Peer Community In Registered Reports

Evidence for the role of predictive coding in subjective tinnitus

*A recommendation by **Chris Chambers** based on peer reviews by **Will Sedley**, **Pia Brinkmann** and **Emilie Cardon** of the STAGE 2 REPORT:*

L. Reisinger, G. Demarchi, S. Rösch, E. Trinka, J. Obleser, N. Weisz (2024) Registered Report: Are anticipatory auditory predictions enhanced in tinnitus and independent of hearing loss? OSF, ver. version 3, peer-reviewed and recommended by Peer Community in Registered Reports. https://osf.io/9wqjh

Submitted: 22 February 2024, Recommended: 27 March 2024

Cite this recommendation as:
Chambers, C. (2024) Evidence for the role of predictive coding in subjective tinnitus. *Peer Community in Registered Reports*, 100727. 10.24072/pci.rr.100727

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Subjective tinnitus is a common disorder in which people experience a persistent sound in the absence of any external source. The underlying causes of tinnitus are debated – although the condition is strongly associated with hearing loss resulting from auditory damage, much remains to be understood about the neural processes that give rise to the phantom perception. Various classes of neurophysiological theories have been proposed, including the "altered gain" model – in which neurons in the auditory pathway increase their responsiveness to compensate for reduced auditory input following hearing loss – and the "noise cancellation" model – in which disrupted feedback connections from limbic regions are unable to tune out phantom signals. Although these theories account for much observed data, they have not been conclusively supported, and their ability to explain tinnitus is limited by the fact that hearing loss and tinnitus can arise independently and at different times. In the current study, Reisinger et al. (2024) tested an emerging alternative theory based on a Bayesian predictive-coding framework (Sedley et al., 2016) in which the alteration of perceptual priors leads the auditory system to expect a sound that, if functioning normally, it should not expect. Using magnetoencephalography (MEG) in a sample of tinnitus patients (and carefully-matched controls for age, gender, and level of hearing loss), they asked whether tinnitus is associated with anticipatory brain activation, tuned to the carrier-frequency of an expected auditory stimulus. Specifically, the authors predicted that if the predictive-coding framework is correct then individuals with tinnitus should show different regularity-dependent pre-activations of carrier-frequency-specific information compared to the control group, while tone carrier-frequencies should be processed normally in tinnitus patients. They also predicted that any such pre-activations should not be related to levels of reported subjective tinnitus distress, as measured with the short version of the Tinnitus Questionnaire (mini-TQ). The results broadly confirmed the hypotheses, with some caveats. Statistically

significant differences in regularity-dependent pre-activations were observed between the tinnitus and control groups, however – curiously – the effects appear to be driven by below-chance decoding in the control group, complicating the interpretration. At the same time, consistent with expectations, frequency processing did not differ significantly between individuals with and without tinnitus, and the observed pre-activations were not significantly related to tinnitus distress. Overall, the findings cautiously support the conclusion that chronic tinnitus is associated with maladaptively upregulated predictive neural processing, and that this phenomenon is unlikely to be explained by either tinnitus distress or hearing loss. The Stage 2 manuscript was evaluated over one round of in-depth review. Based on detailed responses to the reviewers' comments, the recommender judged that the manuscript met the Stage 2 criteria and awarded a positive recommendation. **URL to the preregistered Stage 1 protocol:** https://osf.io/6gvpy
Level of bias control achieved: Level 3. *At least some data/evidence that was used to the answer the research question had been previously accessed by the authors (e.g. downloaded or otherwise received), but the authors certify that they had yet observed any part of the data/evidence prior to Stage 1 IPA.* **List of eligible PCI RR-friendly journals:**

- Brain and Neuroscience Advances
- Cortex
- F1000Research
- Imaging Neuroscience
- In&Vertebrates
- NeuroImage: Reports
- Peer Community Journal
- PeerJ
- Psychology of Consciousness: Theory, Research and Practice
- Royal Society Open Science

References:

1. Reisinger, L., Demarchi, G., Rösch, , S., Trinka, E., Obleser, L., & Weisz, N. (2024). Registered Report: Are anticipatory auditory predictions enhanced in tinnitus and independent of hearing loss? [Stage 2] Acceptance of Version 3 by Peer Community in Registered Reports. https://osf.io/9wqjh

2. Sedley, W., Friston, K. J., Gander, P. E., Kumar, S., & Griffiths, T. D. (2016). An integrative tinnitus model based on sensory precision. Trends in Neurosciences, 39, 799-812. https://doi.org/10.1016/j.tins.2016.10.004

Reviews

Evaluation round #2

DOI or URL of the preprint: **https://osf.io/ue64s**
Version of the preprint: version 2

Authors' reply, 26 March 2024

Download author's reply
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Decision by Chris Chambers, posted 26 March 2024, validated 26 March 2024

Minor Revision

Thank you for your careful revisions. The manuscript is now almost ready for Stage 2 recommendation but I would like to request two final revisions.

