Alternative Tinnitus Management Techniques Developed from Volitional Control Over the Activity of the Auditory Cortex

Nelson, Jeremy T

2018 Military Health Research Symposium (MHSRS) in Kissimmee, Florida on August 20-23, 2018

SSgt Erin Toth
INSTRUCTIONS FOR COMPLETING SF 298

1. REPORT DATE. Full publication date, including day, month, if available. Must cite at least the year and be Year 2000 compliant, e.g. 30-06-1998; xx-06-1998; xx-xx-1998.

2. REPORT TYPE. State the type of report, such as final, technical, interim, memorandum, master's thesis, progress, quarterly, research, special, group study, etc.

3. DATES COVERED. Indicate the time during which the work was performed and the report was written, e.g., Jun 1997 - Jun 1998; 1-10 Jun 1996; May - Nov 1998; Nov 1998.

4. TITLE. Enter title and subtitle with volume number and part number, if applicable. On classified documents, enter the title classification in parentheses.

5a. CONTRACT NUMBER. Enter all contract numbers as they appear in the report, e.g. F33615-86-C-5169.

5b. GRANT NUMBER. Enter all grant numbers as they appear in the report, e.g. AFOSR-82-1234.

5c. PROGRAM ELEMENT NUMBER. Enter all program element numbers as they appear in the report, e.g. 61101A.

5d. PROJECT NUMBER. Enter all project numbers as they appear in the report, e.g. 1F665702D1257; ILIR.

5e. TASK NUMBER. Enter all task numbers as they appear in the report, e.g. 05; RF0330201; T4112.

5f. WORK UNIT NUMBER. Enter all work unit numbers as they appear in the report, e.g. 001; AFAPL30480105.

6. AUTHOR(S). Enter name(s) of person(s) responsible for writing the report, performing the research, or credited with the content of the report. The form of entry is the last name, first name, middle initial, and additional qualifiers separated by commas, e.g. Smith, Richard, J, Jr.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES). Self-explanatory.

8. PERFORMING ORGANIZATION REPORT NUMBER. Enter all unique alphanumeric report numbers assigned by the performing organization, e.g. BRL-1234; AFWL-TR-85-4017-Vol-21-PT-2.

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES). Enter the name and address of the organization(s) financially responsible for and monitoring the work.

10. SPONSOR/MONITOR'S ACRONYM(S). Enter, if available, e.g. BRL, ARDEC, NADC.

11. SPONSOR/MONITOR'S REPORT NUMBER(S). Enter report number as assigned by the sponsoring/monitoring agency, if available, e.g. BRL-TR-829; -215.

12. DISTRIBUTION/AVAILABILITY STATEMENT. Use agency-mandated availability statements to indicate the public availability or distribution limitations of the report. If additional limitations/ restrictions or special markings are indicated, follow agency authorization procedures, e.g. RD/FRD, PROP, IAR, etc. Include copyright information.

13. SUPPLEMENTARY NOTES. Enter information not included elsewhere such as: prepared in cooperation with; translation of; report supersedes; old edition number, etc.

14. ABSTRACT. A brief (approximately 200 words) factual summary of the most significant information.

15. SUBJECT TERMS. Key words or phrases identifying major concepts in the report.

16. SECURITY CLASSIFICATION. Enter security classification in accordance with security classification regulations, e.g. U, C, S, etc. If this form contains classified information, stamp classification level on the top and bottom of this page.

17. LIMITATION OF ABSTRACT. This block must be completed to assign a distribution limitation to the abstract. Enter UU (Unclassified Unlimited) or SAR (Same as Report). An entry in this block is necessary if the abstract is to be limited.
Alternative Tinnitus Management Techniques Developed from Volitional Control Over the Activity of the Auditory Cortex

Matthew S. Sherwood, PhD
Emily E. Diller, MS; Subhashini Ganapathy, PhD; Jeremy T. Nelson, PhD; Jason G. Parker, PhD
**Tinnitus**

- Lots of Debate
- Difficult to Study
  - Subjective
  - Highly Variable
- Various Models
  - Bottom-up Deafferentation
  - Top-Down Deficiencies
- Critical Gap in Treatment Technologies/Therapies
Our Therapeutic Idea

Phase 1
- Train control over the activity of the primary auditory cortex using functional MRI neurofeedback
- Assess changes in behavioral and neural measures
- Determine control methods resulting in greatest behavioral/neural effects

Phase 2
- Develop a simple application to train control methods in the absence of neurofeedback
- Determine changes in behavioral and neural measures
- Compare effects with functional MRI neurofeedback
Findings from Functional Neuroimaging

