

Gating Mechanism in Tinnitus: Explored in Surgery-Induced Unilateral Deafness in Adult Humans

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Introduction

Tinnitus

- Perception of sound in the absence of an external sound source (e.g. high pitched ringing noise)¹
- Prevalent amongst the elderly², knowledge of pathophysiology incomplete³ and cure yet to be found¹

Noise-cancellation (NC) mechanism⁴

- Hearing loss → central auditory system (CAS) hyperactivity → tinnitus signal
- Failure of the so-called noise-cancellation circuitry of the auditory brain to cancel neural noise (i.e. tinnitus signal)
- Thalamic reticular nucleus (TRN) – key component – activity directly measurable from sleep spindles⁹
- Mechanism may explain why some people with hearing loss experience tinnitus while others do not

Unilateral Deafness (UD)

- Surgery-induced UD patients allow an opportunity to bypass confounding factors from hearing loss
- Vestibular schwannoma removal surgery can lead to UD that is immediate and complete⁵

Electroencephalography (EEG)

- Non-invasive and objective method of measuring macroscopic brain activity⁶
- Can measure spontaneous/resting-state CAS activity and auditory evoked potentials (AEPs: e.g. auditory brainstem response (ABR) and cortical auditory evoked potential (CAEP))

Gap in Knowledge

- Surgery-induced UD offer a rare opportunity to explore the NC mechanism in humans*

Aims

To assess the predictions of the Noise-Cancellation Mechanism⁴ in Humans with UD

- Study 1: To compare spontaneous CAS activity in UD humans with (UDT) and without tinnitus (UD)*
Study 2: To indirectly assess the noise-cancellation mechanism by comparing auditory evoked potentials in noise
Study 3: To directly assess the TRN's role in the noise-cancellation mechanism by comparing sleep spindle activity*

*As stated in the poster, for the purposes of space and simplicity, studies 1 and 3 will be omitted

Study 2 : Indirect Assessment of NC mechanism

Hypothesis

- CAEP P1-N1 complex, exhibits amplitude effects to sound heard in noise as a function of signal to noise ratio (SNR: effects are subtractive)⁷. ABR exhibits amplitude effects to sound heard in noise as a function of both SNR and absolute level (effects are additive)⁸
- Comparing AEPs from generators above and below the thalamus level may offer an indirect means to test the NC model in humans
- If a failure of NC circuitry is related to the perception of tinnitus, we hypothesise an absence of the subtractive effect in P1-N1 data in UDT individuals compared to UD individuals, and controls, but no such changes in the ABR in all three groups (Figure 1)

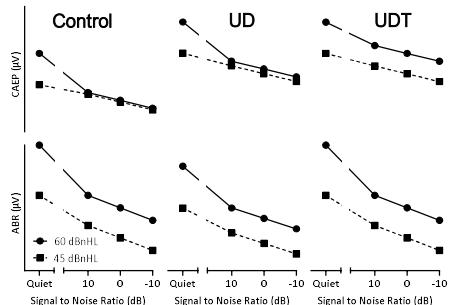


Figure 1 | Schematic of the hypothesised effects of varying signal to noise ratios on CAEP and ABR amplitudes across three study groups. Compare this to Figure 5 if TRN is gating a tinnitus signal (UD without tinnitus), then the CAEPs should show a subtractive effect in noise, and ABRs an additive effect. But if TRN is not gating tinnitus in UD with tinnitus, both the CAEPs and ABRs should show an additive effect in noise

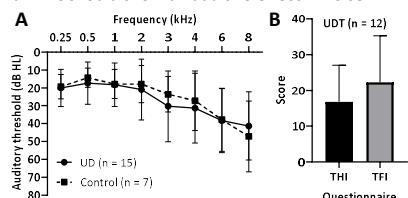


Figure 2 | A) Mean (± SD) auditory thresholds (dB HL) between control (broken line) and all UD participants (solid line; intact ear tested), and B) Mean (± SD) tinnitus handicap inventory (THI) and tinnitus functional index questionnaire (TFI) scores from the UDT (n = 12) group. Mean THI/TFI scores indicate minimal tinnitus suffering

Methods

Participants

- 15 UD participants recruited from the Canterbury District Health Board database, New Zealand
- 7 control participants recruited from various regions of Canterbury, New Zealand
- All participants went through pure tone audiometry and UDT participants completed the tinnitus handicap inventory (THI) and tinnitus functional index questionnaires (TFI) (Figure 2)
- University of Canterbury Ethics approval HREC Ref. HEC 2021/68/LR-PS

Acquisition Procedure

- 64-channel BioSemi ActiveTwo system
- 400 trials of 1 kHz tone burst CAEP and 6000 trials of broadband (0.1 – 8 kHz) chirp ABR
- 60 and 45 dBnHL stimulus intensities each at Quiet and 3 SNRs: -10, 0 and +10 dB SNR

