Editorial

In continuation of our first Newsletter, this editorial will provide highlights from several selected articles of the publications concerning hearing loss between January and April 2014.

There was only one randomized controlled trial (RCT) reported among the 48 hits between January and April 2014. Marshak et al. (2014) performed a prospective, RCT to investigate the role of intratympanic Dexamethasone (ITD) in the prevention of Cisplatin (Cis)-induced hearing loss. Employing a within-subject design, ITD was injected into one ear (randomly selected) and compared to the opposite non-treated ear (served as control) of 26 patients with neoplastic disease. Baseline (before Cis) audiometry and Distortion Product Otoacoustic Emissions (DPOAEs) tests were compared to follow-up assessments between the ITD and control ears after Cis treatments. Of the 15 subjects completing the study, pure tone threshold (PTT) at 8000 Hz and pure tone average threshold at 4000 to 8000 Hz significantly increased in both the ITD and control ears. However, a significant increase in the PTT at 6000 Hz was observed in the control but not in the ITD group. Results also revealed a significant decrease in the DPOAE average signal-to-noise ratio (SNR) for the f2 frequencies 7031 and 8391 Hz.

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and SNR average for 4000 to 8000 Hz for control but not ITD ears. Based on the findings the authors conclude that ITD might have potential in the reduction of Cis-induced hearing loss.

Hammer et al. (2014) estimated that 104 million Americans were at risk of noise induced hearing loss (NIHL) in 2013. While Hammer’s research team identified a number of opportunities to lower noise exposures, they recommend additional research to identify appropriate exposure limits. Verbeek et al. (2014) assessed biomedical databases consisting of 19 studies with 82,794 participants and found the overall quality of these studies is “low to very low” and better legislation, implementation, and technical evaluations of hearing loss prevention programs are needed. This assessment is further echoed by Neitzel et al. (2014) and Reddy et al. (2014) both urging for better metrics and subject questionnaire data, and by Stewart et al. (2014), Sekhar et al. (2014), and Gilles & Paul (2014) all proposing better early education and intervention in youth (and parents).

In February 2014 the Institute of Medicine (IOM) released a report to the Department of Veterans Affairs (VA) regarding the long-term health effects of blast exposures (http://www.iom.edu/Reports/2014/Gulf-War-and-Health-Volume-9-Long-Term-Effects-of-Blast-Exposures.aspx). The IOM assessed relevant scientific information to draw conclusions regarding the strength of the scientific evidence of an association between exposure to blast and human long-term (6 months or greater) health effects. The IOM also provided recommendations to VA and the Department of Defense addressing recommendations for future research. The IOM assessed the effects of blast exposure on several organ systems reporting on psychologic, psychiatric, nervous system, auditory, vestibular, ocular, cardiovascular, respiratory, digestive system, genitourinary, dental, musculoskeletal, and rehabilitation outcomes.

Regarding auditory and vestibular systems, IOM concluded on the basis of its evaluation that there is:

1. Limited/suggestive evidence of an association between exposure to blast and long-term effects on the tympanic membrane and auditory thresholds.
2. Inadequate/insufficient evidence of an association between exposure to blast and tinnitus and long-term effects on central auditory processing.
3. Inadequate/insufficient evidence of an association between exposure to blast and long-term balance dysfunction and vertigo.

The IOM’s recommendations focused on the gaps in the evidence base related to how blast affects human health short- and long-term. The IOM stressed the importance of conducting research emphasizing multisystem injury patterns and the need to understand the clinical significance of cross-system interactions.

Meltser et al. (2014) made an interesting biological discovery that nocturnal mice exhibited permanent threshold shift (PTS) only at night but not during daylight. This self-sustained circadian rhythm can be reversed by administrating a TrkB activator resulting in preservation of inner hair cell’s ribbon synapses and recovery of PTS after night noise. Tagoe et al. (2014) discovered changes in myelination and conduction velocity of auditory nerve after exposure to loud noise in rats.
Pharmaceutically, Lu et al. (2014) reported N-acetylcysteine (NAC) and 2,4-disulfonyl α-phenyl tertiary butyl nitrore (HPN-07) combination is promising in treating NIHL in rats by reducing both temporary threshold shift (TTS) and PTS after 115 dB octave-band noise for 1 hour. Polony et al. (2014) reported rasagiline, an FDA-approved MAO-B inhibitor, can protect ototoxicity in mice by enhancing dopamine release from the lateral olivocochlear (LOC) fibers.

There were a number of special interest articles. Schmidt et al. (2014) found that hearing levels (based on pure tone audiometry @ 3, 4, 6 kHz) of symphony orchestra musician were correlated with noise exposure (NE) levels (instrument played), age and gender. They found that 29 of 363 ear tested had an additional threshold increase of 6.3 dB associated with the highest NE level. However, most of the musicians had better hearing than predicted from ISO 1999 for noise-induced PTS, but the authors suggested that musicians still had a work-related risk of developing NIHL to the same extent as industrial NE.

Golf enthusiasts using the newer generation metal clubs do not have to concern themselves for developing hearing loss from the explosive impulsive sounds from hitting the ball down the range. Zhao and Bardsley (2014) provided a low estimated risk to hearing after a cross-sectional study based on the sound pressure levels and frequency responses produced from various metal club drivers on impact with golf balls (daily noise exposure level using the drivers described was less than 2%). Good news to us amateur golfers; NIHL is quite unlikely from golf.

Finally, there were two articles that examined genetic factors that may underlie human ear susceptibility to NIHL. Shen et al. (2014) investigated whether presence of a polymorphism (mutation) for the base excision repair gene for hOGG1 (a key enzyme that eliminates 8-oxoG which causes damage to cochlear hair cell DNA and is essential for developing NIHL) may increase susceptibility for hearing loss. Polymorphism was genotyped among 612 workers with NIHL and 615 workers with normal hearing. In summary, data suggested that the hOGG1 Cys/Cys genotype may be a genetic susceptibility marker for NIHL (at least in their Chinese Han population). Kowalski et al. (2014) explored an interesting candidate gene for NIHL susceptibility; CDH23-encoding cadherin 23, a stereocilia tip links component. Subjects included 314 worst-hearing and 313 best-hearing exposed to occupational noise, selected out of 3,860 workers database. Five single nucleotide polymorphisms (SNPs) in CDH23 were genotyped. A main effect of genotype was obtained for one SNP (SNP rs3752752). The association was stronger in the younger subjects and in those exposed to impulse noise. Additionally, the CC genotype was more frequent among susceptible subjects, whereas genotype CT appeared more often among resistant to noise subjects. Interestingly, the effect of these polymorphisms was not modified by the environmental and individual factors except for blood pressure (although this needs to be further investigated). Effect of smoking was an independent factor determining NIHL development. The study results confirm that CDH23 genetic variant may modify the susceptibility to NIHL. The authors caution that the differences between the 2 study groups may not be totally related to noise susceptibility but there may also age-related cochlear changes involved.

Ronald Jackson, Ph.D. – Naval Medical Center San Diego
Jian Zuo, Ph.D. – St. Jude Children’s Research Hospital
Prevention of Cisplatin-Induced Hearing Loss by Intratympanic Dexamethasone: A Randomized Controlled Study.

Marshak T, Steiner M, Kaminer M, Levy L, Shupak A.