1. On a close reading I noticed that the study design table (Table 1 in the registered Stage 1 manuscript) has been removed from the Stage 2 manuscript. This table is very useful for readers so please restore it to the main text (not as supplementary information) and I suggest also adding a column to the right that summarises the actual outcome (e.g. hypothesis confirmed or disconfirmed).

2. In Q4 of the submission checklist you noted that the data are publicly archived at https://gin.g-node.org/lisareisinger/tinnitus_predictions/. You also stated: *"Study data contains the preprocessed data, since raw data is not fully anonymous and therefore we are not allowed to publicly share these files. Our file storage does not allow to rename raw data and hence we decided to share the preprocessed data and the script for the preprocessing, so that reviewers can reconstruct our analysis pipeline up to the shared data (including ICA, filtering and epoching of the data). File names refer to the group (tinn = Tinnitus; notinn = Control group)."*

The link to the data repository is not stated in the manuscript and in any case returns a 404 error https://gin.g-node.org/lisareisinger/tinnitus_predictions/ Also, the link to the materials repository (https://gitlab.com/lisareisinger/tinnitus_predictions/) does not appear to be stated in the manuscript.

Please therefore include a section at the end of the manuscript called "Data and materials availability" that includes correct, up-to-date links to the repository (or repositories) containing the data, code and materials. In addition, you note in the checklist that the raw data cannot be publicly archived, presumably due to an ethical restriction. If so, then to achieve TOP Level 2 compliance (see PCI RR policy here), the nature of this barrier needs to be stated in the manuscript and the conditions readers must meet to access the raw data (if it can be shared at all, even on request). Therefore please add a template statement to the data and materials availability section as follows: "The conditions of our ethics approval do not permit public archiving of the raw study data. Readers seeking access to the data should contact [contact person or committee]. Access will be granted to named individuals in accordance with ethical procedures governing the reuse of sensitive data. Specifically, requestors must meet the following conditions to obtain the data [insert any conditions, e.g. completion of a formal data sharing agreement, or state explicitly if there are no conditions]."

Once you have made these changes I will issue Stage 2 acceptance without delay.

Evaluation round #1

DOI or URL of the preprint: https://osf.io/u5e6v
Version of the preprint: version 1

Authors' reply, 14 March 2024

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Decision by Chris Chambers, posted 11 March 2024, validated 11 March 2024

Revision invited

The three reviewers from Stage 1 kindly returned to evaluate your Stage 2 submission, and the good news is that all of them are broadly satisfied with the completed manuscript. I concur and I believe your submission will be suitable for final Stage 2 recommendation following a round of careful revision. Enclosed you will find some helpful comments from the reviewers to improve the clarity and degree of detail, primarily concerning specific aspects of the results and discussion. In revising, please avoid making any changes to the approved Stage 1 parts of the manuscript unless doing so is necessary to correct a factual error, resolve a lack of clarity, or in to make a minor typographic/grammatical change (e.g. changing future tense to past tense).

Reviewed by Will Sedley, 07 March 2024

This report is a great example of the scientific process. The hypotheses and aims were well laid out, based on prior work. Methods were well-planned in advance also, and deviations from the methods of the prior study are well-justified, and their importance clearly discussed. The aim of the study was to replicate previous novel and exciting findings with respect to possible tinnitus mechanisms, in the form of auditory predictive tendencies, and eliminate hearing loss as the explanation (which has turned out to be the basis of most previously reported 'tinnitus' studies that were not rigorously controlled). The study achieves its aims, in an independent group of participants, replicating the original findings. This is a big achievement. The discussion strikes a good balance of recognising the potential importance of the findings, whilst openly acknowledging the remaining uncertainties, and being clear between what its findings demonstrate, and what is still speculation.

I am supportive of publication, but would recommend some minor and moderate revisions first.

Moderate:

Given that matching for hearing was the particular focus and novelty of this study, it would be useful to have more information about hearing matching, for instance:

- Were the groups only compared in terms of hearing for the average pure tone threshold across all frequencies (for each ear), or were significant differences in individual frequencies sought?
- Can the authors please provide a figure showing the group mean and standard error of the hearing profiles for each ear?

