P055

TINNITUS AND HYPERACUSIS: COGNITIVE APPROACHES

Neural Mechanisms of Alertness Deficits In Relation to Tinnitus

A.SKRZATEK, L.HOBEIKA, S.DUPONT, C.GALLEA, A.LONDERO & S.SAMSON

Paris Brain Institute / CNRS UMR 7225 / INSERM 1127 / Sorbonne Université, Paris; PSITEC - Psychology: Interactions, Time, Emotions, Cognition / ULR 4072 / Université de Lille; Institut Pasteur / Hearing Institute / Université Paris Cité, Paris / AP-HP / INSERM / Fondation Pour l'Audition / IHU reConnect / F-75012 Paris, France

Abstract

Chronic tinnitus has been linked to attention difficulties, yet no clear correlates of these deficits have been identified in the brain[10]. In a recent study, we used the Attentional Network Test (ANT)[3] to compare the functioning of the attentional subsystems in 100 patients with chronic tinnitus (> 3 months) matched to 100 controls (Hobeika et al., in prep). We evidenced that tinnitus (but not hearing loss) was associated with **deficits of alerting cue and of sustained attention**, linked respectively to phasic and tonic alertness. These mechanisms are modulated by noradrenergic systems in the brain, thereby controlling levels of arousal. The aim of the study was to identify the changes in functional brain connectivity underlying these alertness deficits. The association of the behavioural evaluation and the resting state fMRI has shown for the first time that the differences in attentional abilities between tinnitus patients and healthy controls are related to the functional connectivity of brain regions particularly related to tinnitus. We also confirmed differences between groups in attentional, executive and default mode networks.

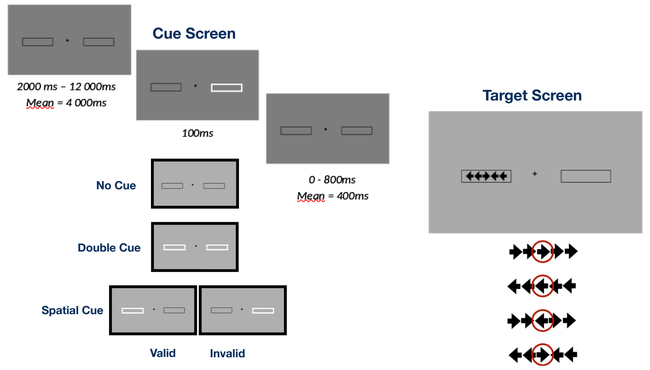
Objectives

Distinguish **functional connectivity changes related to alertness (phasic and/or tonic) in chronic tinnitus** by examining resting state fMRI in regions specific to alerting effect, hearing and tinnitus, while controlling for hearing loss and emotional state.

Methods et Materials

- **Chronic Tinnitus Patients** (N=25) and **Healthy Controls** (N=25) matched for age and sex (mean age 42 ± 11)
- All patients presented a moderate to severe chronic subjective tinnitus (mean THI score = 48) with no severe hearing loss

FIGURE 1 | Attentional Network Task (revised)[3]. The goal is to report the direction of the center arrow (red circle) on the Target Screen. Trials vary depending on cueing conditions (No Cue, Double Cue, Spatial Cue - Valid or Invalid) and target direction.



Variables Of Interest

- **Alerting score** = No Cue - Double Cue
- **Reaction Time Variability** (RTs standard deviation)

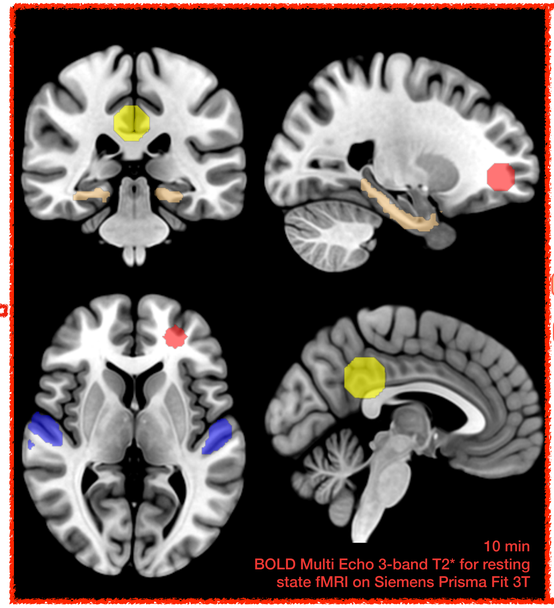


Figure 2 | Selected network-specific brain hubs for resting state functional connectivity (FC) seed-to-brain analysis

