Altered listening changes the way we predict the auditory environment

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Impact paragraph
This dissertation assessed how altered listening changes how we predict the auditory environment that affects everyday life behavior. The findings suggest that aging and tinnitus affect multiple facets of prediction in audition, such as formal (‘what’) and temporal (‘when’) predictions.

Scientific impact
The research performed for this dissertation is mostly of fundamental nature and aimed to unravel the mechanisms underlying altered predictions in audition due to aging or phantom sound perception (tinnitus). Empirical studies employed oddball sequences consisting of tones differing in pitch that were presented either with regular or randomly timed inter-stimulus intervals. Although the experimental paradigms might seem to be of low ecological validity, the results can inform our understanding of audition in everyday life. For example, when hearing the beeps of the parking assistant in a car, the temporal distances and the pitch of the beeps inform about how close the car is to another object. Likewise, when participants in a swimming competition prepare and hear ‘take your marks’ followed by a beep, expectations about ‘what’ and ‘when’ certain auditory stimuli are delivered are formed. Such adaptation of behavior based on auditory ‘what’ and ‘when’ predictions changes during aging and might become more difficult, as indicated by the findings presented here. Moreover, in persons who experience tinnitus, classical sensory gating seems largely intact, which, however, depends on the tinnitus severity. In addition, adapting to auditory ‘what’ and ‘when’ predictions seems intact for earlier auditory EEG/ERP components, but affected in later components, potentially indicating altered selective attention. However, those results might depend on the severity of the tinnitus as well. Considering these results could lead to adaptations of auditory signals, such as, for example, warning signals in the parking assistant.

Potential clinical impact
Tinnitus prevalence increases with age and with hearing loss. Therefore, educating people about how to protect their hearing and thereby fostering healthy aging might reduce the development of tinnitus. There is currently also no cure for tinnitus and the precise etiology is still unknown (Langguth et al., 2013). Accordingly, further research into tinnitus, pursuing similar approaches as in the current dissertation are needed to explore underlying mechanisms and treatment options for persons with tinnitus.
Currently, there are multiple ways to treat tinnitus (Langguth et al., 2013). The reported research in this dissertation might inform ongoing work on a promising new alternative treatment possibility for persons with refractory tinnitus, which is deep brain stimulation (DBS) (Smit et al., 2016). DBS is an invasive method where electrodes are implanted in specific subcortical structures, such as the MGB, and alter neural functioning via high frequency stimulation. Animal research in noise-exposed rats (i.e., the animal model of tinnitus) is promising and suggests that DBS of the MGB can suppress thalamocortical synchronization as an underlying mechanism of tinnitus suppression (van Zwieten et al., 2021). Currently at the Maastricht University Medical Center +, the first human study of DBS targeting the auditory thalamus is performed and first patients have been included (van Zwieten et al., 2022). I am, together with my supervisors and colleagues, part of this project.

The urgent need for new alternative treatment options, which include DBS for persons with refractory tinnitus, cannot be underestimated as incidents of suicide or euthanasia linked to tinnitus have been documented in the past (Lewis, Stephens, & McKenna, 1994), but continue to occur until today (van Veen, Weerheim, Mostert, & van Delden, 2018).

**Economic impact**

In general, tinnitus is a debilitating condition and worldwide more than 740 million adults are affected by it, while more than 120 million suffer from the condition (Jarach et al., 2022). This means that the global burden of tinnitus is at the scale of leading causes of years lived with disabilities, which also encompass hearing loss, migraine, lower back, or neck pain (Vos et al., 2017). Due to the high prevalence rates, healthcare costs to help persons suffering from tinnitus are correspondingly high. It has been found that the costs for the Dutch health care system for tinnitus are higher than for chronic lower back pain (Maes et al., 2013). A systematic review found five studies conducted in the US (2), the Netherlands (2) and the UK (1) that evaluated healthcare costs for tinnitus management (Trochidis et al., 2021). The results showed that 1544-3429 Euros were spent for mean annual healthcare costs, while indirect costs due to the lack of productivity, were higher (2565-3702 Euros) (Trochidis et al., 2021). In Germany, mean public health care costs per patient were around 2207 Euros (adding a loss of 2301 Euros due to sick leave) for a group consisting of chronic tinnitus patients of the Berlin Charité (Tziridis, Friedrich, Brüeggemann, Mazurek, & Schulze, 2022). In addition, persons with tinnitus missed more than double the amount of work days of an average German
employee (Tziridis et al., 2022). Conducting research and educating about tinnitus, its potential causes, treatment options and the possible impact of tinnitus on everyday life, is therefore crucial to not only improve the quality of life but to also reduce global disease burden and healthcare costs.

**Current societal impact**

The findings presented in this dissertation were disseminated at conferences and shared with the general public via social platforms and the webpage of the laboratory. The findings were shared with the scientific community via articles published in international peer-reviewed journals that are openly accessible for scientists and the interested reader. The projects were presented at various occasions, ranging from invited lectures provided to university students or talks at faculty research days to more informal presentations at the Women Researcher’s Festival or at the Pint of Science Maastricht. These activities will be continued considering the potential implications of this work for education about (healthy) aging, hearing loss, or the treatment of tinnitus.