Direct mapping of the cortical tinnitus network


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Introduction
Tinnitus occurs when damage to the peripheral auditory system leads to spontaneous brain activity that is interpreted as sound. Many types of brain activity show abnormalities in association with tinnitus, but it is not clear which of these relate to the phantom sound itself, as opposed to co-occurring factors or secondary consequences. Direct demonstration of the core tinnitus correlates requires high-precision recordings of neural activity combined with a behavioral paradigm in which the perception of tinnitus is manipulated and accurately reported upon by the subject. This has thus far not been possible in animal or human research. Here we present extensive intracranial recordings from an awake, behaving tinnitus patient during short-term modifications in perceived tinnitus loudness, permitting a robust characterization of the core tinnitus brain network.

Methods
A 50-year-old male patient with moderate-to-severe bilateral hearing loss (Fig. 1) and longstanding bilateral tinnitus underwent diagnostic electrophysiological and imaging studies (Fig. 2). A 22-channel subdural grid was implanted to assess brain activity during awake hearing tests (Fig. 2). Tinnitus was modulated by a 10-min inter-stimulus interval white noise stimulus. Auditory and tinnitus modulations were associated with clear demonstration of a distributed cortical ‘tinnitus system’, which involved both auditory and non-auditory regions, and all新冠 of oscillatory frequency bands. Tinnitus modulations were associated with complex restructuring of widespread within- and between-region coupling. The extended cortical areas found to be involved with tinnitus change are in general agreement with recent proposals of a tinnitus network of brain regions [2].

References

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1 Tinnitus characteristics and experimental paradigm

- **Power changes with tinnitus suppression**
- **Delta phase locking value changes with tinnitus suppression**
- **Local cross-frequency coupling changes with tinnitus suppression**
- **Summary of findings and proposed tinnitus networks**

**A pre-operative brain reconstruction is shown with electrode locations (black dots) estimated from the post-implantation CT and MRI scans. Circled electrodes denote significant power changes in a given frequency range following tinnitus suppression (see legend).**

Data-band (1-4 Hz) inter-channel phase locking value (PLV) changes coinciding with tinnitus suppression. Significant PLVs were summarized using a principal component analysis with one positive (red) and two negative (blue, cyan) PCs. Direction of PLV change is shown in the legend. Each principal component indicates two separate acts of electrode weights (solid and dashed circles), the size of the circle the magnitude of PLV change.

- **Left hemisphere.** i and ii) As described in Fig. 2.
- **Right hemisphere.** i) As described in Fig. 2.

**2 Power changes with tinnitus suppression**

**3 Delta phase locking value changes with tinnitus suppression**

**4 Local cross-frequency coupling changes with tinnitus suppression**

- Significant changes in local cross-frequency envelope coupling occurring with tinnitus suppression. Representation of α-ω are described in Fig. 2. Electrode sites with significant coupling changes are outlined with green boxes in Fig. 2 (A)-(D). Higher frequency leading posterior superior temporal gyrus 164 - lateral Heschl’s gyrus 173 - posterior medial temporal lobes. The plots are in polar coordinates on the complex plane with the horizontal axis representing real-valued (non-lagged) coupling, and the vertical imaginary (phase-lagged) coupling. Distance from the origin is the magnitude of coupling and the angle the phase delay associated with the coupling. Coupling on the right-hand side is positive, and on the left is inverse or ‘anti-coupling’. Above the origin denotes the lower frequency leading, and below the origin the higher frequency leading. Coupling was measured from the phase-locking value using the envelope data from the different frequencies. Significant changes in magnitude were shown with the size of the circle and changes in angle as rotation of the arrow. Red is baseline and black is during tinnitus suppression.

- The number by each plot indicates the electrode number at which coupling is illustrated, and the Greek letters show which frequency bands the coupling being illustrated is between. HGS = Heschl’s gyrus. STG = superior temporal gyrus. PHC = parahippocampal cortex. PLV = phase-locking value.

**5 Summary of findings and proposed tinnitus networks**

- **Summary of findings shown in (a), (c), and (d).** A schematic of the network used in (b), (c), and (d) is the brain activity characterizing each tinnitus sub-network (a), and the anatomical distribution of each of these sub-networks according to this categorization scheme (d). While text boxes with solid and dashed outlines indicate superficial and deep areas respectively.

- **Three tinnitus networks are proposed.** Tinnitus Driving Network (TDN), Tinnitus Perception Network (TPN), Tinnitus Memory Network (TMN), with interaction hub sites linking them together. STG = primary somatosensory cortex, IPC = inferior parietal cortex, STG = superior temporal gyrus, HG = Heschl’s gyrus, MTG = middle temporal gyrus, aMTL = anterior medial temporal lobe, PHC = parahippocampal cortex, TP = temporal pole. See Fig. 4 for frequency bands.