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Review

Neuroanatomical abnormalities in chronic tinnitus in the human brain

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ABSTRACT

In this paper, we review studies that have investigated brain morphology in chronic tinnitus in order to better understand the underlying pathophysiology of the disorder. Current consensus is that tinnitus is a disorder involving a distributed network of peripheral and central pathways in the nervous system. However, the precise mechanism remains elusive and it is unclear which structures are involved. Given that brain structure and function are highly related, identification of anatomical differences may shed light upon the mechanism of tinnitus generation and maintenance. We discuss anatomical changes in the auditory cortex, the limbic system, and prefrontal cortex, among others. Specifically, we discuss the gating mechanism of tinnitus and evaluate the evidence in support of the model from studies of brain anatomy. Although individual studies claim significant effects related to tinnitus, outcomes are divergent and even contradictory across studies. Moreover, results are often confounded by the presence of hearing loss. We conclude that, at present, the overall evidence for structural abnormalities specifically related to tinnitus is poor. As this area of research is expanding, we identify some key considerations for research design and propose strategies for future research.

Contents

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1. Introduction

Tinnitus, also known as "ringing in the ears", is a prevalent hearing disorder that can be characterised by the perception of a sound, like a tone or noise, in the absence of a corresponding external sound source. Symptoms can be acute (onset within the last 3 months) or chronic (typically lasting longer than 12 months). In rare cases, an objective source can be identified that is susceptible to treatment. In the majority of cases, however, tinnitus is subjective and occurs as an idiopathic condition of which the precise mechanism remains unknown. In clinical practice, common factors that affect the psychological and emotional well-being of people with tinnitus are fear, stress, anxiety, and depression, which in turn can cause sleep deprivation, poor concentration, and cognitive dysfunction (Baguley et al., 2013).

Tinnitus is a heterogeneous disorder with regard to its aetiology, presenting symptoms, and perceptual characteristics. In many cases tinnitus appears related to hearing loss, as both symptoms often occur together. Approximately 90% of people with chronic tinnitus have some form of hearing loss (Davis and Rafaie, 2000). Moreover, the acoustic characteristics of the tinnitus percept correspond to the region of hearing loss: a high-pitched tinnitus tends to be accompanied by high-frequency hearing loss (Sereda et al., 2011). At the same time, several observations indicate that tinnitus has neural correlates in the brain, regardless of peripheral damage that might trigger it. First, in many cases, tinnitus persists, and may even become worse, after the transection of the eighth cranial nerve, which destroys cochlear input to the brain (House and Brackmann, 1981; Baguley et al., 2013). Second, About 10% of people with tinnitus have normal hearing thresholds ($\leq$20 dB hearing level on frequencies from 0.25 to 8 kHz), at least on standard clinical audiometric examination (Barnea et al., 1990), while many people with hearing loss never develop tinnitus. However, since clinical audiometry is a rather crude measure of cochlear integrity, it is not a reliable marker for determining aetiology. Finally, tinnitus loudness measures obtained psychophysically are not strongly associated with tinnitus-related distress (Hiller and Goebel, 2006; Andersson, 2003). Therefore, detectable damage to the auditory periphery by itself seems neither sufficient nor required to give rise to chronic tinnitus, indicating extra-auditory modulation of the auditory sensation.

Tinnitus reflects a complex interplay of peripheral and central auditory mechanisms (e.g. Noreña and Farley, 2013). Fig. 1 displays the central auditory pathway that transmits auditory signals. It starts at the hair cells in the cochlea, from where signals are conveyed along the auditory nerve to the cochlear nucleus, superior olivary complex, inferior colliculus (IC) in the midbrain, the medial geniculate body (MGB) in the thalamus, in order to finally arrive at the auditory cortex.

One subtype of tinnitus appears to be associated with aberrant neural reorganisation at various stages of the central auditory system following deafferentation caused by peripheral hearing loss. Such reorganisation may take the form of plastic changes in the strength of existing synapses, the awakening of dormant synapses, or the growth of new connections altogether. Such changes may allow neurons tuned to sound frequencies that are affected by hearing loss to start responding to input from nearby intact frequency regions. It has previously been argued that this leads to a shift of the neuron's characteristic frequency, resulting in an over-representation of frequencies near the edge of the hearing loss (Eggermont and Roberts, 2004). However, recent human functional magnetic resonance imaging (MRI) evidence disputes that tonotopic map reorganisation is necessary for tinnitus (Langers et al., 2012). At the same time, neural synchronicity is increased when a disproportionately large population of neurons responds to the same input. Animal studies have also revealed tinnitus-related changes in neural activity at various stages of the auditory pathway that result from the imbalance between the excitatory and

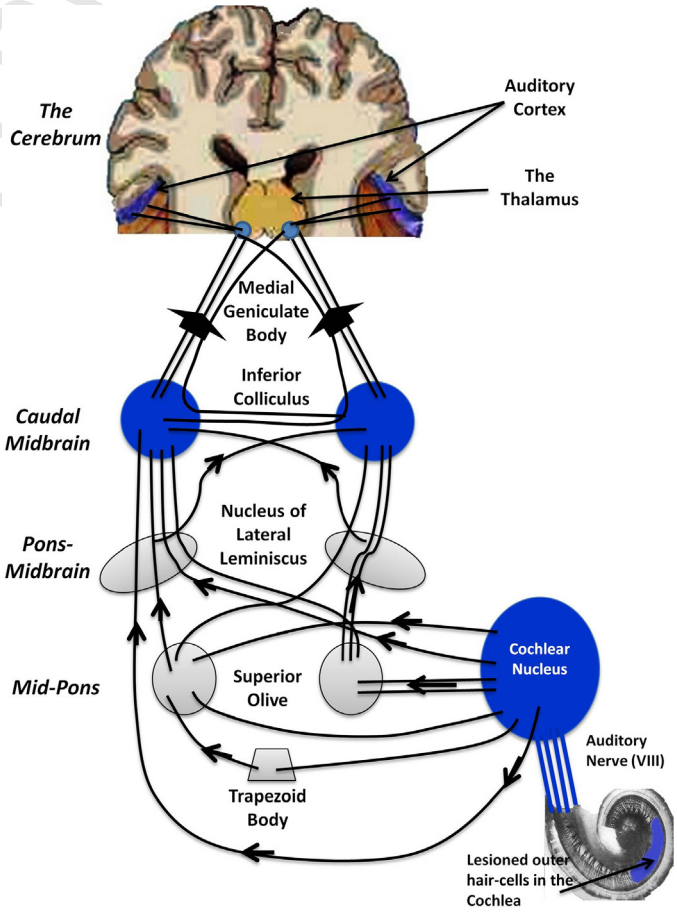

Fig. 1. Pathways and structures involved in tinnitus. Schematic of the ascending auditory pathways showing structures involved in tinnitus, from the cochlea to the auditory cortex in the brain. Human, but mainly animal studies of tinnitus have revealed increase in spontaneous activity, burst firing, and synchronous discharges at various stages of this pathway following lesions of the hair cells in the cochlea. These areas with structural and functional change in tinnitus are shown in blue, according to the review by Eggermont (2013). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.) Q3