OBJECTIVE: To examine the role of intratympanic Dexamethasone (ITD) in the prevention of Cisplatin-induced hearing loss.

DESIGN: Prospective randomized controlled clinical trial.

SETTING: Tertiary referral center.

SUBJECTS AND METHODS: Twenty-six patients suffering from a neoplastic disease for which the treatment protocol included Cisplatin were recruited. Prior to each Cisplatin treatment session ITD was injected to the baseline randomly assigned ear while the other ear of the same patient served as the control. Audiometry and Distortion Product Otoacoustic Emissions (DPOAEs) test results of the baseline and follow-up examinations were compared within and between the study and control ears.

RESULTS: The cumulative dose of Cisplatin was greater than 400 mg for the 15 subjects who completed the study. The pure tone threshold at 8000 Hz and pure tone average threshold at 4000 to 8000 Hz significantly increased in both the study (P < .005, P < .03, respectively) and control ears (P < .01, P < .005, respectively). Significant increase in the pure tone threshold for 6000 Hz was observed in the control (P < .02) but not in the study group. Within the groups comparison also revealed significant decrease in the DPOAE average signal-to-noise ratio (SNR) for the f2 frequencies 7031 (P < .04) and 8391 Hz (P < .04) and SNR average for 4000 to 8000 Hz in the control (P < .04) but not in the study ears.

CONCLUSIONS: ITD significantly attenuated hearing loss at 6000 Hz and decreased the outer hair dysfunction in the DPOAE f2 range of 4000 to 8000 Hz. ITD might have potential in the reduction of Cisplatin-induced hearing loss.

Environmental noise pollution in the United States: developing an effective public health response.

Hammer MS, Swinburn TK, Neitzel RL.

BACKGROUND: Tens of millions of Americans suffer from a range of adverse health outcomes due to noise exposure, including heart disease and hearing loss. Reducing environmental noise pollution is achievable and consistent with national prevention goals, yet there is no national plan to reduce environmental noise pollution.

OBJECTIVES: We aimed to describe some of the most serious health effects associated with noise, summarize exposures from several highly prevalent noise sources based on published estimates as well as extrapolations made using these estimates, and lay out proven mechanisms and strategies to reduce noise by incorporating scientific insight and technological innovations into existing public health infrastructure.
DISCUSSION: We estimated that 104 million individuals had annual LEQ(24) levels > 70 dBA (equivalent to a continuous average exposure level of >70 dBA over 24 hr) in 2013 and were at risk of noise-induced hearing loss. Tens of millions more may be at risk of heart disease, and other noise-related health effects. Direct regulation, altering the informational environment, and altering the built environment are the least costly, most logistically feasible, and most effective noise reduction interventions.

CONCLUSION: Significant public health benefit can be achieved by integrating interventions that

Gulf War and Health, Volume 9: Long-Term Effects of Blast Exposures
Institute of Medicine (IOM) of the National Academies, released February 13, 2014

The wars in Iraq and Afghanistan are known for the enemy’s reliance on improvised explosive devices (IEDs). It is estimated that explosive weaponry accounts for 75 percent of all US military casualties. Since 2001, more than 1,000 US soldiers in the Afghanistan war have been killed in action and nearly 10,000 wounded in action - causing a variety of injuries - because of IEDs. From March 2003 to November 2011, more than 2,000 US soldiers in the Iraq war were killed in action and close to 22,000 wounded in action due to IEDs.

Concerned about the long-term health effects of exposure to blast, the Department of Veterans Affairs asked the IOM to assess the relevant scientific information and to draw conclusions regarding the strength of the evidence of an association between exposure to blast and health effects. The IOM’s report makes recommendations for future research on the topic.

Interventions to prevent occupational noise-induced hearing loss: A Cochrane systematic review.

Verbeek JH, Kateman E, Morata TC, Dreschler WA, Mischke C.

OBJECTIVE: To assess the effectiveness of interventions for preventing occupational noise exposure or hearing loss compared to no intervention or alternative interventions.
DESIGN: We searched biomedical databases up to 25 January 2012 for randomized controlled trials (RCT), controlled before-after studies and interrupted time-series of hearing loss prevention among workers exposed to noise.
STUDY SAMPLE: We included 19 studies with 82,794 participants evaluating effects of hearing loss prevention programs (HLPP). The overall quality of studies was low to very low, as rated using the GRADE approach.
RESULTS: One study of stricter legislation showed a favorable effect on noise levels. Three studies, of which two RCTs, did not find an effect of a HLPP. Four studies showed that better use of hearing protection devices in HLPPs decreased the risk of hearing loss. In four other studies, workers in a HLPP still had a 0.5 dB greater hearing loss at 4 kHz (95% CI - 0.5 to 1.7) than non-exposed workers. In two similar studies there was a substantial risk of hearing loss in spite of a HLPP.
CONCLUSIONS: Stricter enforcement of legislation and better implementation of HLPPs can reduce noise levels in workplaces. Better evaluations of technical interventions and long-term effects are needed.

Methods for evaluating temporal trends in noise exposure.
Neitzel RL, Galusha D, Dixon-Emst C, Rabinowitz PM.

OBJECTIVE: Hearing conservation programs have been mandatory in many US industries since 1983. Since then, three program elements (audiometric testing, hearing protection, and training) have been the focus of much research. By comparison, little has been done on noise exposure evaluation.

DESIGN: Temporal trends in time weighted average (TWA) exposures and the fraction of measurements exceeding 85 dBA were evaluated by facility, by exposure group within facility, and by individual worker within facility.

STUDY SAMPLE: A large dataset (> 10 000 measurements over 20 years) from eight facilities operated by a multinational aluminum manufacturing company was studied.

RESULTS: Overall, exposures declined across locations over the study period. Several facilities demonstrated substantial reductions in exposure, and the results of mean noise levels and exceedance fractions generally showed good agreement. The results of analyses at the individual level diverged with analyses by facility and exposure group within facility, suggesting that individual-level analyses, while challenging, may provide important information not available from coarser levels of analysis.

CONCLUSIONS: Validated metrics are needed to allow for assessment of temporal trends in noise exposure. Such metrics will improve our ability to characterize, in a standardized manner, efforts to reduce noise-induced hearing loss.

Development of the hearing protection assessment (HPA-2) questionnaire.
Reddy R, Welch D, Ameratunga S, Thorne P.

BACKGROUND: Noise-induced hearing loss (NIHL) remains an important occupational health issue as the second most commonly self-reported occupational injury or illness. The incorrect and inconsistent use of hearing protection devices (HPDs) compromises their effectiveness in preventing NIHL.

AIMS: To describe the development of an easily administered yet robust questionnaire to investigate factors that influence HPD use.

METHODS: A hearing protection assessment (HPA-2) questionnaire was developed using items based on themes identified in our previous research. These fell into two classes: supports and barriers to wearing HPD, which formed two scales within the questionnaire. The questionnaire, which also included demographic items, was administered to workers from 34 manufacturing companies. The internal consistency of the scales was tested, and factor analysis was conducted to investigate the underlying structure of the scales.
**RESULTS:** Of the 1053 questionnaires distributed, 555 completed questionnaires were received giving a response rate of 53%. The Cronbach’s alpha for the barriers scale ($\alpha = 0.740$) and supports scale ($\alpha = 0.771$) indicated strong internal reliability of the questionnaire. The supports and barriers were further described as five key factors (risk justification, HPD constraints, hazard recognition, behaviour motivation and safety culture) that influence hearing protection behaviour. Workers who reported always using HPDs had more supports across these factors, while those who did not always wear HPDs reported more barriers.

