Mismatch Negativity and P300: Biomarkers of Target Engagement for Transcranial Direct Current Stimulation in Schizophrenia

Walter Dunn1, Yuri Rasovskyy2, Jonathan Wyner3, Allan D. Wej2, Marco Iacoboni2, Gerhard Helleman2, Michael F. Green4

1. Department of Psychiatry, Menninger Clinic, Topeka, KS, USA
2. Ahmanson-Lovelace Brain Mapping Center, University of California, Los Angeles, CA, USA
3. Department of Psychiatry and Behavioral Sciences, UCLA School of Medicine for Transcience and Human Behavior, Los Angeles, CA, USA
4. Department of Neurology, University of California, Los Angeles, CA, USA

Introduction

Schizophrenia is an illness characterized by deficits in attention, executive functioning, and social cognition. Treatment options are limited and many patients fail to respond adequately to available therapies. Developing new targets and adjunctive treatments to those that have been shown to be effective may help achieve better outcomes for this illness. In animal models, transcranial direct current stimulation (tDCS) can modulate neurotransmitter levels and may target auditory processing dysfunction in schizophrenia. Potential targets include the prefrontal cortex, thalamus, and auditory processing circuitry.

Subjects pay attention to a series of standard tones and signal when a deviant tone is heard. Two groups of participants were assigned to one of 3 conditions: anodal, cathodal, or sham stimulation.

Materials and Methods

Subjects:
- 12 participants assigned to one of 3 groups: anodal, cathodal, sham
- Patients:
  - Illness duration (years): 19.8 ± 13.8
  - Duration of education (years): 13.5 ± 2.98
  - Parental education (years): 19.8 ± 13.8
- Gender: 6 males, 6 females
- Age: 24.8 ± 10.9
- BPRS: Brief Psychiatric Rating Scale; SANS: Scale for the Assessment of Negative Symptoms; SAPP: Scale for the Assessment of Positive Symptoms

Screening

EEG Results

Mismatch Negativity

Mean MMN amplitude at baseline and post-tDCS; changes in amplitude not significant (p=0.08).

Table 1: Mismatch Negativity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mean MMN Amplitude (µV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>4.91 ± 3.68</td>
</tr>
<tr>
<td>Cathodal</td>
<td>7.91 ± 2.95</td>
</tr>
<tr>
<td>Anodal</td>
<td>6.04 ± 3.04</td>
</tr>
</tbody>
</table>

P300 Results

Mean P300 amplitude at baseline and post-tDCS; changes in amplitude not statistically significant (p=0.05).

Table 2: P300 Results

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mean P300 Amplitude (µV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>0.42 ± 1.04</td>
</tr>
<tr>
<td>Cathodal</td>
<td>-1.41 ± 0.62</td>
</tr>
<tr>
<td>Anodal</td>
<td>2.10 ± 0.57</td>
</tr>
</tbody>
</table>

Future Directions

Direct Current Stimulation in Schizophrenia

Transcranial direct current stimulation (tDCS) in the prefrontal cortex could modulate auditory processing dysfunction in schizophrenia. If replicated, this suggests that MMN could serve as a biomarker of target engagement for tDCS treatment of auditory processing deficits in schizophrenia as MMN reflects an early stage process (pre-attentional) in the pathway of auditory processing.

Acknowledgements

NARSAD Independent Investigator Award to Yuri Rasovsky

Funding provided by VA VISN 23 MERIT

References