Feasibility of Auditory Cortical Stimulation for the Treatment of Tinnitus

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Outline

• Background
• Materials and Method
• Results
• Discussion & Conclusion
Background
Background

• Recent studies have examined the role of direct and indirect CNS stimulation for the suppression of tinnitus
  – Transcranial magnetic stimulation (TMS)
  – Direct current stimulation of the auditory cortex
Background

• Objectives
  – To investigate the feasibility and safety of an implantable epidural cortical stimulator for the treatment of severe tinnitus
    • 2-contact electrode, connected to a fully implantable stimulator, placed over the secondary auditory cortex contralateral to the side of tinnitus percept
Materials and Method
Patients

• **Inclusion criteria:**
  
  – *Adults (n = 8) with,*
    
    • constant tinnitus of at least 1 year
    • tinnitus reaction questionnaire score greater than 33
    • tinnitus was predominantly unilateral
    • a frequency less than 8,000 Hz
Patients

• Exclusion criteria:
  – Active Ménière’s disease
  – Intracranial neoplasm
  – Current substance abuse
  – Medical conditions preventing safe implantation
Setting

- Setting:
  - Tertiary care referral center
Study Design

• Study design:
  – Prospective, controlled, single-blinded study of cortical stimulation for 4 weeks, and then an open-label stimulation period
Study Design

Preimplantation Testing
Preimplantation Testing

• **Baseline audiometric evaluation:**
  - pure-tone thresholds to bone and air
  - word recognition testing
  - tinnitus loudness matching
  - tinnitus pitch matching
  - determination of minimum masking level

• **Questionnaire evaluation:**
  - TRQ at initial evaluation
  - TRQ, Tinnitus Handicap Questionnaire (THQ) and Beck Depression Inventory before implantation
Preimplantation Testing

• Subjects underwent functional magnetic resonance imaging (fMRI) scanning to localize the site of maximal response to the tinnitus frequency in the auditory cortex.

• The target region was merged with a 3-dimensional anatomic MR image and uploaded onto the surgical navigation system.
Study Design

Initial evaluation; TRQ

Implantation

CROSSOVER

ON

2 wk

OFF

2 wk

OPEN LABEL STIMULATION

8 wk

12-wk evaluation

OFF

ON

TRQ; THQ; BDI

audiometry

TRQ; THQ; BDI

Audiometric testing

Audiometry testing
Surgical Implantation

• Surgical implantation of an investigational epidural electrode over the posterior superior temporal gyrus using fMRI targeting
Study Design
Stimulation

• 4-week crossover control period
  - a 2-week stimulation period alternated with a 2-week sham period in random order to which subjects were blinded

• Open-label stimulation period
  - continuous stimulation with parameter adjustments to maximize tinnitus suppression
Study Design

Initial evaluation; TRQ

Implantation

CROSSOVER

ON

OFF

2 wk

2 wk

OPEN LABEL STIMULATION

8 wk

12-wk evaluation

TRQ; THQ; BDI

Audiometric testing

TRQ; THQ; BDI

audiometry
Postimplant Evaluation

• Main Outcome Measure:
  – Subjective measures
    • rating of tinnitus severity, loudness, and device efficacy
  – Objective measures
    • Hearing thresholds, tinnitus frequency, loudness, and minimum masking levels
    • Outcome measures using the THQ, TRQ, BDI
Results
Results

Subject Characteristics
# Results

## Subject Characteristics

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>M/F</th>
<th>PTA (dB)</th>
<th>Side</th>
<th>Duration (yr)</th>
<th>Frequency (Hz)</th>
<th>Loudness (dB)</th>
<th>Minimum masking level (dB)</th>
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<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>M</td>
<td>87</td>
<td>R</td>
<td>14</td>
<td>4,700</td>
<td>102</td>
<td>65</td>
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<tr>
<td>2</td>
<td>56</td>
<td>F</td>
<td>33</td>
<td>L</td>
<td>13</td>
<td>2,150</td>
<td>41</td>
<td>59</td>
</tr>
<tr>
<td>3</td>
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<td>F</td>
<td>62</td>
<td>R</td>
<td>3</td>
<td>2,600</td>
<td>29</td>
<td>74</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>M</td>
<td>17</td>
<td>L</td>
<td>12</td>
<td>6,400</td>
<td>52</td>
<td>72</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>M</td>
<td>68</td>
<td>R</td>
<td>10</td>
<td>2,000</td>
<td>66</td>
<td>69</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>M</td>
<td>17</td>
<td>B (L&gt;R)</td>
<td>17</td>
<td>6,400</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>F</td>
<td>53</td>
<td>L</td>
<td>48</td>
<td>3,400</td>
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<td>8</td>
<td>67</td>
<td>M</td>
<td>NR</td>
<td>L</td>
<td>9</td>
<td>6,400</td>
<td>41</td>
<td>64</td>
</tr>
</tbody>
</table>

