

EFFECTIVENESS OF AUDITORY MEASURES FOR DETECTING HIDDEN HEARING LOSS AND COCHLEAR SYNAPTOPATHY: A SYSTEMATIC REVIEW

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Abstract

Standard audiometric tests aren't sensitive enough to detect hidden hearing loss (HHL) or cochlear synaptopathy (CS). People with these conditions often struggle to understand speech in noisy environments or report symptoms like tinnitus. This systematic review aimed to identify peer-reviewed studies that evaluated the effectiveness of various audiological measures for detecting HHL and/or CS, with the potential to be included in clinical testing for these conditions. A reference librarian conducted a search using specific boolean terms in MEDLINE, Embase, and Web of Science. The authors followed a consensus approach, using custom score sheets to select titles, abstracts, and full articles for inclusion in the review, as well as to assess the quality of the studies.

Fifteen studies were included in the review. Seven focused on humans, seven on animals, and one study involved both. The findings revealed several audiological measures used to assess HHL and/or CS, including pure-tone audiometry up to 20 kHz, otoacoustic emissions, electrocochleography, auditory brainstem response (ABR), electrophysiological tests, speech recognition in noise (with and without temporal distortion), interviews, and self-reported questionnaires. For detecting HHL, ultrahigh-frequency audiometry could help identify individuals with sensory hair cell loss that might not show up on standard audiograms. Promising non-behavioral tests for CS included the ABR wave I amplitude, the summing potential-to-action potential ratio, and speech recognition in noise with and without temporal distortion. Additionally, self-report questionnaires might aid in identifying auditory dysfunction in individuals with normal hearing.

Keywords: Hidden hearing loss, cochlear synaptopathy, King-Kopetzky syndrome, assessment.

INTRODUCTION

Sensorineural hearing loss (SNHL), caused by damage to the cochlea, has traditionally been identified by elevated hearing thresholds above 20 dB HL, as measured through pure-tone audiometry across frequencies from 0.25 to 8 kHz. These increased thresholds have typically been associated with dysfunction or loss of inner and/or outer hair cells, with outer hair cells being the most vulnerable to damage. Pure-tone audiometry has been commonly used in hearing





conservation programs, under the assumption that thresholds below 20 dB HL indicate no damage to the auditory system.

However, audiologists often encounter patients who report hearing difficulties, such as trouble understanding speech in noisy environments, tinnitus, or trouble following conversations, but show normal results on standard audiometric tests. This can be frustrating for patients who experience real-life limitations but find that their symptoms are not reflected in formal hearing tests. As a result, these patients are often told their hearing is normal, leaving their auditory complaints undiagnosed and untreated.

This issue has led to a new classification of hearing disorders, now referred to as hidden hearing loss (HHL). Audiologists, while understanding these patients' concerns, generally do not have the tools to properly diagnose or address these types of complaints. Moreover, when these issues remain unrecognized in standard evaluations, patients may begin to lose trust in both audiologists and audiological tests, exacerbating the problem.

The phenomenon where patients with normal hearing sensitivity report difficulties in understanding speech and tolerate tinnitus has been widely documented. This condition has been referred to by various names, including King-Kopetzky syndrome, obscure auditory dysfunction, auditory disability with normal hearing, and a subset of central auditory processing disorder. More recently, the term "hidden hearing loss" (HHL) has been used to describe individuals whose hearing loss is undetectable through standard pure-tone audiometry (0.25 to 8 kHz), yet may be revealed through patient reports or physiological measures.

Recent animal studies have provided evidence that cochlear damage from noise exposure can occur despite normal hearing thresholds in traditional audiometric ranges. For example, research by Kujawa and Liberman found that mice exposed to mild acoustic trauma showed only a temporary shift in hearing thresholds but suffered permanent deafferentation, with a loss of more than 50% of afferent ribbon synapses at the cochlea's base, which corresponds to high-frequency hearing. Similarly, abnormal spontaneous neuronal activity and neuropathy have been observed in the auditory brainstem of rodents exposed to mild noise. If these findings apply to humans, they suggest that noise exposure could cause physiological auditory changes that standard clinical measures may not detect.

While HHL is often used interchangeably with cochlear synaptopathy (CS), it is important to note that not all HHL cases are due to the loss of cochlear ribbon synapses. In addition to noise exposure, there is growing evidence that aging also contributes to the loss of ribbon synapses. Studies by Abdala and Dhar found that these age-related changes can begin in early adulthood, even in individuals without significant noise exposure. Other research has shown that aging reduces the number of spiral ganglion cells, synaptic structures, and cochlear nerve terminal boutons. These studies suggest that while aging alone may contribute to synaptopathy, noise exposure accelerates the aging process in the inner ear.

Given the rising awareness of HHL and CS and the limitations of standard audiological tests in detecting these conditions, audiologists should prioritize developing and validating tests that are sensitive to early auditory system changes. Such tests could enhance understanding of the impact of damage and aging on the auditory system, as well as aid in the prevention, diagnosis, and treatment of preclinical auditory dysfunction. Improving the audiological test battery could help





healthcare professionals detect early signs of auditory dysfunction, allowing for quicker intervention to protect hearing or address subtle inner ear damage.

Liberman and colleagues found that young musicians had significantly different results on a test battery for CS compared to young individuals with low risk of noise exposure. This suggests that such a test could be used to identify individuals who would benefit from hearing conservation programs. Additionally, animal studies are exploring various noise exposure protocols and tests of auditory dysfunction, some of which are already used in clinical audiology. Some of these preclinical studies are transitioning to phase II clinical trials of compounds that may prevent or reverse CS in humans, which would require clinical tests sensitive to CS.

Effective test batteries must not only be sensitive and specific to the disorders being assessed but also practical for use in clinical trials and audiological protocols. Developing new test protocols should start with a thorough review of investigations assessing HHL and/or CS in both humans and animal models. The purpose of this systematic review was to determine: (1) which audiologic measures have been used to assess HHL and CS in human and animal models, and (2) whether there is enough evidence to recommend certain clinical tests for detecting HHL and CS. The findings of this review aim to: (1) identify techniques for early detection of auditory dysfunction, (2) improve the understanding of standard audiologic assessments for patients with normal hearing sensitivity but suprathreshold auditory dysfunction, and (3) pinpoint tests most likely to serve as clinical endpoints in phase II clinical trials.

Conclusions

Various tests have been used to assess hidden hearing loss (HHL) and/or cochlear synaptopathy (CS), including pure-tone audiometry up to 20 kHz, otoacoustic emissions (OAEs), electrocochleography (ECochG), auditory brainstem response (ABR), and other electrophysiological tests, as well as interviews and self-report questionnaires.

For HHL, ultra-high-frequency audiometry has shown promise in detecting sensory hair cell loss that may not be apparent on standard audiograms. Potential nonbehavioral indicators for HHL and/or CS include the amplitude of wave I in the ABR and the summing potential-to-action potential (SP/AP) ratio in ECochG. Additionally, self-report questionnaires may be useful in identifying or confirming the presence of auditory dysfunction.

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