

## **Patterns and Connectivity in Neural Networks: Leveraging Clustering and Replicability to Better Understand Tinnitus**

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One of the hallmarks of tinnitus is its high degree of heterogeneity, marked both by the variable percept and the individual's psychological reaction to it. In this talk, I will explore the latest data from brain imaging studies, primarily functional and structural MRI, to better understand the neural correlates of this heterogeneity. Detecting repeated patterns within tinnitus subgroups or within the greater tinnitus population in contrast to non-tinnitus groups allows us to cluster the larger tinnitus population into smaller subgroups, with possible common mechanisms to mediate tinnitus-related reaction, and to better understand the disorder as a whole. Clustering is possible due to commonality within certain subgroups as detected by replication studies. I will motivate a theoretical model of at least one prominent dimension of variability, that of severity or lack of successful habituation, and provide evidence for this model.

Over the past few decades, we have begun to understand the sensitivities of the neural correlates of tinnitus subgroups varying in severity. Our lab and other labs have used specific subgroups (e.g., mild tinnitus, bothersome tinnitus, those with normal hearing thresholds, with lateralized tinnitus, with gaze-evoked tinnitus, recent-onset tinnitus, pulsatile tinnitus, etc.) to understand how they differ from control groups or other subgroups. Slowly, evidence of invariant correlates of tinnitus as a whole and of the sensitivities related to tinnitus severity in these subgroups is accumulating across different studies. The primary source of reliable evidence appears to be task-based fMRI and resting-state functional connectivity studies, pointing to involvement of auditory, attention, emotion processing and default mode networks in these correlates. However, much work still needs to be done regarding specificities – for instance, how much of tinnitus distress can be attributed to hearing loss? What factors can lead to successful habituation, as recent-onset tinnitus changes to long-term tinnitus? One way to accelerate research in this arena is to use advanced clustering techniques to identify subgroups within a large dataset in an automated fashion based on functional connectivity. I will present preliminary results from our lab using such methodology.

Models of various subgroups or of the larger tinnitus population allow us to refine our understanding of the mechanisms and focus on the sources of intra- and inter-group variability. They also allow us to customize treatment or management options for the appropriate subgroups, thus increasing the possibility of tinnitus habituation.