AN INVESTIGATION OF TINNITUS USING BEHAVIOURAL AND FUNCTIONAL IMAGING MEASURES

A summary of four years

NIHR Nottingham Hearing Biomedical Research Unit

Jeff Davies
My PhD dataset

0 months

3 months

6 months

QUESTIONNAIRE

Very often

Often

Sometimes

Rarely
Exclusions n=28
• metal implant n=9
• claustrophobic n=5
• neurological n=7
• withdrew n=7

Tinnitus participants assessed for eligibility n=70

Hearing aid n=29
No hearing aid n=13

Visit 1 MRI scan and behavioural tests (0 months)

Visit 2 MRI scan and behavioural tests (3 months)

Visit 3 MRI scan and behavioural tests (6 months)

No tinnitus participants assessed for eligibility n=28

Hearing aid n=14
No hearing aid n=13

Exclusions n=1
• withdrew n=1

No tinnitus participants assessed for eligibility n=28

Hearing aid n=29
No hearing aid n=13

Visit 1 MRI scan and behavioural tests (0 months)

Visit 2 MRI scan and behavioural tests (3 months)

Visit 3 MRI scan and behavioural tests (6 months)
Aims

Original research aims were focused on investigating the benefits of different sound and psychological-based tinnitus intervention strategies.

Our research questions:

1. How effective is amplification for hearing loss in alleviating tinnitus handicap? And does perceived tinnitus pitch affect hearing aid efficacy in the management of tinnitus?

2. Does chronic tinnitus reliably alter patterns of resting-state auditory network activity?

3. Does the amygdala respond differently to emotionally evocative sound in chronic tinnitus patients?
My PhD studies

Study 1
• How effective is amplification for hearing loss in alleviating tinnitus handicap? A prospective questionnaire-based evaluation within a UK clinic

Study 2
• Auditory network connectivity in tinnitus patients: a resting-state fMRI study

Study 3
• Exploring the amygdala response to emotionally evocative soundscapes in people with tinnitus: a sound-evoked fMRI study
Study 1

How effective is amplification for hearing loss in alleviating tinnitus handicap? A prospective questionnaire-based evaluation within a UK clinic

Background

- Underlying hearing loss is common in those who report tinnitus
- Hearing aids are frequently used for tinnitus management
- Although the weight of evidence to support the benefit of hearing aids is high (Shekhawat et al., 2013), the general quality of evidence is poor (Hoare et al. 2014).
  - study design
  - patient demography
  - fitting strategies
  - sub-optimal outcome measures
- Only one study has targeted a UK-based NHS patient group despite the NHS being the main provider of hearing aids in the UK
Chronic tinnitus subjects  
n=56

Hearing aid intervention group  
n=42

No hearing aid controls  
n=14

(Pre-fit) 0 months

(Pre-fit) 3 months

(Pre-fit) 6 months

Pure tone audiometry  
Tinnitus Handicap Questionnaire,  
Hyperacusis Questionnaire, Beck Anxiety  
Inventory, Beck Depression Inventory,  
pitch / loudness measures

Tinnitus Handicap Questionnaire, Beck  
Anxiety Inventory, Beck Depression  
Inventory,  
pitch / loudness measures

Tinnitus Handicap Questionnaire, Hyperacusis Questionnaire, Beck Anxiety  
Inventory, Beck Depression Inventory  
pitch / loudness measures
### STUDY 1

