Some Ongoing tDCS Studies

Kelvin O. Lim, M.D.
Drs. T.J. and Ella M. Arneson Endowed Chair
Professor and Vice Chair for Research
Department of Psychiatry
and
Minneapolis VA Medical Center
kolim@umn.edu
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
tDPS enhancement of working memory

Pascual-Leone et al., 2005

\[ p = .0042 \]

\[ p = .015 \]
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 cm²) 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
Enrolled (n = 17)
Began Cognitive Training (n = 15)
Allocated to TDCS vs. Sham (n = 12)

Assessed for Eligibility (n = 26)
Eligible (n = 18)

1 Withdrawn from TDCS due to physical illness

TDCS Assigned (n = 7)
Completers (n = 6)
Analyzed (n = 6)

1 Withdrawn from Sham after getting a job

Sham Assigned (n = 5)
Completers (n = 4)
Analyzed (n = 4)
# Sample Demographic and Clinical Characteristics

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

Fecteau et al., JNeurosci, 2007

32%
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 $25 \, \text{cm}^2$ 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: $t(7)=2.51$, $p=.04$, $d=.92$
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