

**1685a USE OF THE KURTOSIS STATISTIC TO BETTER ESTIMATE THE EFFECT OF NOISE AND SOLVENT PROFESSIONAL EXPOSURE ON HEARING THRESHOLD**

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**Introduction** The aim of this exploratory study was to examine whether the kurtosis metric can contribute to investigations of the effects of combined exposure to noise and solvents on human hearing thresholds.

**Methods** Twenty factory workers exposed to noise and solvents along with 20 workers of similar age exposed only to noise in southern China were investigated using pure-tone audiometry (1000–8000 Hz). Exposure histories and shift-long noise recording files were obtained for each participant. The data was used in the calculation of their Cumulative Noise Exposure (CNE) which was adjusted using the kurtosis data recorded for each worker. Passive samplers were used to collect solvent concentrations for each worker exposed to solvents over the full work shift.

**Results** We observed an interaction between noise exposure and solvents for the hearing threshold at 6000 Hz. This effect was observed only when the CNE level was adjusted by the kurtosis metric.

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**1685b HEARING PROCESS**

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**Introduction** Many workers suffer from hearing dysfunctions, even if their exposure to noise and chemicals is within the established exposure limits. The mechanisms of action for combined exposure possible can be determined by sound perception indicators, and in this sense the appropriate health assessment can be performed.

**Methods** This exposure is based on the review of medical literature about the hearing process.

**Result** The hazardous synergistic effects of some chemicals and noise can be well understood with a deep knowledge of the hearing process. Pure-tone air-conduction audiometry is the most used method to check the state of the worker's auditory system, but it has been proven to be insufficient when hearing loss is due to a combined exposure to noise and ototoxic agents, since it does not allow the source of the problem to be correctly identified.

**Discussion** The hearing system can be affected not only by the noise, but also by its combination with ototoxic chemical agents, this damage can affect from the cochlea to the higher auditory pathways. It's important to use tools that evaluate the auditory system comprehensively, using tests that help to

differentiate between the individual or the combined effects of noise and chemicals on hearing, such as the distortion product otoacoustic emissions. Furthermore, exposure limits to noise and ototoxic chemical agents lower than those set out in should be considered, taking into account their synergistic effect.

**1685c OTOACOUSTIC EMISSIONS ARE SENSITIVE TO OXIDATIVE STRESS IN HUMANS EXPOSED TO NOISE AND STYRENE**

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**Introduction** Evidence for synergistic interaction between noise and styrene in inducing cochlear damage can be found in the literature. At present a mechanistic explanation of such an interaction is not available, although animal studies are shedding light on the phenomenon. At the aim of clarifying the effect of simultaneous exposure to noise (mild level) and styrene on the cochlear functionality, distortion product otoacoustic emissions (DPOAEs) were used as biomarkers of the cochlear status. In this work, the correlation between the DPOAE level and blood concentration of oxidative stress biomarkers is studied in a sample of subjects professionally exposed to styrene. This study is aimed at investigating the role of the oxidative stress in the inner ear damage in workers exposed to styrene.

**Methods** Nine subjects exposed to styrene in a fibreglass factory and eight control subjects were enrolled in this study. The mean age was the same in the exposed and control groups. The airborne concentration of styrene was evaluated by means of ambiental and personal samplers. The end shift urinary concentration of the phenylglyoxylic (PGA) and mandelic acid (MA) was also evaluated. Distortion product otoacoustic emissions were measured in the exposed workers and in a control group. The DPOAE component generated by a nonlinear mechanism, characterised by zero latency, and the long-latency component, generated by a linear reflection mechanism, were separately analysed, using a time-frequency domain wavelet filter for component unmixing.

The urinary concentration of the DNA and RNA oxidation products, namely 8-oxo-7,8-dihydroguanine (oxoGua), 8-oxo-7,8-dihydro-20-deoxyguanosine (oxodGuo), and 8-oxo-7,8-dihydroguanosine (oxoGuo), were evaluated and correlated to the DPOAE level.

**Results** A statistically significant negative correlation was found between the DPOAE level and the PGA and MA urinary concentration. A dose response relation was proposed correlating the styrene concentration, the exposure duration and the DPOAE level, used as outcome variables.

High levels of the oxidative damage biomarkers were found in the workers exposed to high levels of styrene. Significant negative correlation was found between the otoacoustic emission distortion component levels and the concentration of the oxoGuo biomarker.

**Conclusions** This experiment confirms that the styrene exposure is responsible for cochlear dysfunctionality. A quantitative relation between the styrene exposure and the reduction of cochlear functionality, expressed in terms of DPOAE amplitude, can be found. Exposure-induced damage of the cochlear amplifier is shown in the mid-frequency range, confirming the results of animal experiments, in which hair cells in the middle turn of the cochlea were damaged. Hearing damage is consistent with the outer hair cell apoptosis pathway associated with oxidative stress.

