

Application for the Research Award Tinnitus & Hearing

Functional MRI Neurofeedback for Chronic Tinnitus: Clinical Description and Significance

Tinnitus, often experienced as a phantom auditory perception or “ringing in the ears,” affects up to 15% of the adult population in industrialized countries. Among them, 1–2% suffer from severe, chronic forms that significantly impair quality of life. Despite the high prevalence, no universal cure currently exists. Cognitive Behavioral Therapy (CBT) is recognized as the standard treatment, aiming to reduce distress through cognitive reframing, yet it does not directly address the underlying neural hyperactivity that characterizes chronic tinnitus.

Recent advances have suggested that maladaptive plasticity in the auditory cortex is central to the persistence of tinnitus symptoms. Real-time functional MRI (fMRI) neurofeedback (NF) has emerged as a novel approach, enabling patients to gain volitional control over aberrant brain activity by providing real-time visual feedback of their own auditory cortex activation. Earlier pilot studies indicated feasibility (Haller *et al.*, 2010), but larger controlled trials were needed.

The *NeuroTin* clinical trial (NCT05737888), conducted at Geneva University Hospitals (HUG) and EPFL (Campus Biotech, Geneva, Switzerland), represents the first prospective randomized study directly comparing real-time fMRI NF to CBT in patients with severe chronic tinnitus. Forty-three participants were randomized to receive either 15 individualized weekly sessions of fMRI NF or 10 weekly group CBT sessions. The primary outcome was change in the Tinnitus Handicap Inventory (THI), with additional measures of depression, anxiety, sleep quality, and general functioning.

Our results demonstrated that fMRI NF significantly outperformed CBT. At 6 months, participants in the fMRI NF arm showed a mean reduction of 28 points on the THI, compared with a 12-point reduction for CBT. Importantly, benefits in the fMRI group persisted at 12 months, whereas CBT effects diminished. Participants of the fMRI NF group also showed improvements in depression, anxiety, sleep quality, and overall functioning, highlighting the broader psychosocial impact of this approach. Functional MRI analyses confirmed

successful downregulation of auditory cortex activity at the group level, supporting the hypothesized mechanism of action.

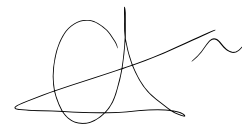
Clinically, these results are highly significant. They suggest that fMRI NF may represent the first non-invasive therapy capable of directly targeting the neural correlates of tinnitus, offering longer-lasting relief than CBT. While the technique requires specialized MRI infrastructure and trained staff, its implementation has already begun: we are currently integrating this protocol into clinical care at HUG and at a private clinic in Geneva (with Prof. Sven Haller and Prof. Pascal Senn), representing a pioneering step towards translation into standard practice. For patients with severe, refractory tinnitus, fMRI NF provides a promising therapeutic avenue where few effective options exist today.

In summary, this work demonstrates that fMRI NF is not only feasible but clinically superior to CBT for reducing tinnitus distress. By coupling advanced neuroimaging with patient-driven brain regulation, this method opens new perspectives for precision neuromodulation in psychiatry and neurology. The ongoing implementation in Geneva underlines its clinical relevance and translational potential for improving patient care worldwide.

I hope that this methodology can be brought further into other clinics, and that the continued work in advanced neuroimaging analysis of the large data set collected in this study will further inform fMRI NF procedures for specific tinnitus phenotypes.

I thank the Stiftung Tinnitus & Hören committee for considering my application.

Sincerely,

A handwritten signature in black ink, consisting of a large, stylized 'G' followed by a horizontal line and a small flourish.

Dr. Gninenko Nicolas