**CONCLUSIONS:** The HPA-2 questionnaire may be useful in both research and interventions to understand and motivate hearing protection behaviour by identifying and targeting supports and barriers to HPD use at different levels of the ecological model.

**Shooting habits of youth recreational firearm users.**

Stewart M, Meinke DK, Snyders JK, Howerton K.

**OBJECTIVE:** This study surveyed youth recreational firearm users (YRFUs) regarding shooting habits, reported use of hearing protection devices (HPDs), self-assessed auditory status, and attitudes about firearm noise and hearing loss.

**DESIGN:** A descriptive study using a 28-item survey administered by personal interview.

**STUDY SAMPLE:** Two-hundred and ten youth aged 10 to 17 years responded.

**RESULTS:** Seventy-eight percent of those surveyed began shooting before the age of ten. The majority reported using large caliber firearms capable of rapid fire for both hunting and target practice. Most youths in this study were not aware of, and therefore, were not utilizing HPDs specifically designed for the shooting sports. Ten percent of subjects reported constant tinnitus and 45% notice tinnitus occurred or worsened after shooting. Although the majority of YRFUs reported good or perfect hearing, a small percentage (4-5%) of youth reported having only ‘fair’ hearing.

**CONCLUSION:** YRFUs are putting themselves at risk beginning at a young age for noise-induced hearing loss (NIHL) and tinnitus based on self-reported shooting habits and inconsistent use of HPDs during both target practice and hunting activities. This research highlights the need for early education and intervention efforts to minimize the risk of NIHL in youth.

**Parental perspectives on adolescent hearing loss risk and prevention.**

Sekhar DL, Clark SJ, Davis MM, Singer DC, Paul IM.

**IMPORTANCE:** Data indicate that 1 in 6 adolescents have high-frequency hearing loss, which is typically noise related and preventable. Parental participation improves the success of adolescent behavioral interventions, yet little is known about parental perspectives regarding adolescent noise-induced hearing loss.

**OBJECTIVE:** To perform a survey to determine parental knowledge of adolescent hearing loss and willingness to promote hearing conservation to discern information that is critical to design adolescent hearing loss prevention programs.


**DESIGN, SETTING, AND PARTICIPANTS:** A cross-sectional, Internet-based survey of a nationally representative online sample of parents of 13- to 17-year-olds.

**INTERVENTIONS:** A survey conducted with the C.S. Mott Children's Hospital National Poll on Children's Health, a recurring online survey.

**MAIN OUTCOMES AND MEASURES:** Parental knowledge of adolescent hearing loss and willingness to promote hearing conservation.

**RESULTS:** Of 716 eligible respondents, 96.3% of parents reported that their adolescent was slightly or not at all at risk of hearing problems from excessive noise, and 69.0% had not spoken with their adolescent about noise exposure, mainly because of the perceived low risk. Nonetheless, to protect their adolescents' hearing, more than 65.0% of parents are either willing or very willing to consider limiting time listening to music, limiting access to excessively noisy situations, or insisting on the use of hearing protection (earplugs or earmuffs). Higher parental education increased the odds of promoting hearing-protective strategies. Parents were less likely to insist on hearing protection for older adolescents. Parents who understood that both volume and time of exposure affect hearing damage were more likely to have discussed hearing loss with their adolescent (odds ratio [OR], 1.98; 95% CI, 1.29-3.03). The odds of discussing hearing loss were also increased for those who were willing or very willing to limit time listening to music (OR, 1.88; 95% CI, 1.19-2.26) and to insist on hearing protection (OR, 1.92; 95% CI, 1.15-3.18) compared with parents who were very unwilling, unwilling, or neutral.

**CONCLUSIONS AND RELEVANCE:** Despite the rising prevalence of acquired adolescent hearing loss, few parents believe their adolescent is at risk. Those with higher education are more willing to promote hearing conservation, especially with younger adolescents. To create effective hearing conservation programs, parents need better education on this subject as well as effective and acceptable strategies to prevent adolescent noise exposure.

**Effectiveness of a preventive campaign for noise-induced hearing damage in adolescents.**


Gilles A, Paul V de H.

**OBJECTIVES:** Many studies have documented a high incidence of hearing loss and tinnitus in adolescents after recreational noise exposure. The prevalence of noise-induced symptoms is in contradiction to the low preventive use of hearing protection. The effects of preventive campaigns on the attitudes toward noise in young people are under debate. The aim of the present study is to investigate whether a preventive campaign can alter attitudes toward noise in adolescents and whether this results in an increase of hearing protection use in this population.

**METHODS:** A cohort of 547 Flemish high school students, aged 14 to 18 years old, completed a questionnaire prior to and after a governmental campaign focusing on the harmful effects of recreational noise and the preventive use of hearing protection. At both occasions the attitudes toward noise and toward hearing protection were assessed by use of the youth attitudes toward noise scale (YANS) and the beliefs about hearing protection and hearing loss (BAHPHL), respectively. These questionnaires fit into the model of the theory of planned behavior which provides a more clear insight into the prediction of a certain behavior and the factors influencing that behavior.
RESULTS: The score on the YANS and the BAHPHL decreased significantly (p<0.001) implying a more negative attitude toward noise and a more positive attitude toward hearing protection. The use of hearing protection increased significantly from 3.6% prior to the campaign to 14.3% (p=0.001) post campaign in students familiar with the campaign.

CONCLUSIONS: Measurable alteration of all the variables in the theory of planned behavior caused an increase of the intentions to use hearing protection as well as the actual use of hearing protection. The present study shows the usefulness of the theory of planned behavior to change and guide adolescents’ preventive actions toward noise damage. In addition, preventive campaigns can establish attitude and behavioral adjustments. However, the long term effects of preventive campaigns should be investigated in future research.

TrkB-Mediated Protection against Circadian Sensitivity to Noise Trauma in the Murine Cochlea.

Meltzer I, Cederroth CR, Basinou V, Savelyev S, Lundkvist GS, Canlon B.

Noise-induced hearing loss (NIHL) is a debilitating sensory impairment affecting 10%-15% of the population, caused primarily through damage to the sensory hair cells or to the auditory neurons. Once lost, these never regenerate [1], and no effective drugs are available [2, 3]. Emerging evidence points toward an important contribution of synaptic ribbons in the long term coupling of the inner hair cell and afferent neuron synapse to maintain hearing [4]. Here we show in nocturnal mice that night noise overexposure triggers permanent hearing loss, whereas mice overexposed during the day recover to normal auditory thresholds. In view of this time-dependent sensitivity, we identified a self-sustained circadian rhythm in the isolated cochlea, as evidenced by circadian expression of clock genes and ample PERIOD2::LUCIFERASE oscillations, originating mainly from the primary auditory neurons and hair cells. The transcripts of the otoprotecting brain-derived neurotrophic factor (BDNF) showed higher levels in response to day noise versus night noise, suggesting that BDNF mediated signaling regulates noise sensitivity throughout the day. Administration of a selective BDNF receptor, tropomyosin-related kinase type B (TrkB), in the night protected the inner hair cell's synaptic ribbons and subsequent full recovery of hearing thresholds after night noise overexposure. The TrkB agonist shifted the phase and boosted the amplitude of circadian rhythms in the isolated cochlea. These findings highlight the coupling of circadian rhythmicity and the TrkB receptor for the successful prevention and treatment of NIHL.