**1685d COCHLEOTOXICITY AND NEUROPHARMACOLOGY OF AROMATIC SOLVENTS CAN POTENTIATE NOISE-INDUCED HEARING LOSS**

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The toxic mechanisms involved in solvent-induced hearing loss are not well-known, even though, today, the disturbances of  $K^+$  recycling and the generation of reactive oxygen species in the organ of Corti are considered as determinant. The cochleotoxic effects of these pollutants shows up after a long-lasting exposure and ends up by the phagocytosis of outer hair cells (OHCs) initiated by the supporting cells. Because of the lipid peroxidation which takes place within the OHC membranes, the latter are more vulnerable to noise. As a result, a solvent exposure can exacerbate the traumatic effects of noise at the level of the organ of Corti. Such a phenomenon is not the only one capable of explaining the synergistic effects of a co-exposure to noise and solvents. Indeed, solvents can also disturb the function of the middle-ear acoustic reflex which protects against continuous high-intensity noises by contracting the stapes muscle and thereby reduces the amount of acoustic energy penetrating into the cochlea.

Recently, it has been shown that solvents like benzene, toluene, ethylbenzene and xylenes disturb the function of the middle-ear reflex and therefore allow noise to be more cochlea-traumatic. These neuropharmacological effects are likely due to an action of the pollutants on the targeted neuroreceptors of the acoustic reflex circuit. The interaction 'pollutants vs receptors' would be determined by the stereo-specificity rather than by the lipophilicity of the molecules. Both cochleotoxic and neuropharmacological phenomena can induce the traumatic effect of the noise on the organ of Corti. Partial disruption of the organ of Corti, or temporary disturbances of the reflex by solvents, both can increase the risk of occupational deafness encountered by co-exposed workers. Despite these statements, the European hearing conservation programs have not changed their concerns about the co-exposures to noise and solvents.

**1685e NANOTECHNOLOGY IN EAR DISEASES: PROMISING AND CHALLENGING ISSUES**

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**Introduction** Nanotechnology and nanomedicine are innovative and rapidly developing areas, aimed to develop nanoscale structures and devices whose physico-chemical properties may be useful for pathological diagnosis and treatment. To date, almost no effective remedies are available for inner ear diseases, i.e. sensorineural hearing loss and vertigo, that are common and disabling conditions caused by the degeneration of sensory-neural transducer epithelial cells and nerve cells. In this scenario, nanotechnology attracted increasing scientific interests for its potential to improve existing treatments, but also raised concerns on possible, still not-fully explored, adverse effects exerted by nanomaterials on the auditory system. Therefore, aim of this work is to provide a comprehensive overview of existing evidence concerning biological interactions between nano-based applications and ear structures.

**Methods** A systematic search and revision of experimental *in vitro* and *in vivo* studies addressing possible effects exerted by nano-enhanced remedies on auditory system was performed in the Pubmed, Scopus, and ISI Web of Science databases.

**Results** Nanoparticle-based systems proved a high potential for inner ear delivery of various therapeutic agents in animal models and were reported to exert a significant protection against drugs- (i.e. cisplatin) as well as noise-induced hearing loss. However, nanomaterials were also able to induce ototoxic effects on cultured cochlear epithelium, as well as middle and inner ear mucosa permeability changes, associated with hearing loss in animals trans-tympanically treated with nanoparticles.

**Discussion** Conflicting results emerged concerning nanotechnology applications in otology. Nano-enhanced systems may provide benefits to ear disease treatments, overcoming inner ear anatomic inaccessibility, minimising systemic treatment side effects, allowing a specific and sustained drug release in inner ear fluids. However, other investigations are necessary to deeply assess nano-ototoxicity risks particularly in relation to nanomaterial physico-chemical characterisation, and verify issues of biocompatibility, drug release profile, and biosafety before achieving a successful clinical application.

**1685f HOW DOES MECHANICAL VIBRATION REACH THE COCHLEA?**

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**Introduction** Several epidemiological studies highlighted a synergistic interaction between noise and mechanical vibration exposure.<sup>1</sup> The etiologic mechanism is still missing. Moreover, the measured transmissibility from the hand to the head seems to be poor. At the shoulder, frequency over 30 Hz are practically suppressed. If there are not any vibration left, how can mechanical energy interact with the cochlea? The aim of this speculation is to approach the transmission of vibration from entering point to the cochlea from a different point of view.

**Proposed methods** In the seminar on hand-arm vibration exposure<sup>3</sup> to isolated and repeated shock vibrations held in October 2015 in Beijing it was suggested that a wider spectral component of mechanical vibration may travel in the blood vessels and impair vasoregulation and nerve terminations in