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Revisiones

# Hidden Hearing Loss, Cochlear Synaptopathy and Occupational Noise

## Pérdida Auditiva Oculta, Sinaptopatía Coclear y Ruido Ocupacional

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Authors declare have no conflicts of interest.

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## Resumen

**Introducción:** La sinaptopatía coclear por exposición a ruido (SCER) es definida como una alteración funcional transitoria o permanente de las sinapsis en cinta de las células pilosas internas de la cóclea. Este artículo tiene el objetivo de comentar la utilidad de la identificación temprana de la pérdida auditiva oculta por SCER basado en marcadores audiológicos y en la metodología usada en grupos clínicos para su búsqueda.

**Método:** Revisión de la literatura relacionada en bases científicas y la narración descriptiva de los resultados.

**Resultados:** La SCER produce una pérdida auditiva oculta en pacientes con audiograma normal, principalmente obreros o individuos expuestos a niveles de ruido intenso. Los principales estudios de identificación de la SCER han sido realizados principalmente en estudiantes universitarios o en músicos.

**Conclusiones:** Son necesarios ajustes en la política de salud auditiva para una amplia identificación temprana de la SCER en las poblaciones en riesgo para la pérdida auditiva oculta y luchar por una regulación del daño.

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**Palabras clave:** Pérdida auditiva oculta; Sinaptopatía coclear; Ruido ocupacional.

## Abstract

**Introduction:** Cochlear synaptopathy after noise exposure (CSNE) is defined as the transient or permanent functional damage to the ribbon synapsis of the inner hair cells of the cochlea. This article has the objective of comment the usefulness of early identification of the hidden hearing loss after CSNE based on audiological markers and in changes in the clinical methodology in clinical groups for its searching.

**Method:** Review of related literature in scientific databases and narrative description of results.

**Results:** CSNE results in a hidden hearing loss in patients with normal pitch audiogram, mainly workers or individuals exposed to high noise levels. The main studies of identification have been performed mainly in groups of students from college or musicians.

**Conclusions:** Is necessary adjustments in hearing health policy for an wide early identification of CSNE in at risk populations for the identification of the hidden hearing loss and fight for its damage regulation.

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**Keywords:** Hidden hearing loss; Cochlear synaptopathy; Occupational noise.

## Introduction

The inner hair cells of the cochlea have a very special synapsis in “ribbon” fashion. This structure has been the point of attention for the study of cochlear synaptopathy by noise exposure (CSNE). Auditory fibers joined to synapsis go to the ganglionic neurons of the cochlea. The increased excitotoxicity of glutamate in the ribbon synapsis is the most accepted basis of an alteration due to a temporal variation in the auditory threshold, without damage of the inner hair cells which produce a dysfunction on both the auditory fibers and the ganglionic neurons.<sup>(1)</sup> In this case, the structures more susceptible to be damaged are the auditory fibers located near the modiolus. The auditory fibers are thinner and transfer at a low stimuli rate in order to codify sounds of high loudness or supra-threshold.<sup>(2)</sup> This finding was confirmed by Schaette and McAlpine,<sup>(3)</sup> in women with tinnitus and normal audiograms who showed lower amplitude of the first wave of the auditory brainstem responses (ABR) at supra-threshold intensity (see Table 1). These authors used for the first time the term: “hidden hearing loss” (HHL) based on the fact that tinnitus was present because of cochlear damage despite a normal audiogram.

