Physiological mechanisms of hyperacusis: an update

Hyperacusis is a debilitating hearing disorder that affects up to 10% of the general population. Advancing diagnosis and treatment of hyperacusis requires a better understanding of its underlying neural mechanisms. This is complicated by the diversity in both its cause and clinical presentation. This update will discuss recent efforts to model distinct forms of hyperacusis in animals to help elucidate potential mechanisms underlying this diverse disorder.

Hyperacusis encompasses a wide range of reactions to sound and, as such, its definition has been amorphous. Four subtypes of hyperacusis have recently been identified based on clinical presentation: excessive loudness, annoyance, fear, and pain [1]. Hyperacusis is often associated with hearing loss and the phantom sensation of tinnitus. Sound tolerance disturbances are observed, however, across a wide range of neurological disorders. These include neurodevelopmental disorders like Williams syndrome and autism spectrum disorders (ASD), psychiatric disorders like depression and post-traumatic stress disorder (PTSD), as well as chronic pain disorders like fibromyalgia, migraine, and complex regional pain syndrome (see Figure 1). Thus, hyperacusis is diverse in both its etiology and expression, and it is imperative to consider this diversity when attempting to define its physiological mechanisms.

Loudness hyperacusis, where moderately intense sounds are judged to be excessively loud, is the best characterised form of the disorder. Evidence points to excessive central gain enhancement as a major mechanism underlying loudness hyperacusis. In order to maintain sensitivity across an enormous range of intensities, central auditory neurons adapt their responsiveness, or ‘gain’, with changes to auditory input. If these gain control mechanisms are dysregulated, hearing loss can cause a maladaptive over-amplification of peripheral input, resulting in higher spontaneous and/or stimulus-evoked neural activity, which may present as tinnitus and/or hyperacusis, respectively (see Figure 2). Numerous studies in humans and animal models have found a paradoxical increase in sound-evoked activity following hearing loss, in regions spanning from the cochlear nucleus to the auditory cortex. In a recent study, my colleagues and I used a novel behavioural-electrophysiological paradigm to demonstrate that changes to...
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In hyperacusis, noxacus mechanisms mediate pain; (2) if targeting these peripheral mechanisms can rescue or reduce pain hyperacusis; and (3) whether auditory pain becomes centralised over time, similar to chronic pain disorders.

Continued refinement of the clinical definition for hyperacusis has greatly informed current approaches to understanding the physiological basis of the disorder. A fundamental question that remains for hyperacusis research is whether different forms of hyperacusis are mechanistically distinct disorders with overlapping presentation, or if they converge on a common pathophysiological mechanism. Current evidence suggests that different forms of hyperacusis may be mediated by distinct mechanisms. Future work must directly examine the various aspects of hyperacusis (loudness, emotion, pain) within the same subjects in order to determine how they may, or may not, overlap. Additionally, efforts must be made to model hyperacusis of etiology unrelated to hearing loss. For instance, there are well-developed genetic models of autism that may provide a novel avenue for examining mechanisms of decreased sound tolerance. With continued research, the field is positioned to make great insights into the pathophysiological mechanism of hyperacusis and, most importantly, develop novel therapies for this often devastating disorder.

References