Neurostimulation techniques including rTMS, tDCS, and tACS for treating auditory hallucination in schizophrenia: a systematic review

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Introduction

- Schizophrenia is a chronic, debilitating psychiatric illness that distorts affect, thought, and perception. It has a lifetime prevalence of 0.3-0.5%.
- According to the 2017 Canadian Schizophrenia Guidelines, antipsychotic medications are the first line treatment; however, 25-30% of patients have medication-refractory psychosis.
- Clozapine is recommended for such patients, but the question still remains whether this is the best treatment option available.
- Neurostimulation has emerged in recent years as a potential treatment alternative.
- In this review, we examine 3 techniques: rTMS, tDCS, and tACS.

Methods

- PsychINFO was searched from inception to March 10, 2020.
- The following search terms and their synonyms were used: schizophrenia, hallucination, neurostimulation, neuromodulation, rTMS, repetitive transcranial magnetic stimulation, tDCS, transcranial direct current stimulation, tACS, transcranial alternating current stimulation
- Inclusion criteria:
  - Randomized, sham-controlled trials that use DSM-IV or DSM-5 criteria for schizophrenia in adult patients
  - Outcomes must include positive symptoms of psychosis (e.g., delusions and hallucinations)
  - Must use outcome scale that measures auditory hallucinations
  - Studies must also specify which areas of the brain were stimulated and how the control groups were stimulated while blind
  - Published in English
- Exclusion criteria:
  - Systematic reviews, meta-analyses, case reports, editorials, and letters to the editor

Results

<table>
<thead>
<tr>
<th>Source</th>
<th>Brain area stimulated</th>
<th>Active rTMS parameters</th>
<th>Area of brain stimulated</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffman et al 2003 (1)</td>
<td>Left TP area</td>
<td>24 90% of motor threshold, 1 Hz, 8 min on day 1, 12 min on day 2, 16 min for next 7 days</td>
<td>After day 8, 75% of active group had positive response (defined as a decrease in 50% on HCS), while only 17% of sham had response, which was statistically significant. Effects endured for at least 15 weeks for 50% of patients.</td>
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<td>Poleli et al 2005 (2)</td>
<td>Left TP cortex</td>
<td>10 90% of motor threshold, 1 Hz, 2000 stimulations per day, total 5 days</td>
<td>A significant reduction in AHRS score for the active group (-13.1±0.8) and no decrease for the sham group (1±5.2) was found. There was a 70% response rate (response defined as a 20% reduction in AHRSs maintained until 1 month; at 2 months, that figure dropped to 50%.</td>
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<td>de Jesus et al 2011 (3)</td>
<td>Left TP cortex</td>
<td>17 90% of motor threshold, 1 Hz, 8 min on day 1, 16 min on day 2, 20 min for next 18 days</td>
<td>After 80 days, the active group’s mean AHRS was reduced from 31.0±3.6 to 27.1±3.4 whereas the sham group’s AHRS was similarly reduced from 26.8±7.6 to 25.4±8.8, which was a non-significant difference.</td>
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<td>Hoehn et al 2011 (4)</td>
<td>Left TP area</td>
<td>62 90% of motor threshold, 1 Hz, 20 min daily, 5 days per week, total 3 weeks</td>
<td>No significant difference in AHRS scores of any of the 3 groups. That is, in the MRI group, AHRS dropped from 26.8 to 22.6 in TP group, 26.3 to 22.7 in sham group, 27.4 to 24.1.</td>
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<td>Koops et al 2016 (5)</td>
<td>Left TP cortex</td>
<td>71 Theta-burst rTMS, 80% of motor threshold, 3-pulse burst at 50 Hz, given every 200 ms. Once daily for 5 days</td>
<td>No significant interaction effect with treatment group for F(2,124) = 0.19, P = 0.83; therefore, both the active rTMS and sham groups had the same reduction in hallucinations.</td>
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</tbody>
</table>

Conclusions

- rTMS is the more established modality, and recent larger studies have shown negative results for treating auditory hallucinations in schizophrenia.
- tDCS is expensive and portable, but still considered to be in its infancy in terms of application for psychiatric disorders. Like rTMS, tDCS can be targeted to a specific area of the brain.
- tACS is the least studied of the three modalities in this review and no RCTs on tACS met criteria for this systematic review.

References