

## Changes in Resting-State fMRI Activity during Salicylate-Induced Tinnitus and Sound Stimulation

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**Target audience:** This study is mainly for the readers who work on functional MRI and tinnitus.

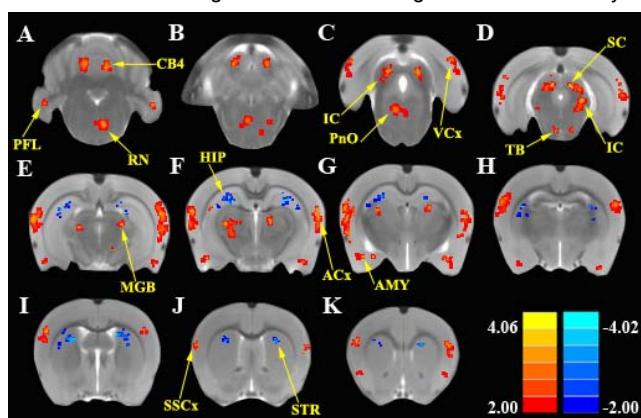
**Purpose:** The neural mechanisms that give rise to the phantom sound of tinnitus are poorly understood, but recent studies suggest that low frequency neural oscillatory activity contributes to tinnitus generation. To explore this issue, we measured the amplitude of low-frequency fluctuations (ALFF) in resting-state functional magnetic resonance imaging (fMRI) during salicylate-induced tinnitus and during sound stimulation.

**Methods:** Rats were scanned with a 7.0 T MRI system; 15 were treated with 300 mg/kg of salicylate to induce tinnitus and the remaining 15 were injected with saline as controls. Baseline fMRI scans were collected with music stimulation (85 dB SPL Leq) and without music. Afterwards, the measurements were repeated 2 h after salicylate or saline treatment. Statistical parametric mapping was used to determine which regions of the brain showed significant changes in ALFF activity due to salicylate or music stimulation.

**Results:** Salicylate induced significant bilateral increases of ALFF activity in several auditory region (auditory cortex (ACx), medial geniculate body (MGB), inferior colliculus (IC), trapezoid body (TB)) as well as several non-auditory regions (paraflocculus (PFL), reticular nucleus (RN), lobules 4 of cerebellum (CB4), superior colliculus (SC), visual cortex (VCx), somatosensory cortex (SSCx), amygdala (AMY)). In contrast, salicylate significantly decreased ALFF activity in the hippocampus (HIP) and striatum (STR). Furthermore, salicylate treatment enhanced (hyperactivity) the ALFF neural responses to music stimuli in several brain regions, including the ACx, IC, MGB, TB and SSCx.

**Discussion:** Salicylate significantly increased ALFF oscillatory activity in several auditory and non-auditory regions previously implicated in tinnitus, but also identified new regions of aberrant ALFF activity in visual and somatosensory cortex, sensory areas known to interconnect with auditory cortex. Music stimulation tended to potentiate the salicylate-induced hyperactivity in the ALFF responses in many auditory areas. Taken together, these results suggest that tinnitus may result from large increases in low-frequency neural oscillations within the central auditory pathway together with aberrant neural oscillations in the amygdala, paraflocculus and visual and somatosensory cortices.

**Conclusions:** Resting-state ALFF fMRI might be used to identify the aberrant neural networks in humans who suffer from severe, debilitating tinnitus.



**Figure 1:** Significant differences in ALFF between 2h-salicylate injection and 2h control without music. The red regions stood for higher ALFF and the blue regions stood for lower ALFF in salicylate group.