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Review

An integrative model of tinnitus based on a central gain controlling neural sensitivity

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ABSTRACT

The purpose of the current review is to propose a model highlighting the putative connections between hearing loss and the phantom perception of tinnitus (tinnitus being accompanied by hearing loss in the majority, if not all, subjects). Sensory deprivation is followed by dramatic functional and structural changes in the auditory system. Notably, while cochlear injuries are accompanied by a reduced activity in the cochlear nerve, neural activity is increased at virtually all levels in the central auditory system. We suggest that this central hyperactivity could result from a central gain increase; the general purpose of this gain modulation being to adapt neural sensitivity to the reduced sensory inputs, preserving a stable mean firing and neural coding efficiency. However, maintaining neural homeostasis at all costs, in the event of an auditory system sensory deprivation, could be done at the price of amplifying "neural noise" due to the overall increase of gain (or sensitivity), ultimately resulting in the generation of tinnitus. The clinical implications of this model are also presented.

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1. Introduction

Hearing loss represents a major sensory deficit as it is largely prevalent in the general population, and can dramatically impair life quality; its social and economic impacts in developed countries is also considerable (estimated between 1% and 3% of the gross domestic product) (Ruben, 2000a,b; Anon, 2006; Mackenzie and Smith, 2009).

The main cause of hearing loss is ageing (presbyacusis); the increase of lifespan in developed countries increases the prevalence of sensory deficits. In addition to ageing, hearing loss can also be induced by exposure to loud noise. This is especially true in industrialized countries and for people living in urban environments where noisy situations are ubiquitous. Leisure-sound induced hearing loss is a very serious concern as compelling evidence has been provided for significant and increased risks of hearing loss with the widespread use of personal music players or similar devices (Daniel, 2007; Cazals et al., 2008). Finally, hearing loss can be induced by many other causes such as viral infection, ototoxic drugs (antibiotics, chemotherapy...), and cochlear ischemia. In summary, noise exposure (and other causes) will ultimately add to the damages caused by ageing to produce a hearing loss sooner and worse than would have occurred from age alone.

Cochlear insults result in an elevation of auditory thresholds and in a deterioration of the spectro-temporal decomposition of acoustic stimuli, which lead to diminished sound audibility and impaired speech understanding, especially in noise (Moore, 1995). In addition, cochlear insults have been suggested to cause or act as a trigger in the generation of "aberrant perceptions" such as tinnitus (auditory perception which is not related to any acoustic stimulus in the environment) and hyperacusis (overestimation of loudness, in which acoustic stimuli of moderate level are considered as being too loud or painful) (Noreña and Chery-Croze, 2007). The prevalence of tinnitus increases with age, peaking at around 14% between 60 and 69 years of age (prevalence slightly deceases after 69 years of age) (Shargorodsky et al., 2010). Tinnitus dramatically impairs the quality of life, leading in the most severe cases to depression or even suicide (Tyler and Baker, 1983; Folmer et al., 1999; Folmer and Griest, 2000; Sanchez et al., 1999). The annoyance caused by tinnitus can be even further increased by hyperacusis, which accompanies tinnitus in about 40% of cases (Dauman and Bouscau-Faure, 2005). The high prevalence of tinnitus and hyperacusis in the general population of industrialized countries and their large impact on the quality of life of subjects makes the need to develop effective therapies urgent. In this context, understanding the neurophysiological mechanisms of these "aberrant perceptions" is a critical endeavor which will facilitate this goal. In addition, tinnitus and hyperacusis are interesting and original phenomena in the sense that understanding these "distorted percepts" can shed some lights on the general mechanisms of auditory processing, especially when the auditory system is facing a sensory deprivation.

The aim of the present paper is manifold. First of all, we will review the current state of knowledge about the aberrant perceptions, especially tinnitus, which may result from sensory deprivation. Namely, we will present an overview of the "audiology of tinnitus" as it gives crucial insights to orient and inspire the search for the detailed mechanisms of tinnitus. Second, as cochlear insults are thought to act as a trigger or cause of tinnitus and hyperacusis, we will synthesize the knowledge regarding the effects of cochlear insults on peripheral (cochlear nerve) and central neural activity of the auditory system. Third, we will present an overview of the vast repertoire of mechanisms which could account for these central changes and provide a conceptual framework to interpret them. In brief, we propose that neural hyperactivity observed after hearing loss could result from an increase of a central gain which controls neural sensitivity in order to preserve neural homeostasis and neural coding efficiency. Fourth, we will present the view that tinnitus and hyperacusis could be a "side-effect" of this homeostatic plasticity. Finally, clinical implications of this model will be presented.

2. The audiology of tinnitus

By the "audiology of tinnitus", we refer to the studies carried out in human subjects which examined the characteristics of tinnitus, in terms of its psychoacoustic properties (pitch, loudness, maskability, residual inhibition), its putative causes and time course of occurrence. Knowledge of the audiology of tinnitus is a necessary pre-requisite and a starting point for studies addressing the neurophysiological mechanisms of tinnitus. We will see that some characteristics and properties of tinnitus (comorbidity between hearing loss and tinnitus, and the properties of tinnitus pitch, for instance) constitute guidelines for any explanatory model trying to account for tinnitus occurrence (Norena et al., 2002). This paragraph aims at providing the reader an overview of the most relevant