Auditory nerve perinodal dysmyelination in noise-induced hearing loss.

Tagoe T, Barker M, Jones A, Allcock N, Hamann M.

Exposure to loud sound (acoustic overexposure; AOE) induces hearing loss and damages cellular structures at multiple locations in the auditory pathway. Whether AOE can also induce changes in myelin sheaths of the auditory nerve (AN) is an important issue particularly because these changes can be responsible for impaired action potential propagation along the AN. Here we investigate the effects of AOE on morphological and electrophysiological features of
the centrally directed part of the rat AN projecting from the cochlear spiral ganglion to brainstem cochlear nuclei. Using electron microscopy and immunocytochemistry, we show that AOE elongates the AN nodes of Ranvier and triggers notable perinodal morphological changes. Compound action potential recordings of the AN coupled to biophysical modeling demonstrated that these nodal and perinodal structural changes were associated with decreased conduction velocity and conduction block. Furthermore, AOE decreased the number of release sites in the cochlear nuclei associated with the reduced amplitudes of EPSCs evoked by AN stimulation. In conclusion, AN dysmyelination may be of fundamental importance in auditory impairment following exposure to loud sound.

Antioxidants Reduce Cellular and Functional Changes Induced by Intense Noise in the Inner Ear and Cochlear Nucleus.

J Assoc Res Otolaryngol. 2014 Feb 5. [Epub ahead of print]

Lu J, Li W, Du X, Ewert DL, West MB, Stewart C, Floyd RA, Kopke RD.

The present study marks the first evaluation of combined application of the antioxidant N-acetylcysteine (NAC) and the free radical spin trap reagent, disodium 2,4-disulfophenyl-N-tert-butylnitronate (HPN-07), as a therapeutic approach for noise-induced hearing loss (NIHL). Pharmacokinetic studies and C-14 tracer experiments demonstrated that both compounds achieve high blood levels within 30 min after i.p. injection, with sustained levels of radiolabeled cysteine (released from NAC) in the cochlea, brainstem, and auditory cortex for up to 48 h. Rats exposed to 115 dB octave-band noise (10-20 kHz) for 1 h were treated with combined NAC/HPN-07 beginning 1 h after noise exposure and for two consecutive days. Auditory brainstem responses (ABR) showed that treatment substantially reduced the degree of threshold shift across all test frequencies (2-16 kHz), beginning at 24 h after noise exposure and continuing for up to 21 days. Reduced distortion product otoacoustic emission (DPOAE) level shifts were also detected at 7 and 21 days following noise exposure in treated animals.Noise-induced hair cell (HC) loss, which was localized to the basal half of the cochlea, was reduced in treated animals by 85 and 64 % in the outer and inner HC regions, respectively. Treatment also significantly reduced an increase in c-fos-positive neuronal cells in the cochlear nucleus following noise exposure. However, no detectable spiral ganglion neuron loss was observed after noise exposure. The results reported herein demonstrate that the NAC/HPN-07 combination is a promising pharmacological treatment of NIHL that reduces both temporary and permanent threshold shifts after intense noise exposure and acts to protect cochlear sensory cells, and potentially afferent neurites, from the damaging effects of acoustic trauma. In addition, the drugs were shown to reduce aberrant activation of neurons in the central auditory regions of the brain following noise exposure. It is likely that the protective mechanisms are related to preservation of structural components of the cochlea and blocking the activation of immediate early genes in the auditory centers of the brain.

Protective effect of rasagiline in aminoglycoside ototoxicity.


Sensorineural hearing losses (SNHLs; e.g., ototoxicant- and noise-induced hearing loss or presbycusis) are among the most frequent sensory deficits, but they lack effective drug therapies. The majority of recent therapeutic approaches focused on the trials of antioxidants and reactive oxygen species (ROS) scavengers in SNHLs. The rationale for these studies was the prominent role of disturbed redox homeostasis and the consequent ROS elevation. Although the antioxidant therapies in several animal studies seemed to be promising, clinical trials have failed to fulfill expectations. We investigated the potential of rasagiline, an FDA-approved monamine oxidase type B inhibitor (MAO-B) inhibitor type anti-parkinsonian drug, as an otoprotectant. We showed a dose-dependent alleviation of the kanamycin-induced threshold shifts measured by auditory brainstem response (ABR) in an ototoxicant aminoglycoside antibiotic-based hearing loss model in mice. This effect proved to be statistically significant at a 6-mg/kg (s.c.) dose. The most prominent effect appeared at 16kHz, which is the hearing sensitivity optimum for mice. The neuroprotective, antiapoptotic and antioxidant effects of rasagiline in animal models, all targeting a specific mechanism of aminoglycoside injury, may explain this otoprotection. The dopaminergic neurotransmission enhancer effect of rasagiline might also contribute to the protection. Dopamine (DA), released from lateral olivocochlear (LOC) fibers, was shown to exert a protective action against excitotoxicity, a pathological factor in the aminoglycoside-induced SNHL. We have shown that rasagiline enhanced the electric stimulation-evoked release of DA from an acute mouse cochlea preparation in a dose-dependent manner. Using inhibitors of voltage-gated Na+, Ca channels and DA transporters, we revealed that rasagiline potentiated the action potential-evoked release of DA by inhibiting the reuptake. The complex, multifactorial pathomechanism of SNHLs most likely requires drugs acting on multiple targets for effective therapy. Rasagiline, with its multi-target action and favorable adverse effects profile, might be a good candidate for a clinical trial testing the otoprotective indication.

**Hearing Loss in Relation to Sound Exposure of Professional Symphony Orchestra Musicians.**

Ear Hear. 2014 Mar 5. [Epub ahead of print]

Schmidt JH, Pedersen ER, Paarup HM, Christensen-Dalsgaard J, Andersen T, Poulsen T, Bælum J.

**OBJECTIVES:** The objectives of this study were to: (1) estimate the hearing status of classical symphony orchestra musicians and (2) investigate the hypothesis that occupational sound exposure of symphony orchestra musicians leads to elevated hearing thresholds.

**DESIGN:** The study population comprised all the musicians from five symphony orchestras. Questionnaires were filled in by 337 subjects, and 212 subjects performed an audiometric test. For a group of 182 musicians (363 ears) the results of the audiometry was analyzed in relation to the individual exposure, which was estimated on the basis of sound measurements and questionnaire data regarding the exposure time. The mean hearing threshold at the frequencies 3, 4, and 6 kHz, corrected for age and sex, was used as outcome.

**RESULTS:** The musician ears with the highest exposure (29 of 363) had an additional threshold shift of 6.3 dB compared with the 238 ears with lowest exposure. The observed hearing loss of musicians was smaller compared with the noise-induced permanent threshold shift (NIPTS) predicted from ISO1999. A remaining confounding effect of age after ISO 7029 age corrections could be observed to explain the difference in observed and predicted NIPTS. However, the observed hearing loss difference between the left and the right ear of musicians was 2.5 dB (95% confidence interval 1.5-3.6), which was similar to the NIPTS predicted from ISO1999. Most of the
musicians had better hearing at 3, 4, and 6 kHz for age than expected, however, 29 ears with the highest exposure above 90.4 dBA with a mean exposure time of 41.7 years had significantly elevated hearing thresholds. Trumpet players and the left ear of first violinists had significantly elevated hearing thresholds compared with other musicians.