What does is mean that controls have a negative anticipatory decoding accuracy difference between ordered and random? This is the one part that sits slightly uneasily with me. I do not doubt the findings, but rather I just wonder what it means that people are either 'un-representing', or 'contra-representing' upcoming stimuli based on learned regularities. As just one possibility of many, could this be because in the random condition it is more likely that the upcoming stimulus was presented 2-3 stimuli back (the probability of the immediately preceding stimuli clearly being exactly 25% in each condition, and therefore equivalent)? I am finding it hard to reconcile something that is less negatively predictive of the upcoming stimulus being an anticipatory prediction. Or, do the authors think that there are two opposing processes here? The authors do highlight this point and make quite a lot of discussion already about it, so perhaps they do not feel in a position to speculate further, but I would encourage them to ensure they have considered all possibilities as fully as they can.

Minor:

In the discussion, I wonder about including the following considerations for future work

- Attention as another explanation for differences in tinnitus vs. control groups. (Though, MMN studies in tinnitus show diminished responses to sub-tinnitus frequency ranges in people with tinnitus in passive

listening paradigms, which is hard to reconcile with increased predictive tendencies).

- Measuring hyperacusis scores in participants (but, these typically correlate with tinnitus distress, which already has not shown a significant correlation)?

I think that future work using tones around the tinnitus frequency could be highly informative, as it would allow probing of specific differential anticipatory activations between tinnitus and non-tinnitus tones, and might highlight correlates of tinnitus frequency predictions themselves, to complement the existing findings relating to auditory predictive tendencies more generally.

Minor

Abstract:
Clarify whether 80 is number per group or total number of participants (i.e. the latter)

Introduction:
Lines 85-90: Mention some other work (e.g. Adjamian et al. 2012) finding no differences in resting-state delta or gamma between tinnitus and hearing-matched controls.

Results:
Line 650: Please make it clear how hearing loss was controlled for in this statement (e.g. by removing the effect of hearing loss by linear regression)?

Discussion:
Line 687: 'indication' should be 'indicating'
Line 692: A full stop and space is missing
The discussion spends a lot of words repeating the main findings, and could perhaps be streamlined somewhat, without losing content or clarity.

Reviewed by Pia Brinkmann, 01 March 2024

Download the review

Reviewed by Emilie Cardon, 06 March 2024

In this stage 2 registered report, participants with tinnitus are shown to display relatively enhanced tone frequency specific pre-activation (i.e. larger differences in decoding accuracy) compared to matched tinnitus-free controls. The authors have carefully complied with their registered Stage 1 study design. Analytical methods have been performed as described in the Stage 1 protocol. Furthermore, the authors have presented their results completely and transparently.

Throughout this report, I have identified some minor issues where information may be lacking or interpretation of the findings might be improved upon. I have outlined these items below. Additionally, I recommend a careful readthrough to identify some very minor grammatical errors (some of which I have also addressed below).

Results

Figure 4 and the corresponding results section (L502 onwards): Overall, it seems that the primary outcome of this report (the difference in decoding accuracy) shows quite a bit of between-subject variability. Even at the time point with the most pronounced group differences (panel B of Fig. 4), these differences in decoding accuracy show a significant amount of variation, with the distributions for both groups (Tinnitus vs. No Tinnitus) overlapping considerably. Could the authors address this considerable variability and offer some

potential explanations for the observed variation? Are there parameters present in the current dataset that are potentially associated with the difference in decoding accuracy, and that could offer some more insight? Or do the authors hypothesize that this between-subject variability is largely driven by factors that were not investigated in the context of this study?

L560 “Together, with the result reported by Partyka et al. (2019), our results strongly support the notion that unspecific distress due to tinnitus is not a good explanation for tinnitus”: This seems to be a typo – could it be that the authors meant that “unspecific distress due to tinnitus is not a good explanation for the identified differences in decoding accuracy”, for example?

L646 and following: Here, tinnitus presence is significantly predicted by the mean difference in decoding accuracy. Could, potentially, the opposite be done, i.e. predict the mean difference in decoding accuracy by group (Tinnitus vs. No Tinnitus)? Would this give us some insight into how much of the between-subject variability in this difference in decoding accuracy (see also my comment above) is explained by the presence of tinnitus, versus the proportion of the variance that would have to be explained by other factors? It might be interesting to have such insights in order to compare the current results to other established differences between tinnitus patients and controls based on evoked MEG or EEG that currently exist in the literature.

Discussion

L686 What would this “neural prediction score” entail specifically? Do the authors propose a concrete numerical score, e.g. the values that are shown in Figure 4B, to be used in future applications? Or is this a broader concept?

L687 “indication” does not make sense grammatically here, did the authors meant to write “indicating”?

L746 “As they follow the onset the subsequent tone”: I think an ‘of’ may be missing here.