Offline Data Analysis

- Ocular artefact correction with vertical electro-oculogram
- EEG bandpass filtered between 1 – 40 Hz and 100 – 3000 Hz for CAEP and ABR respectively
- EEG segmentation: -200 to +600 ms and -10 to +20 ms relative to stimulus for CAEP and ABR respectively for stimulus-locked analysis and subsequent weighted averaging

Study 2 : Indirect Assessment of NC mechanism (continued)

Results

- General trend – with the inclusion of noise, P1-N1 and wave V amplitudes decreases (Figures 3 and 4)
- CAEP P1-N1 amplitudes varied with SNR in both the control and UDT groups but not in the UD group. The ABR wave V amplitudes varied according to the stimulus level and noise in the UD group only (Figure 4)

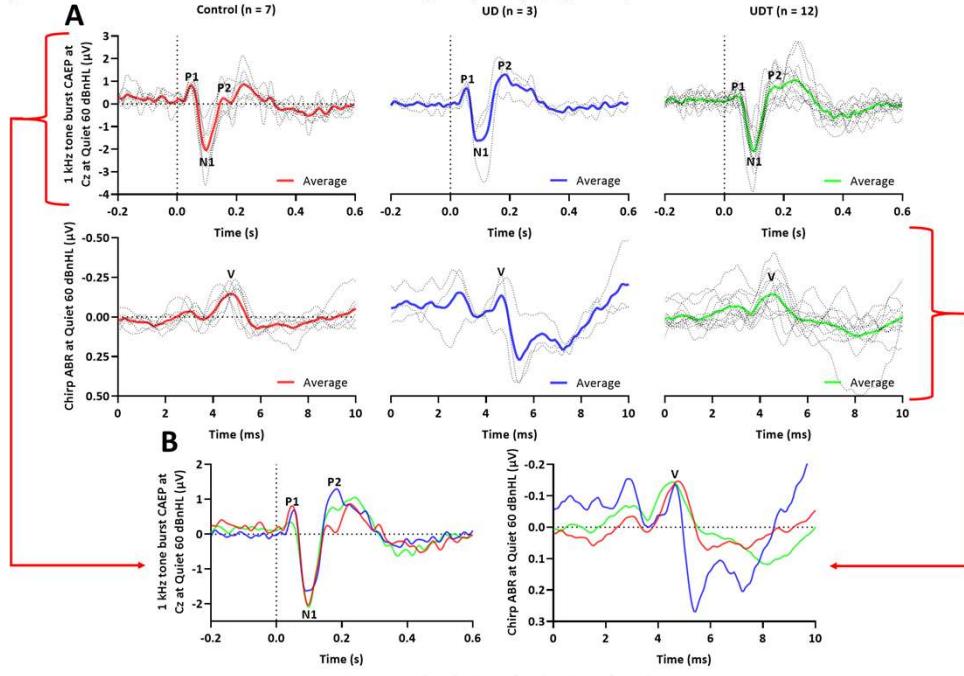


Figure 3 | A) Raw (dotted line) and grand average (solid line) cortical auditory evoked potentials (CAEP) at Cz location (top row) and auditory brainstem responses (ABR) (bottom row) both at Quiet 60 dBnHL stimulus condition across 3 study groups. A) was used to generate B), the same grand average traces of CAEP at Cz and ABR across 3 study groups overlaid on each other. CAEP and ABR peak to peak amplitudes were used to generate Figure 4

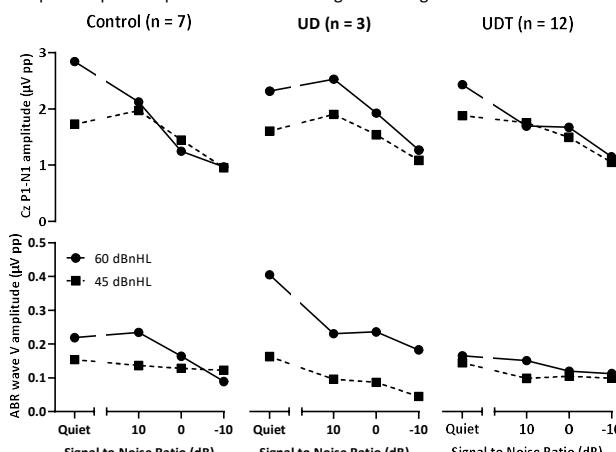


Figure 4 | CAEP Cz P1-N1 peak to peak amplitude (first row) and ABR Wave V peak to peak amplitude (second row) across four stimulus conditions across three study groups

Discussion

- Auditory thresholds between study groups were quite similar and THI and TFI scores of 17 and 22 indicate minimal tinnitus suffering
- Preliminary findings are:
 - CAEP (subtractive) and ABR (additive) in controls reflect the effect of noise as expected
 - UDT is contrary to our expectations as both ABR and CAEP follow a subtractive pattern
 - UD is preliminary with only three participants, but early indications are both ABRs and CAEPs following an additive pattern

Next steps:

- Further data collection from control and UD participants
- Data analysis of nap study for sleep spindle analysis – study 3

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