**CONCLUSION:** Most of the symphony orchestra musicians had better hearing than expected but they had a work-related risk of developing additional noise-induced hearing loss. The additional NITPS of the left ear compared with the right ear was at the expected level based on the cumulated sound exposure and ISO1999, indicating that performing music may induce hearing loss to the same extent as industrial noise.

**Real-ear acoustical characteristics of impulse sound generated by golf drivers and the estimated risk to hearing: a cross-sectional study.**

Zhao F, Bardsley B.

**OBJECTIVES:** This study investigated real-ear acoustical characteristics in terms of the sound pressure levels (SPLs) and frequency responses in situ generated from golf club drivers at impact with a golf ball. The risk of hearing loss caused by hitting a basket of golf balls using various drivers was then estimated.

**DESIGN:** Cross-sectional study.

**SETTING:** The three driver clubs were chosen on the basis of reflection of the commonality and modern technology of the clubs. The participants were asked to choose the clubs in a random order and hit six two-piece range golf balls with each club. The experiment was carried out at a golf driving range in South Wales, UK.

**PARTICIPANTS:** 19 male amateur golfers volunteered to take part in the study, with an age range of 19-54 years.

**OUTCOME MEASURES:** The frequency responses and peak SPLs in situ of the transient sound generated from the club at impact were recorded bilaterally and simultaneously using the GN Otometric Freefit wireless real-ear measurement system. A swing speed radar system was also used to investigate the relationship between noise level and swing speed.

**RESULTS:** Different clubs generated significantly different real-ear acoustical characteristics in terms of SPL and frequency responses. However, they did not differ significantly between the ears. No significant correlation was found between the swing speed and noise intensity. On the basis of the SPLs measured in the present study, the percentage of daily noise exposure for hitting a basket of golf balls using the drivers described above was less than 2%.

**CONCLUSIONS:** The immediate danger of noise-induced hearing loss for amateur golfers is quite unlikely. However, it may be dangerous to hearing if the noise level generated by the golf clubs exceeded 116 dBA.

**A Functional Ser326Cys Polymorphism in hOGG1 Is Associated with Noise-Induced Hearing Loss in a Chinese Population.**

DNA damage to cochlear hair cells caused by 8-oxoguanine (8-oxoG) is essential for the development of noise-induced hearing loss (NIHL). Human 8-oxoG DNA glycosylase 1 (hOGG1) is a key enzyme in the base excision repair (BER) pathway that eliminates 8-oxoG. Many epidemiological and functional studies have suggested that the hOGG1 Ser326Cys polymorphism (rs1052133) is associated with many diseases. The purpose of this investigation was to investigate whether the hOGG1 Ser326Cys polymorphism in the human BER pathway is associated with genetic susceptibility to NIHL in a Chinese population. This polymorphism was genotyped among 612 workers with NIHL and 615 workers with normal hearing. We found that individuals with the hOGG1 Cys/Cys genotype had a statistically significantly increased risk of NIHL compared with those who carried the hOGG1 Ser/Ser genotype (adjusted OR = 1.59, 95% CI = 1.13-2.25) and this increased risk was more pronounced among the workers in the 15- to 25- and >25-year noise exposure time, 85-92 dB(A) noise exposure level, ever smoking, and ever drinking groups; similar effects were also observed in a recessive model. In summary, our data suggested that the hOGG1 Cys/Cys genotype may be a genetic susceptibility marker for NIHL in the Chinese Han population.

Genetic variants of CDH23 associated with noise-induced hearing loss.

Kowalski TJ, Pawelczyk M, Rajkowska E, Dudarewicz A, Sliwinska-Kowalska M.

OBJECTIVES: Noise-induced hearing loss (NIHL) is a complex disease resulting from the interaction between external and intrinsic/genetic factors. Based on mice studies, one of the most interesting candidate gene for NIHL susceptibility is CDH23-encoding cadherin 23, a component of the stereocilia tip links. The aim of this study was to analyze selected CDH23 single nucleotide polymorphisms (SNPs) and to evaluate their interaction with environmental and individual factors in respect to susceptibility for NIHL in humans.

METHODS: A study group consisted of 314 worst-hearing and 313 best-hearing subjects exposed to occupational noise, selected out of 3,860 workers database. Five SNPs in CDH23 were genotyped using real-time PCR. Subsequently, the main effect of genotype and its interaction with selected environmental and individual factors were evaluated.

RESULTS: The significant results within the main effect of genotype were obtained for the SNP rs3752752, localized in exon 21. The effect was observed in particular in the subgroup of young subjects and in those exposed to impulse noise; CC genotype was more frequent among susceptible subjects, whereas genotype CT appeared more often among resistant to noise subjects. The effect of this polymorphism was not modified by none of environmental/individual factors except for blood pressure; however, the latter one should be further investigated. Smoking was shown as an independent factor determining NIHL development.

CONCLUSION: The results of this study confirm that CDH23 genetic variant may modify the susceptibility to NIHL development in humans, as it was earlier proven in mice. Because the differences between the 2 study groups were not necessarily related to susceptibility to noise but they also were prone to age-related cochlear changes, these results should be interpreted with caution until replication in another population.
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Weldon School of Biomedical Engineering, Purdue University, 206 South Martin Jischke Drive, West Lafayette, IN 47907, USA. Department of Speech, Language, and Hearing Sciences, Purdue University, 500 Oval Drive, West Lafayette, IN 47907, USA. Electronic address: mheinz@purdue.edu.

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Fetoni AR, Bielefeld EC, Nicotera T, Henderson D.
Institute of Otolaryngology, Catholic University of Rome, Largo A. Gemelli, 8, Rome, Italy. Electronic address: afetoni@rm.unicatt.it. Department of Speech and Hearing Science, The Ohio State University, Columbus, OH 43210, USA. Roswell Park Cancer Institute, Department of Molecular and Cellular Biophysics, Elm and Carlton Streets, Buffalo, NY 14263, USA. Center for Hearing and Deafness, SUNY at Buffalo, 137 Cary Hall, Buffalo, NY 14214, USA.

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Discipline of Biomedical Sciences, School of Medical Sciences, The University of Sydney, Lidcombe, NSW, 2141, Australia.

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Henry KS, Kale S, Heinz MG.
Department of Speech, Language, and Hearing Sciences, Purdue University West Lafayette, IN, USA. Weldon School of Biomedical Engineering, Purdue University West Lafayette, IN, USA.
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Research Service-151, Loma Linda Veterans Affairs Medical Center, Loma Linda, California, USA.

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Rotman Research Institute, Baycrest Centre for Geriatric Care Toronto, ON, Canada; Department of Psychology, University of Toronto Toronto, ON, Canada; Institute of Medical Sciences, University of Toronto Toronto, ON, Canada.
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Pediatrics, Penn State College of Medicine, Hershey, PA.
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Johnson O, Andrew B, Walker D, Morgan S, Aldren A.
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Dobie RA, Clark WW.
Department of Otolaryngology-Head and Neck Surgery, University of Texas Health Science Center at San Antonio, San Antonio, TX; and Department of Audiology and Communication Sciences, Washington University School of Medicine, St. Louis, MO.

