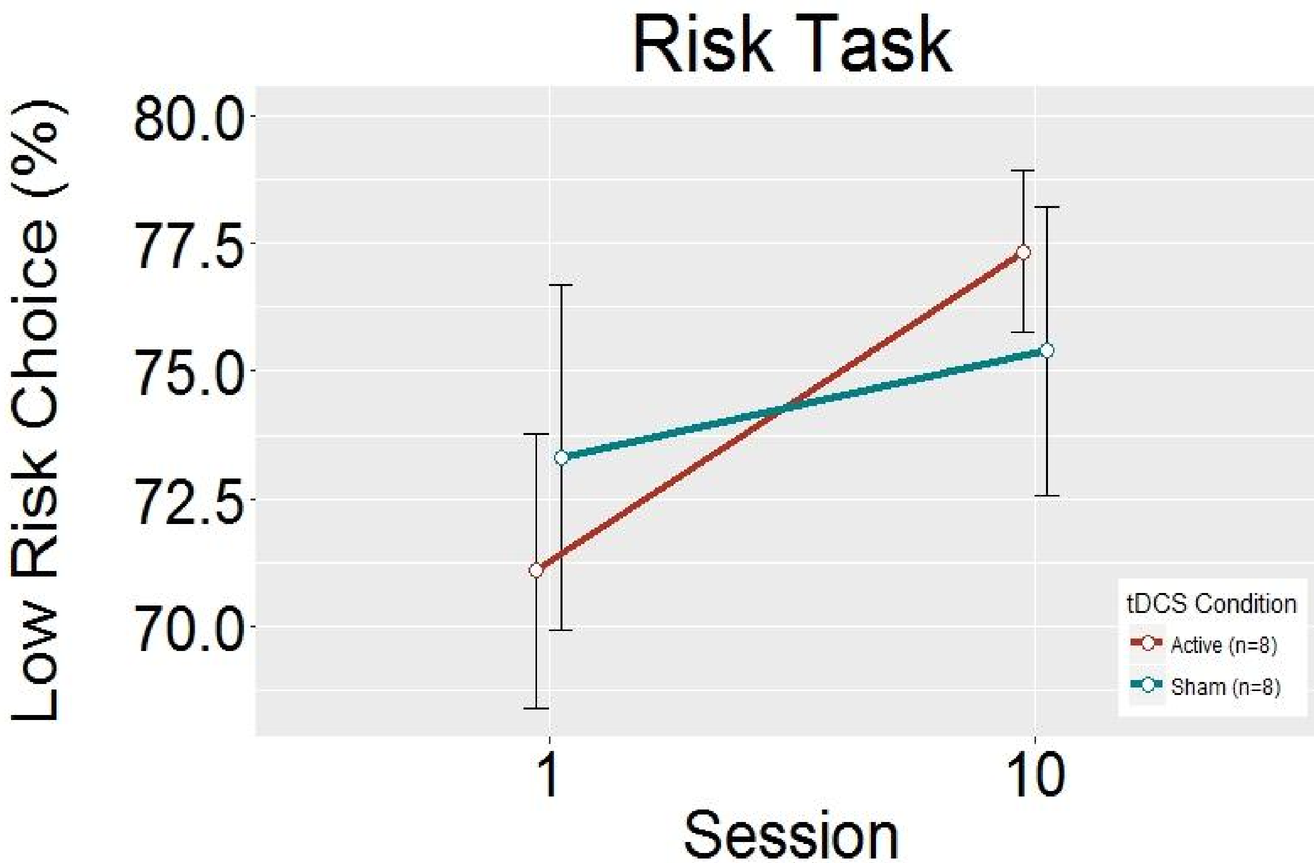
- Neuroelectrics Starstim system
- Two 25 cm^2 saline soaked electrode sponges
- Right anodal (electrode at F4), left cathodal (electrode at F3)
- 2 mA current applied for 20 minutes
- 30 sec ramp up and ramp down
- Sham: Current ramps up, then immediately back down at the beginning and end of stimulation

Trained Task



Within group paired sample t-tests comparing Sessions 1 and 10:
Active group: $t(7)=.99$, $p>.05$, $d=.49$
Sham group: $t(7)=2.51$, $p=.04$, $d=.92$

Untrained Task



Within group paired sample t-tests comparing Sessions 1 and 10:
Active group: t(7)=2.5, p=.04, d=.39
Sham group: t(7)=0.66, p>.05, d=.12

Acknowledgements

- People
  - Tasha Nienow, Ph.D.
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Takeaways

- tDCS well tolerated in clinical populations
- Some effect on learning
- May enhance generalization
- Works in older persons

Issues

- tDCS Montage
- Selection of training tasks
- Dosing
- Matching of above
- Durability
- Enhanced hardware for support of trials
- Optimization for each individual