In 2018 the American Speech and Hearing Association, based on noise interference symptoms, promoted opinions encounters about cases of CSNE versus central auditory processing disorders (CAPD). According with some experts interference in hearing perception by noise is more relevant for clinical purposes in CAPD compared with the synaptopathy.<sup>(4)</sup>

### Operational Variables

For purposes of this article “Occupational noise” is the acoustic energy received by workers in their auditory system in certain industries. It is mainly an unpleasant noise for her/his hearing. The sustained exposure can cause permanent hearing damage. There are four types of occupational noise: continuous, intermittent, impulsive and low frequency noise.<sup>(5)</sup>

On the other hand, “Music” is an intentionally organized acoustic art, whose medium is sound and silence, with core elements of pitch (melody and harmony), rhythm (meter, tempo, and articulation), dynamics, and the qualities of timbre and texture”.<sup>(6)</sup>

### Objective

The goal of this communication was comment the usefulness of early identification of hearing loss of CSNE based on audiological markers and discuss the changes in the used clinical methodology for its searching.

## Methods

Articles addressing “cochlear synaptopathy” and “hidden hearing loss” from peer reviewed journals were identified by each of the authors. Search from literature were performed in PubMed and Google Scholar data bases and articles were selected in three phases: by title, by abstract, and by full text. The search of the articles in scientific journals found around of 330 reports. Results of the screening were discussed among authors and discrepancies were commented until consensus was reached. A critical narrative review of the development of cochlear synaptopathy concept, terminology, and specify the fundamental topics was performed.

## Results

### Noise in Working Centers

The Center for Diseases Control in the United States of America (USA) reported that 22 million workers were exposed to hearing damage by high levels of work noise each year.<sup>(5)</sup> In other example, the Mexican Institute of Social Security (IMSS, for the abbreviation in Spanish) registered hearing damage by noise exposure at working places as the second cause of a typified work disease susceptible of indemnization.<sup>(7)</sup>

The working environment is considered harmful for purposes of clinic audiological evaluation based on what the worker reports. This includes: full time work in a noisy environment, in which loud intensity talking is needed for the worker to be heard by her/his work peers,<sup>(8)</sup> (see Table 1), or whether tinnitus or hearing loss are present at the end of the working day. This last manifestation is known as “transient hearing loss”, in opposite to a “permanent hearing loss”.<sup>(9)</sup>

### **Preventive Measures Against Noise Exposure in Work Environment**

The most common way to prevent hearing loss by noise exposure is occlusion of the external auditory meatus with plugs or headphones, even though it is not the most effective one. Greater effectiveness is reported through reduction of sound emissions from industrial machinery, and through changes in workplaces provided with environmental features that are able to reduce vibrational energy around workers, but these changes are the most expensive. One study of Costa-Meira et al. in 18-65 year-old workers highlighted the disadvantage position of females because of poor use of auditory protection. On the other hand, males use more protection especially either because their socio-economic level is better or because they have had a previous audiological test.<sup>(10)</sup>

### **Detection and Risk Factors**

In the Beaver Dam Offspring Study, Tremblay et al. selected a group of people excluding Hispanics.<sup>(8)</sup> (see Table 1). Although exclusion of Hispanics was later considered as a limitation by the authors themselves in their paper conclusions, they used a four questions scale selected from the Hearing Handicap Inventory for Adults Screening and the Hearing Handicap Inventory for Elderly, and detected as main risk factors: exposure to solvents, metals, and noise, low economic income, less physical activity, substance abuse, several audiological examinations, tinnitus and dizziness. Other study such as the carried-out by Kwon and Lee described also as main risk factors: poor dietary habits, smoking, and co-morbidity with chronic degenerative diseases.<sup>(9)</sup>

Some authors suggest a better tolerance for hearing damage in young subjects because of greater elasticity of the basilar membrane. Although Barrero et al. stated that the opinion is not conclusive,<sup>(11)</sup> these authors observed that the first symptoms of hearing loss appeared in middle-aged workers, and that there may be related with being close to a noise sources at her/his working place.<sup>(11)</sup> There are other reports of age related synaptopathy so there may be a possible overlapping of some risk factors proposed in different studies.