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Tuebingen Hearing Research Center, University of Tuebingen,Tuebingen, Germany.

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Sekhar DL, Clark SJ, Davis MM, Singer DC, Paul IM.
Department of Pediatrics, Penn State College of Medicine, Hershey, Pennsylvania. Department of Pediatrics and Communicable Diseases, University of Michigan Health System, Ann Arbor; Child Health Evaluation and Research Unit, University of Michigan, Ann Arbor. Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania.

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John GW, Grynevych A, Welch D, McBride D, Thorne PR.
Section of Audiology, School of Population Health, University of Auckland, Auckland, New Zealand.

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Sherman CR, Azulay Chertok IR.
Department of Nursing, Shawnee State University, Portsmouth, OH.
FUNDING OPPORTUNITIES

Refer to the HCE website (http://hearing.health.mil/Research/FundingInformation.aspx) for additional hearing-related research funding opportunities.

**NIDCD Research Grants for Translating Basic Research into Clinical Tools (R01)**

**Award Organization:** National Institutes of Health  
**Announcement #:** PAR-14-009  
**Date Released:** May 23, 2014  
**Date Closed:** May 25, 2014  

The NIDCD is encouraging applications which translate basic research findings into clinical tools for better human health in the NIDCD mission areas of hearing, balance, smell, taste, voice, speech and language. The intent of this Funding Opportunity Announcement (FOA) is to provide a new avenue for basic scientists, clinicians and clinical scientists to jointly initiate and conduct translational research projects. The scope of this FOA includes a range of activities to encourage translation of basic research findings which will impact the diagnosis, treatment and prevention of communication disorders. Multi-institutional, multi-disciplinary, and academic-industrial collaborations studies are encouraged. This FOA is not intended for health services/outcome studies, the extension of ongoing clinical research studies, the optimization of current clinical protocols, or pre-translational studies. Connection to the clinical condition must be clearly established and the outcomes of the grant must have practical clinical impact.

**DOD FY14 Combat Casualty Training Initiative Virtual Tissue Advancement Research Program**

**Announcement #:** W81XWH-14-J-PC1-VTA  
**Date Released:** February 12, 2014  
**Date Closed:** June 23, 2014  

The Combat Casualty Training Initiative (CCTI) Virtual Tissue Advancement Research Program Announcement is being offered for the first time in FY14. It seeks to advance the state of research under the CCTI by advancing the state of virtual tissues for use in surgical and other interventional procedure and skill simulation systems. The CCTI is primarily focused on the research and, ultimately, the development of medical training methods, technologies, systems, and competency assessment tools for the attainment and sustainment of military medical readiness. The CCTI advances these goals through research and development projects related to trauma care, surgical procedures, general surgery, and interventional procedures / skills. The results of this effort are intended to improve the fidelity of virtual reality human tissue and anatomical interactions to further the abilities to construct realistic procedural surgical and interventional training systems. It is anticipated that research will lead to better methods to accurately simulate regional anatomic interactions, aggregated tissues (where different tissues connect and interact with each other), organ and structure interactions, organ physical properties as well as structure and tissue properties (here-in-after referred to as ‘human tissue’). Research of the human tissue properties should include a prototype online interactive
knowledge repository or library. Inclusion of an open access interactive research library prototype as part of the research effort will greatly expand the impact of the research. It is also envisioned that such research will lead to more realistic acting surgical and interventional-type simulations for the purposes of providing superior contact, cutting, dissection, approximation, movement and deformation properties that can be measured graphically and ‘haptically’ against known and, in some instances, currently unknown physical standards. Open access, open source or open model approaches are highly encouraged. This announcement is not an attempt to rid the art of creating medical models, but to provide the opportunity for developers and end-users to eventually have access to validated human tissues to create models for the purposes of medical training and education.

Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44])
Award Organization: National Institutes of Health/NIDCD
Announcement #: PA-14-071
Date Released: March 05, 2014
Date Closed: January 08, 2015

This Funding Opportunity Announcement (FOA) issued by the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) and the Administration for Children and Families (ACF) invites eligible United States small business concerns (SBCs) to submit Small Business Innovation Research (SBIR) grant applications. United States SBCs that have the research capabilities and technological expertise to contribute to the R&D mission(s) of the NIH, CDC, FDA or ACF awarding components identified in this FOA are encouraged to submit SBIR grant applications in response to identified topics (see PHS 2014-2 SBIR/STTR Program Descriptions and Research Topics for NIH, CDC, FDA and ACF).

Omnibus Solicitation of the NIH for Small Business Technology Transfer Grant Applications (Parent STTR [R41/R42])
Award Organization: National Institutes of Health/NIDCD
Announcement #: PA-14-072
Date Released: March 05, 2014
Date Closed: January 08, 2015

Notes:
This Funding Opportunity Announcement (FOA) issued by the National Institutes of Health (NIH) invites eligible United States small business concerns (SBCs) to submit Small Business Technology Transfer (STTR) grant applications. United States SBCs that have the research capabilities and technological expertise to contribute to the R&D mission(s) of the NIH awarding components identified in this FOA are encouraged to submit STTR grant applications in response to identified topics (see PHS 2014-2 SBIR/STTR Program Descriptions and Research Topics for NIH.)
NIDCD Research on Hearing Health Care (R21)
Award Organization: National Institutes of Health
Announcement #: PA-14-090
Date Released: May 16, 2014
Date Closed: May 08, 2017

This FOA encourages Research Project Grant (R21) applications from institutions/organizations to support research leading to accessible and affordable hearing health care (HHC). The overarching emphasis is on the acquisition of knowledge that can be rapidly translated into new or enhanced approaches for access, assessment or interventions with a goal to delivering better hearing health care outcomes. Applications should seek quality approaches that are effective, affordable and deliverable to those who need them as well as implementable and sustainable in settings beyond the research environment.

NIDCD Research on Hearing Health Care (R01)
Award Organization: National Institutes of Health
Announcement #: PA-14-091
Date Released: May 05, 2014
Date Closed: May 08, 2017

This FOA encourages Research Project Grant (R01) applications from institutions/organizations to support research leading to accessible and affordable hearing health care (HHC). The overarching emphasis is on the acquisition of knowledge that can be rapidly translated into new or enhanced approaches for access, assessment or interventions with a goal to delivering better hearing health care outcomes. Applications should seek quality approaches that are effective, affordable and deliverable to those who need them as well as implementable and sustainable in settings beyond the research environment.
Phase 3 Clinical Trial: D-Methionine to Reduce Noise-Induce Hearing Loss (NIHL)
This study is currently recruiting participants.
Information Provided by (Responsible Party): Kathleen CM Campbell, PhD, Southern Illinois University
Study Start Date: September 2013
First Received on April 27, 2011

This prospective study is a randomized, double-blind, placebo-controlled Phase 3 clinical trial of oral D-met to reduce noise-induced hearing loss (NIHL) and tinnitus. The goal of the study is to develop a safe, oral pharmacological agent to augment physical hearing protectors for noise exposures that exceed the protective capabilities of ear plugs and/or muffs. The study population is a cohort of Drill Sergeant (DS) instructor trainees during and 22 days after their 11 day weapons training. The primary objective of this study is to determine the efficacy of D-Met in preventing NIHL or reducing tinnitus secondary to a minimum of 500 rounds of M-16 weapons training occurring over an 11 day period.