#### PARTICIPANT PROFILE

<table>
<thead>
<tr>
<th>Measure</th>
<th>HA group (mean, SD)</th>
<th>No HA group (mean, SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.5 (9.3) years</td>
<td>60.9 (8.6) years</td>
<td>2.52</td>
</tr>
<tr>
<td>Gender</td>
<td>25 male: 17 female</td>
<td>9 male: 5 female</td>
<td>-</td>
</tr>
<tr>
<td>Tinnitus pitch (kHz)</td>
<td>6.94 (3.23)</td>
<td>6.82 (3.48)</td>
<td>.992</td>
</tr>
<tr>
<td>Tinnitus loudness (VAS scale)</td>
<td>44.04 (21.13)</td>
<td>46.57 (15.98)</td>
<td>.425</td>
</tr>
<tr>
<td>Tinnitus Handicap Questionnaire (THQ)</td>
<td>38.87 (16.20)</td>
<td>42.8 (20.04)</td>
<td>.508</td>
</tr>
<tr>
<td>Tinnitus duration (years)</td>
<td>16.62 (17.85)</td>
<td>11.39 (12.76)</td>
<td>.550</td>
</tr>
<tr>
<td>Beck Anxiety Inventory (BAI)</td>
<td>4.6 (4.8)</td>
<td>9.9 (12.4)</td>
<td>.140</td>
</tr>
<tr>
<td>Beck Depression Inventory (BDI)</td>
<td>0.98 (1.22)</td>
<td>4.21 (4.66)</td>
<td>.022*</td>
</tr>
<tr>
<td>Hyperacusis Questionnaire (HQ)</td>
<td>13.92 (6.77)</td>
<td>14.92 (8.8)</td>
<td>.857</td>
</tr>
<tr>
<td>Hearing level (0.25 - 4kHz) dB HL</td>
<td>31.07 (12.6)</td>
<td>15.79 (10.0)</td>
<td>.000*</td>
</tr>
<tr>
<td>Hearing level (2 - 8kHz) dB HL</td>
<td>51.09 (15.13)</td>
<td>30.28 (17.5)</td>
<td>.000*</td>
</tr>
</tbody>
</table>
Study 1

AVERAGE HEARING THRESHOLDS

Frequency (Hz)

Hearing Threshold (dB HL)

L HA group
R HA group
L no HA control
R no HA control
### Study 1

How effective is amplification for hearing loss in alleviating tinnitus handicap? A prospective questionnaire-based evaluation within a UK clinic

<table>
<thead>
<tr>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Compared questionnaire scores of hearing aid users and non users at 0, 3 and 6 months</td>
<td>• Global tinnitus handicap scores reduced significantly in the HA group</td>
</tr>
<tr>
<td>• Using GLM / ANCOVA statistics</td>
<td>• Tinnitus pitch did not influence tinnitus handicap change over 6 months</td>
</tr>
<tr>
<td>• Age, sex and BSA average hearing loss used as covariates</td>
<td>• BAI, BDI, HQ and VAS tinnitus loudness did not change significantly</td>
</tr>
</tbody>
</table>
My PhD studies

Study 1
- How effective is amplification for hearing loss in alleviating tinnitus handicap? A prospective questionnaire-based evaluation within a UK clinic

Study 2
- Auditory network connectivity in tinnitus patients: a resting-state fMRI study

Study 3
- Exploring the amygdala response to emotionally evocative soundscapes in people with tinnitus: a sound-evoked fMRI study

Questionnaire based study

fMRI based studies, used the same participant groups
Visit 1 MRI scan and behavioural tests (0 months)

**Exclusions n=17**
- Asymmetrical hearing
- Intermittent tinnitus

**Tinnitus group n=12**
- 5 min resting-state fMRI data
- 15 min sound-evoked fMRI data

**Exclusions n=3**
- Asymmetrical hearing
- Intermittent tinnitus

**No tinnitus controls n=11**
- 5 min resting-state fMRI data
- 15 min sound-evoked fMRI data

Matched on: age, sex, hearing loss, hyperacusis, anxiety and depression
### PARTICIPANT PROFILE

**Tinnitus group**
- n = 12 (7 males)
- 49-73 years (mean: 66)
- bilateral HF SNHL
- No hyperacusis (HQ score < 29)
- BAI mean score 4.3 (SD 3.36)
- BDI mean score 1.1 (SD 1.31)
- All hearing aid users
- No history of neurological disorder
- THQ mean score 43.7 (SD 18.32)

**No tinnitus controls**
- n = 11 (8 males)
- 58-75 years (mean: 68)
- bilateral HF SNHL
- No hyperacusis (HQ score < 29)
- BAI mean score 3.8 (SD 5.34)
- BDI mean score 1 (SD 1.55)
- All hearing aid users
- No history of neurological disorder