Prendergast et al. asked themselves: “is the cochlear synaptopathy by noise exposure present in youths?”<sup>(12)</sup> To answer the question they performed a study in a group of young subjects aged >18 years, with a mean of 23.3 year old, analyzing the possible influence of age in noise exposure. These authors used psychoacoustics tests and evaluated the amplitude of wave I in ABR, in youths with poor evidence of CSNE (Table I). The authors excluded maturational aspects through intersubject variability, and found low frequency of CSNE and stated as a possible explanation the greater vulnerability of some subjects to CSNE. Researchers added a possible recovery factors hypothesis in the ribbon type preganglionic synapsis damage that could be observed in animal models, such as chinchillas exposed to noise.

Among work environment with dangerous activities for hearing are those carried out in factories with noisy machines and heavy equipment as sawmills. Other examples are building construction, mining, and army industries with activities with gun shoots, moreover leisure activities, hunting, and shooting, highlight by their increased risk for hearing damage.

After the youth, some authors identified ageing as a risk factor for hearing injury independent of the type of noise exposure. It has been observed that there is an increased frequency of hearing loss in both genders in older people. Women may show best hearing than men despite environmental noise exposure. Inheritance seems to be related with hearing loss after noise exposure in older age.<sup>(11)</sup> (see Table 1). At the same time, other authors mentioned that inner ear damage by noise exposure affects the left ear more frequently than the right one.<sup>(9)</sup> An a possible explanation of this fact was given by Kwon and Lee,<sup>(9)</sup> who speculate that predominance of hearing loss at the left side was gave by the pro-

tective effect of the left olivo-cochlear fasciculi to the right auditory pathway, which may help to explain why in some audiologic tests, such as the middle ear muscle reflex show asymmetric alterations.<sup>(11)</sup>

Prendergast et al. measured the interaction among intensity and duration of noise in working environment as the main variables of their research.<sup>(12)</sup> Summation of time exposed to noise by the worker was the more important variable in the risk of hearing damage (see Table 1).

Besides physiologic factors, the fine architecture of the structures of the cochlea is damaged by noise by means of metabolic mechanisms which may persist for a long period. The factors that cause damage are: an increase of free radicals, reactive mechanisms to oxygen and nitrogen in the outer hair cells followed by production of cytokines and activation of apoptotic mechanisms. High level of noise produce mechanical adverse effects to injuring the hair cells, the pillar cells, and the tectorial membrane.<sup>(9)</sup>

## Discussion

### General Considerations

CSNE with HHL may be a subtle pathology hard to identify in its beginnings but with important consequences in the hearing health of workers in noisy industries and in individuals exposed to high level of noise in leisure activities such as it will be commented as follows.

The hearing impairment was observed in individuals that even have suspected normal hearing, and was experimented as suboptimal function in their daily hearing. This is why CSNE they belong to the HHL category, although in their paper Tremblay et al. considered better the term: "hearing difficulty" and also found that 12% (n = 682 with age groups between 21 to 67 year-old) had this HHL.<sup>(8)</sup> (see Table 1).

Besides clinical aspects, there are several research unknown fields involved in CSNE research, such as: anatomical, physiological, molecular, biochemical and genetics topics. I.e. Lobarinas et al.,<sup>(13)</sup> emphasized the implications of the ribbon type synopsis in CSNE and its possible role when is damaged, as a predictor of the temporary threshold shifts of more than 30 dB in the first 24 hours after noise exposure in rats that were exposed to noise between 106 to 108 dB between 8 to 16 KHz. The same authors referred to the limited relationship between recreational noise and the decrease of amplitude of wave I of the ABR, they also found inconsistency in this decrease except when there is a significant level of hearing loss or a permanent threshold shift.<sup>(13)</sup>

### Audiological Tests and Groups of Study

Tonal audiogram is the first test of an audiological examination. Cochlear damage by noise exposure causes an increased threshold in high frequencies, firstly in 3, 4 and 6 KHz and a recovery at 8 KHz. Low frequencies can also be altered with the time. Abnormalities in ABR and P300 wave of the event related potentials can also be present.<sup>(9)</sup> Vigilance of risk factors and a synergy with ototoxic drugs and solvents exposure must be performed.<sup>(8)</sup> We join to the proposal of other authors of performing high frequency audiometry and not to limit the study of patients to pure tone audiometry and non-distorted speech audiometry.<sup>(14)</sup> It is also necessary a more precise analysis of audiograms obtained with half an octave in high frequency tones.