Prevention of Noise-Induced Hearing Loss
This study is not yet open for participant recruitment.
Information Provided by (Responsible Party): Judith Lieu, Washington University School of Medicine
Study Start Date: June 2013
First Received on January 23, 2014

Noise-induced hearing loss affects an estimated 5% of the worldwide population, with 30-40 million Americans exposed to hazardous sound or noise levels regularly. Sources of noise may be occupational, blast noise, or recreational. Trauma to the inner ear can occur through transient hearing loss or permanent hearing loss. Although hearing recovers after temporary transient hearing loss, growing evidence suggests that repeated temporary transient hearing loss may lead to a permanent hearing loss. Currently, there are no treatments and there are no known medications that can be used clinically to prevent noise-induced hearing loss in humans. The long-term goal of this research is to find medications that can prevent noise-induced hearing loss. The purpose of the present pilot study is to evaluate zonisamide and methylprednisolone as medications to prevent temporary transient hearing loss in humans.

SPI-1005 for Prevention and Treatment of Chemotherapy Induced Hearing Loss
This study is not yet open for participant recruitment.
Information Provided by (Responsible Party): Sound Pharmaceuticals, Incorporated
Study Start Date: March 2014
First Received on October 7, 2011
Chemotherapy treatment with platinum-based agents is well noted to cause ototoxicity. It is the objective of this study to determine the safety and efficacy of SPI-1005 at three dose levels when delivered orally twice daily for 3 days, surrounding each cycle of platinum chemotherapy in head and neck or non-small cell lung cancer patients to prevent and treat chemotherapy-induced hearing loss and tinnitus.

**Micronutrients to Prevent Noise-Induced Hearing Loss**
This study has been completed.
Information Provided by (Responsible Party): Josef M Miller, University of Michigan
Study Start Date: June 201
First Received on December 11, 2008

Noise-induced hearing loss (NIHL) is a significant clinical, social, and economic issue. Studies in animals have allowed us to identify mechanisms contributing to NIHL, including direct mechanical trauma, free radicals formed in association with metabolic stress, and reduced blood flow. A combination of antioxidant vitamins (beta-carotene, and vitamins C and E) and the mineral magnesium (which acts in part as a vasodilator but also as an antioxidant) is highly effective in preventing NIHL in animals. These studies evaluate efficacy of this intervention in humans.

Hypothesis: Treatment with these micronutrients provides safe, effective attenuation of acute hearing changes induced by exposure to real-world sounds producing temporary (non-permanent) or permanent hearing changes induced by exposure to real-world sounds.

Experiment 1: "Digital Audio Player" studies (University of Florida, Gainesville). Prevention of *temporary* elevations in hearing thresholds, induced by exposure to moderately loud music, will be measured. Subjects will be 70 young adults with equal numbers of male and female participants.

Experiment 2: "Urban warfare" military studies (Karolinska Institutet, Sweden). Prevention of *temporary* elevations in hearing thresholds, induced by automatic gunfire sound inside a concrete bunker, will be measured. Subjects will be 31 adult male or female officers in the Swedish army required to participate in urban combat training regardless of study participation. All subjects are required to wear standard hearing protection during combat exercises.

**TUNE! Teaching the UK About Noise Exposure: A Pilot Study**
This study is enrolling participants by invitation only.
Information Provided by (Responsible Party): London School of Hygiene and Tropical Medicine
Study Start Date: July 2009
First Received on June 5, 2009

In 1986 The Medical Research Council estimated that 4 million UK adolescents were at risk of hearing damage from over-exposure to loud music from personal audio players (PAPs), gigs, clubs, pubs and festivals. Since that time social noise exposure is estimated to have tripled to 19% of young people. The European Commission commissioned a report that estimated 5-10% of personal audio player users are risking permanent hearing loss and tinnitus by listening to music.
at high volumes for more than 1 hour a day for 5 years or more. Up to 246 million PAPs were sold in Europe in 2008, and 200 million mobile phones, many of which now have built-in audio players. Nevertheless, a recent survey showed that only 8% of young people identify hearing loss as a health problem. The Royal National Institute for the Deaf (RNID) undertook two surveys of young people in the UK to analyse listening behaviours as part of their "Don't Lose the Music" campaign. As a consequence they offer listening advice given by flyers at events and online at the dedicated website. There have been no studies to confirm if such advice is effective in reducing noise exposure.

Aim: This study will pilot a methodology for a randomised controlled trial to test the effectiveness of a publically-available online video in changing the listening habits of young music lovers i.e. reduce the volume and number of hours of exposure.

Hypothesis: A video and adapted sound track demonstrating the experience of noise-induced hearing loss and tinnitus accessed online will change the listening habits of 18-25 year-olds.

Prevention of Noise-Induced Damage by Use of Antioxidants
This study is currently recruiting participants.
Information Provided by (Responsible Party): Ethisch Comité UZ Antwerpen, University Hospital, Antwerp
Study Start Date: November 2012
First Received on September 28, 2012

The current study is a double-blind placebo-controlled cross-over study verifying the preventive effect of antioxidants on noise-induced hearing loss (NIHL) and noise-induced tinnitus (NIT). The antioxidants comprise of a mixture of magnesium and n-acetylcystein which should be taken 1h before leisure noise above 100dB for at least 30 minutes.

Early Detection of Noise-Induced Hearing Loss
This study is enrolling participants by invitation only.
Information Provided by (Responsible Party): Department of Veterans Affairs
Study Start Date: January 2010
First Received on November 25, 2009

This study measures sounds produced by the sensory receptors of the inner ear called hair cells. These sounds are called otoacoustic emissions and one special case the investigators are studying are called distortion product otoacoustic emissions (DPOAEs) produced by presenting two tones to the ear. If the ear is damaged by noise exposure DPOAEs are reduced. In this study the investigators are attempting to improve the DPOAE test by adding a third tone to make the test more frequency specific. Whether the third tone helps will be determined by comparing DPOAEs collected with and without the third tone to clinical audiograms. If the addition of the third tone helps then the investigators expect DPOAEs tracked as a function of frequency (DPograms) will more closely match the clinical audiograms.

Antioxidation Medication for Noise-Induced Hearing Loss
This study has been completed.
This study will examine whether oral intake of 1200mg N-Acetylcysteine/day will prevent temporary threshold shift in hearing among workers exposed to noise.

**Study to Evaluate the Safety and Pharmacokinetics of SPI-1005**
This study has been completed.
Information Provided by (Responsible Party): Sound Pharmaceuticals, Incorporated
Study Start Date: May 2006
First Received on October 10, 2011

A study to determine the safety, tolerability, and pharmacokinetics of SPI-1005 capsules in healthy adults.

**Test of a Web-based Intervention to Promote Hearing Protector Use**
This study is ongoing, but not recruiting participants.
Information Provided by (Responsible Party): Marjorie McCullagh, University of Michigan
Study Start Date: November 2011
First Received on October 14, 2011

The purpose of this project is to compare the effectiveness of several approaches to influencing hearing protector use. The goals of this study are to further develop an intervention to promote farmers' use of hearing protectors, and compare the effectiveness of the developed intervention with two alternative approaches to influencing hearing protector use behavior, delivered in various combinations. This study will determine if significant change in hearing protection use can be achieved in a one-shot web-based or protector-supply intervention. Results will determine the need for future program modifications, e.g., inclusion of booster(s).