- $\Delta_{t,m} - \Delta_{c,m} > 0$: Mean signal change between auditory stimulation and no stimulation is elevated in tinnitus patients\(^1,2\)
- $\Delta_s$: elevated steady-state metabolism\(^3,4\)
  - Should result in increased BOLD signal and CBF
- Attentional, emotional and auditory network components are altered\(^5,6\)

\(^1\) Gu et al. (2010). Journal of Neurophysiology, 104(6), 3361-3370.
Real-time fMRI Neurofeedback

Diagram:
- Acquire whole brain BOLD data
- Process whole brain BOLD data
- Quantify contrast from an ROI
- Update subject display
Phase 1: Experimental Methods

27 Healthy Participants
- Written informed consent obtained prior to any experimental procedures

Grouping
Experimental Group (EXP)
- $n = 18$ (mean age $23.2 \pm 1.1$ years, 11 males)
- Supplied real neurofeedback from Primary Auditory Cortex (A1)

Control Group (CON)
- $n = 9$ (mean age $24.4 \pm 2.5$ years, 4 males)
- Supplied sham neurofeedback
Phase 1: Experimental Methods (cont.)

- Session (on separate days)
  - Session 1: Behavioral Assessment
  - Session 2: Neural Assessment
  - Session 3: Real-Time fMRI Neurofeedback Training
  - Session 4: Behavioral Assessment
  - Session 5: Neural Assessment
Experimental Methods (cont.)

Neurofeedback Training

Binaural Auditory Stimulation → ROI Selection → Closed-Loop Endogenous Neuromodulation X 2
Phase 1: Results

[Graph showing the comparison between Group CON and Group EXP. The x-axis represents Session 1 Run 1 and Session 5 Run 2. The y-axis represents A1 De-Activation (z statistic). Asterisks indicate statistical significance: * p < 0.05, ** p < 0.01.]
Phase 1: Results (cont.)
Phase 1: Results (cont.)
Phase 1: Results (cont.)

Attention to Emotion Task

• Assessed impact of emotion on attention
• Calculated the percent change in latency between emotional and neutral trials

![Graph showing change in ΔAE mean latency (%) over sessions](image1)

![Scatter plot showing change in ΔAE mean latency (%) vs. change in A1 control (z statistic)](image2)
Phase 1: Results (cont.)

A1 Response to Auditory Stimulation

- Assessed A1 activation from binaural continuous noise
- Performed a 2x2x2 repeated measures ANOVA
Phase 1: Results (cont.)

Response to Auditory Stimulation
Phase 1: Results (cont.)
Response to Auditory Stimulation
Phase 1: Results (cont.)
Steady-State Perfusion
Phase 1: Results (cont.)

Steady-State Perfusion
Phase 1: Discussion

• Previously, self-regulation via fMRI-NFT of the following have been implicated:
  – Activated cortical volume in A1 and the secondary auditory cortex\(^1\)
  – A1 activation magnitude\(^2\)

• This work indicates self-regulation over A1 deactivation magnitude is achievable using fMRI-NFT in the presence of auditory stimulation

\(^1\) Yoo et al. (2006). NeuroReport, 17(12), 1273-1278.
Phase 1: Discussion (cont.)

- Enhanced emotional response to auditory stimulation has been reported in tinnitus patients\(^1,2\)
  - Improved control over A1 led to a decreased effect of emotionally-charged stimuli on attention
- Tinnitus patients exhibit an elevated response in A1 activation to auditory stimuli\(^3,4\)
  - Attempting volitional control over A1 was found to decrease the A1 activation arising from auditory stimuli
- Tinnitus patients exhibit elevated steady-state metabolism in A1
  - Observed increased perfusion in middle temporal gyrus and superior temporal gyrus

\(^3\) Gu et al. (2010). Journal of Neurophysiology, 104(6), 3361-3370.
Phase 1: Discussion (cont.)

• Enhanced emotional response to auditory stimulation has been reported in tinnitus patients$^{1,2}$
  – Improved control over A1 led to a decreased effect of emotionally-charged stimuli on attention

• Tinnitus patients exhibit an elevated response in A1 activation to auditory stimuli$^{3,4}$
  – Attempting volitional control over A1 was found to decrease the A1 activation arising from auditory stimuli

• Tinnitus patients exhibit elevated steady-state metabolism in A1
  – Observed increased perfusion in middle temporal gyrus and superior temporal gyrus

3 Gu et al. (2010). Journal of Neurophysiology, 104(6), 3361-3370.
Phase 2: Experimental Methods

1. Behavioral Assessment
2. Neural Assessment
3. Control Training
4. Behavioral Assessment
5. Neural Assessment

Session (on separate days)
This research was sponsored by the U.S. Air Force (contract FA8650-16-2-6702).

The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense and its Components. The U.S. Government is authorized to reproduce and distribute reprints for Governmental purposes notwithstanding any copyright notation thereon. The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402.