It is important to take into account that the same pathophysiology of the cochlear synaptopathy is present even when hearing loss is not hidden.<sup>(14)</sup> Moreover, there can be thresholds over the normal range in few frequencies in superficial loss levels.<sup>(15)</sup>

In function of the intensity, the study of phonetically balanced words of Jerger and Hayes described the "roll over" phenomenon identifying a greater neural damage in individuals with tumors such as vestibular Schwannomas.<sup>(16)</sup> In CSNE, mistakes in tests with words could be less dramatic than in tumors at supra threshold levels.

Middle ear muscles reflexes (MEMR) are supra-threshold audiological tests used in the identification of hearing loss. Guest et al. proposed the use of MEMR, being the most sensitive indicators of CSNE and suggest that are related with the amplitude of wave I of ABR in mice.<sup>(17)</sup> However, in human beings,

contrary of what was expected, the authors did not find an association between MEMR and other tests for cochlear synaptopathy or with tinnitus (see Table 1).

Additionally the papers by Prendergrast et al.,<sup>(12)</sup> Lobarinas et al.,<sup>(13)</sup> and Le Prell,<sup>(14)</sup> they state that it is possible, that in order to present CSNE, human beings that have been exposed to high noise, possibly have had previous hearing loss in high frequencies.

### **Laboral Legislation**

The medico-legal aspects in relation to the compensation to which the worker is entitled for the hearing damage caused by exposure to noise in the work environment, specifically assess permanent hearing disorders, that are established based on tonal audiometry in conversational frequencies. The remuneration of the percentage of hearing impairment is made based on binaural loss by averaging the hearing thresholds in the frequencies 500, 1000, 2000, 3000 and/or 4000 Hertz, which are those used in human communication. It shall not be considered hearing loss when the hearing threshold is 25 dB. Practice that is carried out both in Europe and in many countries of America and that does not include any compensation for patients with normal or near-normal audiograms.<sup>(18)</sup> In agreement, the Mexican legislation for noise related hearing loss due to exposure in working environments does not imply indemnization for patients with normal audiograms or near normality. Therefore, this point deserves more attention in the future because it will be the subject of discussion for future legislative policies, which should include personalized prevention and specific treatment strategies based on a comprehensive view of the worker, occupation, genetics and pathology of an individual.

### **Noise and Music**

Musical experience at high sound levels has less frequency of CSNE with respect to workers exposed to industrial environment with noisy machines. This because music in college context can result in a favorable effect for brain plasticity and psychoacoustics performance also. It is believed that industry environment is more aggressive to the inner ear compared with environmental music of several types and with other loud sounds at leisure time. Furthermore, cultural patterns between university people and industry workers could be very different, especially in developing countries. Studies of Skoe and Kraus have considered the possibility that music exerts a protector effect due to educative musical training in early life.<sup>(18)</sup> In this study, one evident benefit was observed in the register of significant improvement of ABR in the studied subjects.<sup>(19)</sup>

## **Conclusions**

This review shows fundamental topics in the state of the scientific knowledge in relation to the pathophysiology and the identification of CSNE based in observations carried-out in laboratory animals, since in human beings with normal audiometrical and electrophysiological tests the results are not completely confirmatory yet.

It is probably that the industrial environment has more dangerous factors for the cochlear synapsis, because of its intrinsic features and also for the type of noise exposure that workers experimented when compared to noise exposure in a college environment, where students listen music often. As this short communication suggests of the knowledge available, it will be probably necessary to adjust the legislation for working centers where noise can result in CSNE type of cochlear damage.