Tinnitus:
- Parahippocampus[6]
- dorsal Posterior Cingulate (dPC)[7]

Alerting:
- Right Orbito-Frontal Cortex (OFC)[4]

Hearing:
- Left and Right Auditory Cortices (AC)

Results

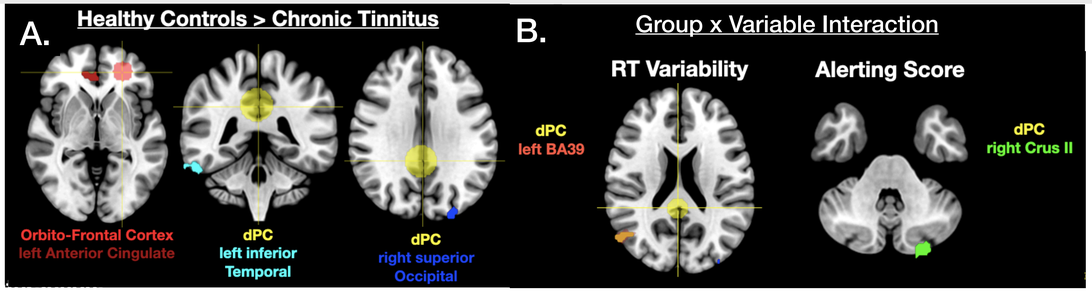


FIGURE 3 | A. FC differences between groups. B. Interaction between group factor and Variables Of Interest. fMRI seed-to-brain analyses of FC corrected at the cluster level (Family Wise Error ≤ 0.05)

Conclusion

- **FC differences** between individuals with and without tinnitus **in attentional, executive and default mode networks,** as presented in the triple network[1,2] and the updated tinnitus habituation[5,8,9] models
- **Altered FC of tinnitus-related hub (dPC) in default mode network linked to alertness differences** between groups, suggesting a possible vulnerability of tinnitus patients to develop alertness deficits
- Controlling for hearing loss and emotional state, yet still relatively small sample (N=25)
- **Future Perspective**: relating to the existing tinnitus resting state literature through seed-to-seed analysis within and between networks[5,8,9] & evaluating arousal anomalies through noradrenergic Receptor Enhanced Analysis of Connectivity Targets (REACT)

References

1. De Ridder D, Vanneste S, Song JJ, Adhia D. Tinnitus and the Triple Network Model: A Perspective. Clin Exp Otorhinolaryngol. 2022
2. De Ridder D, Vanneste S. The Bayesian brain in imbalance: Medial, lateral and descending pathways in tinnitus and pain: A perspective. Prog Brain Res. 2021
3. Fan J, McCandliss BD, Sommer T, Raz A, Posner MI. Testing the efficiency and independence of attentional networks. J Cogn Neurosci. 2002
4. Haupt M, Ruiz-Rizzo AL, Sorg C, Finke K. Phasic alerting effects on visual processing speed are associated with intrinsic functional connectivity in the cingulo-opercular network. Neuroimage. 2019
5. Husain, F.T. Neural networks of tinnitus in humans: elucidating severity and habituation. Hearing research. 2016.
6. Mohan A, Leong SL, De Ridder D, Vanneste S. Symptom dimensions to address heterogeneity in tinnitus. Neurosci Biobehav Rev. 2022
7. Moring JC, Husain FT, Gray J, Franklin C, Peterson AL, Resick PA, Garrett A, Esquivel C, Fox PT. Invariant structural and functional brain regions associated with tinnitus: A meta-analysis. PLoS One. 2022
8. Schmidt SA, Carpenter-Thompson J, Husain FT. Connectivity of precuneus to the default mode and dorsal attention networks: A possible invariant marker of long-term tinnitus. Neuroimage Clin. 2017
9. Shahsavarani, S., Schmidt, S. A., Khan, R. A., Tai, Y., & Husain, F. T. Salience, emotion, and attention: the neural networks underlying tinnitus distress revealed using music and rest. Brain research. 2021
10. Stevens, C., Walker, G., Boyer, M., & Gallagher, M. Severe tinnitus and its effect on selective and divided attention. International journal of audiology. 2007

Acknowledgments: Fondation Pour l'Audition, Fondation Des Gueules Cassées