B indicates both; F, female; L, left; M, male; R, right.

54y/o

15.7yr

<8000Hz
Results

Crossover Control Period
Subjective rating of device effectiveness during the 4-week blinded crossover period

(0-100 numeric rating scale)
Graphic representation of performance on the TRQ at baseline and treatment Weeks 2, 4, and 12
Graphic representation of performance on the THQ at baseline and treatment Weeks 2, 4, and 12
Results Summary

• 4-week blinded period:
  – No effects of stimulation
Results

Open-Label Stimulation Period
Pure-tone averages, word recognition scores, at baseline and at treatment Week 12
Results Summary

• No change noted in pure-tone average and word recognition score
• No surgical or stimulation-related complications
Objective measures of tinnitus loudness, minimum masking level, and tinnitus frequency scores, at baseline and at treatment Week 12
Results Summary

• Objective measures of tinnitus loudness remained fairly Stable
Subjective rating of device effectiveness and tinnitus loudness during an 8-week open-label stimulation period

(0-100 numeric rating scale)
Results Summary

• **Continuous chronic stimulation:**
  - 2 patients ⇒ persistent reduction of pure-tone tinnitus
  - 6 patients ⇒ short periods of total tinnitus suppression
Graphic representation of performance on the BDI at baseline and treatment Week 12
Results Summary

• Significant improvements in the BDI and tinnitus questionnaires
Discussion & Conclusion
Discussion & Conclusion

• *This study suggest,*
  – CNS stimulation is feasible and warrants further investigation as a tinnitus intervention
  – perception of tinnitus may be multifactorial, involving separate pathways for emotional and auditory perception
Discussion & Conclusion

• Noticeable improvement in subjective ratings but unchanged objectives measures, due to
  – cortical stimulation influences emotional centers independent of an effect on the percept
  – Placebo effect related to the surgical intervention or continued physician contact
Thanks for your attention!!
Summary of subject responses to cortical stimulation using objective, subjective, and outcome measures of tinnitus at 12 weeks

<table>
<thead>
<tr>
<th>Subject</th>
<th><strong>Objective Measures</strong></th>
<th><strong>Subjective Measures</strong></th>
<th><strong>Quality of Life Measures</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Loudness (dB)</td>
<td>Masking Level (dB)</td>
<td>Effectiveness (0–100)</td>
</tr>
<tr>
<td>1</td>
<td>-22 (−21%)</td>
<td>2 (−4%)</td>
<td>65 (NA)</td>
</tr>
<tr>
<td>2</td>
<td>29 (−72%)</td>
<td>10 (−17%)</td>
<td>30 (NA)</td>
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<tr>
<td>3</td>
<td>21 (−71%)</td>
<td>6 (−8%)</td>
<td>5 (NA)</td>
</tr>
<tr>
<td>4</td>
<td>-7 (−12%)</td>
<td>-38 (−53%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>5</td>
<td>21 (−32%)</td>
<td>2 (−3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>6</td>
<td>-10 (−16%)</td>
<td>5 (−9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>7</td>
<td>15 (−69%)</td>
<td>10 (−58%)</td>
<td>20 (NA)</td>
</tr>
<tr>
<td>8</td>
<td>-9 (−21%)</td>
<td>-32 (−50%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Notes:**
- NA: Not applicable
- Percentages are relative to baseline or expected values.
Conclusion

• Additional studies will investigate,
  – improve current delivery to the auditory cortex
  – identify characteristics predicative of postimplantation efficacy
  – require more robust control periods to distinguish the effects of cortical stimulation from the potential placebo effects of surgical intervention