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**Table 1.** Main studies of subjects with risk factors or probability of cochlear synaptopathy after noise exposure.

Year	Author	N	Gender	Age in the study	Subjects	Inclusion criteria	Tests	Studied frequencies	Observations
2015	Costa-Meira et al.	2,429 workers in residential area in Brasil 299 positive	Both	18- 65 years	12.3% reported noise in work area. 299 workers positive to questions about intensity and duration of exposure	Register in sociodemographic security and health	Questionnaire	Personal report of hearing loss	Females with hearing loss = 39, negative 78. Males with hearing loss = 45, negative 137
2015	Tremblay et al.	2783/686/82	Both	21-67 years	Subgroups that report or not hearing loss with normal pure tone audiogram	Non-hispanics participants Normal audiogram Questionnaire of hearing loss	Audiogram and 4 specific questions. OAE. Words in silence and with competitive ipsilateral message at 8 dB re SRT and 36 dB HL re 2 KHz threshold	0.5-8 KHz including 3 & 6 KHz	Prevalence HHL and risk factors of 12% & 2.9%
2011	Schaette & McAlpine	33	Women	36-33 years	University students and personal	Normal audiogram with and without tinnitus	Audiogram and A. at HF. ABR	0.125-8 KHz and 12-16 KHz	Wave I of ABR <amplitude with tinnitus
2016	Lieberman	34	Both	Average of 25 years	University students of music/communication high/low risk	English speakers, normal audiogram <25 dB	Audiogram and A. at HF. NU6 words at 35 dBHL. S, C, RV, H. DPOAE, ECoG: SP/AP	2-6 KHz and 8-16 KHz	Significant results with words, ECoG: SP/AP
2017	Prendergast et al.	126	Boths	18 to 36 years. Average in men 23.3 years; women 22.9 years	Adults young musicians, or workers of music industry Work in night shows and concerts	Normal hearing till 8 KHz	Hearing threshold <25dB . ABR 80 and 100 dB, FFR 80 dB. Questionnaires of noise exposure	0.25-8 and 16 KHz bilaterally	Wave I of ABR with amplitude decrease, also observed in waves III and V. ABR and FFR not significant in young adults. With high noise women showed thresholds at 16KHz with great effect than men
2019	Guest et al..	70 (19 with tinnitus).	Boths	18 to 39 years	University groups	Patients studied for tinnitus and alterations in word perception	Normal audiometry (<20dB HL in both ears). Tympanograms. Thresholds of MEMR for 1, 2 y 4 KHz	0.25-8 KHz including 3, 6, 10, and 14 KHz.	No evidence of synaptopathy. Tinnitus significant for thresholds of MEMRs
2020	Barrero et al.	1418 Men = 1233 Women = 185	Both	Average of 38 years of age Range 17-66 years Predominant among 29-49 years of age	Workers from different sources and risk factors	Personal data and demography, works with noise and no-occupational (family history of hearing loss).	SAL index/ELI index, OLI overall loss index, percentage index. Audiometry. Questionnaire	Air conducted Pure tone audiometry. Percentage of biaural loss	Great risk of hearing loss in men with history ofl hypoacusis and age effect in front to any type of noise

Footpage Legend

Abbreviations. ABR = auditory brainstem response. A at HF = audiogram at high frequencies. C = compression. dB = decibels. DPOAE = distortion products-oto-acoustic emissions. ECoG = electrocochleogram. ELI = early-hearing loss index. FFR = frequency following responses. H = hyperacusis. HHL = hidden hearing loss. HL = hearing level. KHz = kilohertz. MEMR = middle ear muscles reflex. NU6 = Northwestern University test no. 6. OAE = otoacoustic emissions. OLI = overall loss index. RV = reverberance. S = silence. SAL = speech average loss. SP/AP = summation potential/action potential. SRT = speech reception threshold. W/compr. = word with compression.