* Constant subjective tinnitus (minimum 2 years duration)
  bilateral n = 10, lateralised n = 2
AVERAGE HEARING THRESHOLD

Study 2&3

Frequency (Hz)

Intensity (dB)

125 500 1000 2000 4000 8000 10000 12500

LEF'T TI

LEFT no TI

RIGHT TI

RIGHT no TI
Background

• Most fMRI tinnitus studies investigate sound-evoked brain activity but even at rest the brain is a complex hive of neural activity: processing and exchanging information between spatially distributed but temporally correlated anatomical regions.

• Resting-state fMRI may be better suited at recording activity relating to the “typical” on-going experience of the tinnitus percept.

• Kim et al. (2012) reported reduced functional connectivity between auditory cortices in 4 tinnitus patients.

• We replicate this study using our well matched groups of 12 tinnitus and 11 no tinnitus participants.
Study 2

Auditory network connectivity in tinnitus patients: a resting-state fMRI study

<table>
<thead>
<tr>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 min resting-state data</td>
<td>Robust activity in the bilateral auditory</td>
</tr>
<tr>
<td>We compared patterns of resting-state brain activity amongst our</td>
<td>auditory brain regions was found</td>
</tr>
<tr>
<td>tinnitus and no tinnitus participants</td>
<td></td>
</tr>
<tr>
<td>Used independent component analysis and region of interest analysis</td>
<td>However this did not differ between patient</td>
</tr>
<tr>
<td>Targeted neural activity arising from auditory brain centres (primary and non-primary auditory cortex)</td>
<td>groups (P &gt; 0.05 FWE)</td>
</tr>
<tr>
<td></td>
<td>Presence of tinnitus does not appear to</td>
</tr>
<tr>
<td></td>
<td>modify functional connectivity in the</td>
</tr>
<tr>
<td></td>
<td>auditory network</td>
</tr>
</tbody>
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Questionnaire based study

fMRI based studies, used the same participant groups
Study 3

Exploring the amygdala response to emotionally evocative soundscapes in people with tinnitus: a sound-evoked fMRI study

Background

- Tinnitus is often associated with strong negative feelings, this can lead to the manifestation of a distressing and chronic experience.
- Key to this process is the amygdala, the “feeling and reacting” part of the brain.
- Although several fMRI studies have investigated how the amygdala processes emotional sound stimuli, few have targeted a tinnitus population.
- Results may be restricted due choice of fMRI parameter.
### Study 3

**Exploring the amygdala response to emotionally evocative soundscapes in people with tinnitus: a sound-evoked fMRI study**

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>• 15 minute sound-evoked data</td>
<td>• In comparison to neutral sounds, both pleasant and unpleasant sounds evoked the strongest amygdala activations amongst participants</td>
</tr>
<tr>
<td>• We compared amygdala activity in response to very pleasant, neutral and very unpleasant sound stimuli</td>
<td>• Magnitude of the amygdala’s response to different sounds were similar between tinnitus and no tinnitus participants</td>
</tr>
<tr>
<td>• Used region of interest analysis</td>
<td>• Although a consistent trend for lower activation in the tinnitus group was observed</td>
</tr>
<tr>
<td>• Peak amygdala activity was derived on an individual basis and cross referenced with a probabilistic map to confirm location</td>
<td></td>
</tr>
</tbody>
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Summary

1. How effective is amplification for hearing loss in alleviating tinnitus handicap? And does perceived tinnitus pitch affect hearing aid efficacy in the management of tinnitus? 
Current NHS hearing aids are effective in reducing tinnitus handicap over a 6 month period, regardless of tinnitus pitch

2. Does chronic tinnitus reliably alter patterns of resting-state auditory network activity? No, not after strict control of patient demographics and statistical methods (FWE)

3. Does the amygdala respond differently to emotionally evocative sound in chronic tinnitus patients? The amygdala remains responsive to highly emotional sounds in tinnitus participants but this is comparable to non-tinnitus participants
Thanks for listening!

Acknowledgements

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