**The Effect of Gabapentin on the Sensation and Impact of Tinnitus**
This study has been completed.
Information Provided by (Responsible Party): Tinnitus Research Consortium
Study Start Date: August 2003
First Received on November 18, 2005

This study evaluated the effectiveness of gabapentin in treating tinnitus in two populations: Tinnitus with associated acoustic trauma and tinnitus without associated acoustic trauma. The hypothesis was that gabapentin would decrease both subjective and objective features of tinnitus in the trauma group, but would be less effective in the non-trauma group.

**Hearing Loss Prevention for Veterans (HLPP)**
This study has been completed.
Information Provided by (Responsible Party): Department of Veterans Affairs
Hearing loss is the most prevalent service-connected disability in the VA. It causes communication difficulties, which contribute to isolation, frustration and depression. A major cause of hearing loss is from exposure to high levels of sound, and is referred to as Noise Induced Hearing Loss (NIHL). Veterans have inevitably been exposed to high levels of sound during military service, and even though they may not yet have NIHL, their ears have been damaged. Continued noise exposure in civilian life will result in NIHL. However, it can easily be prevented by avoiding noise or using hearing protection. Most people are unaware that noise damages hearing, and even when they are, they do not use hearing protection. In this study we will use a randomized controlled trial to evaluate the short- and long-term effectiveness of two forms of education about NIHL that we have developed for Veterans. One is a computerized program; the other is a Hearing Conservation Brochure.

**Daily Exposure Monitoring to Prevent Hearing Hearing Loss (DEMON)**
This study is currently recruiting participants.
Information Provided by (Responsible Party): Yale University
Study Start Date: July 2007
First Received on October 22, 2012

The goal of this study is to determine whether daily assessment and feedback of workers' noise exposures leads to more effective use of hearing protection and prevention of noise-induced hearing loss.

**Otoprotection With SPI-1005 for Prevention of Temporary Auditory Threshold Shift**
This study is ongoing, but not recruiting participants.
Information Provided by (Responsible Party): Sound Pharmaceuticals, Incorporated
Study Start Date: September 2011
First Received on October 29, 2011

Exposure to loud sounds can cause hearing loss. The purpose of this research study is to evaluate potential prevention of temporary changes in hearing that may occur after listening to music through an iPod or personal music player. We will measure temporary changes in hearing in subjects who listen to music and take either the study drug, SPI-1005, or a placebo for 4 days. SPI-1005 is a proprietary preparation of ebselen that allows it to be taken by mouth. Ebselen contains the mineral selenium and behaves like Glutathione Peroxidase, an enzyme that helps to rid the body of damaging chemicals caused by loud sounds.

**A Trial of Magnesium Dependent Tinnitus**
This study is ongoing, but not recruiting participants.
Information Provided by (Responsible Party): Michael Cevette, Mayo Clinic
Study Start Date: July 2011
First Received on January 7, 2011
Descriptions of tinnitus date back to the time of ancient Egypt, yet science has failed to unravel the mysterious underlying mechanisms that produce these subjective auditory perceptions of sound. These perceptions may be manifestations of damage resulting from noise exposure, ototoxicity, or other abnormal conditions of the auditory system. However, many individuals have idiopathic tinnitus for which no specific cause can be determined. Although often presenting in conjunction with hearing loss, the magnitude of hearing loss does not necessarily correspond with the severity of tinnitus. In addition, some individuals reporting tinnitus experience concomitant hyperacusis. This relationship suggests these processes may be linked by underlying imbalances at the level of the hair cell. The possible influence of magnesium and its antagonist, calcium, has been discussed in the literature as a contributing factor in the mitigation of noise-induced hearing loss, ototoxicity, and the hyperexcitability of the auditory system (Cevette et al, 2003). Permanent and temporary changes in auditory function have been linked to nutritional deficiencies of magnesium. Magnesium deficiency has resulted in increased susceptibility to noise-induced hearing loss (Ising et al, 1982; Joachims et al, 1983; Joachims et al, 1987; Scheibe et al, 2000), ototoxicity (Vormann and Gunther, 1993), and hyperexcitability (Kruse et al, 1932; Cevette et al, 1989; Bac et al, 1994) of the auditory system.

The recommended daily allowance (RDA) for magnesium in adults is 4.5 mg/kg (Saris et al, 2000); however, all age groups of Americans fall short of the RDA for magnesium by 100 mg daily (Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 1997). This lack of appropriate magnesium intake may have negative consequences. For example, the putative magnesium mechanism within the auditory system involves a metabolic cellular cascade of events. Specifically, magnesium deficiency leads to increased permeability of the calcium channel in the hair cells with a consequent over-influx of calcium, an increased release of glutamate via exocytosis, and overstimulation of N-methyl-D-aspartate receptors on the auditory nerve fibers. Recent studies of both noise-induced hearing loss and idiopathic sensorineural hearing loss have suggested that magnesium supplementation may lessen the severity of tinnitus in patients. Magnesium improved hearing recovery and lessened tinnitus in patients with idiopathic sudden hearing loss (Gordin et al, 2002). More recently, Nageris et al (2004) showed in a well-controlled study that magnesium was a relatively safe and convenient adjunct to corticosteroid treatment for enhancing the improvements of hearing in acute-onset sensorineural hearing loss at a dose of 4 g. The protective effect of magnesium in noise-induced hearing loss has been previously reported (Ising et al, 1982; Scheibe et al, 2000).

Despite these encouraging findings, no controlled study has examined the effect of magnesium supplementation for patients with moderate to severe tinnitus.

Incidence of Tinnitus Amongst Teenagers and Young Adult mp3 Users

This study is currently recruiting participants.
Information Provided by (Responsible Party): Faculdade de Medicina de Valencia
Study Start Date: July 2007
First Received on August 2009

The aim of this study is to compare the incidence of tinnitus between mp3 users and non-users, aged between 15 and 30 years old. 100 patients will be recruited in Valença secondary schools. High frequency audiometry and otoacoustic emissions will be performed. Tinnitus patients will complete the Tinnitus Handicap Inventory questionnaire.
**Efficacy of AM-111 in Patients With Acute Sensorineural Hearing Loss**

This study has been completed.
Information Provided by (Responsible Party): Auris Medical, Inc.
Study Start Date: December 2008
First Received on December 3, 2008

The purpose of the study is to determine whether AM-111 is effective in the treatment of acute inner ear hearing loss (acute sensorineural hearing loss, ASNHL).

**The Effect of Sound Stimulation on Hearing Ability**

This study has been completed.
Information Provided by (Responsible Party): Earlogic Korea, Inc.
Study Start Date: September 2011
First Received on September 9, 2011

In the late 1990s, researchers discovered that acoustic stimuli slow progressive sensorineural hearing loss and exposure to a moderately augmented acoustic environment can delay the loss of auditory function. In addition, prolonged exposure to an augmented acoustic environment could improve age-related auditory changes. These ameliorative effects were shown in several types of mouse strains, as long as the acoustic environment was provided prior to the occurrence of severe hearing loss.

In addition to delaying progressive hearing loss, acoustic stimuli could also protect hearing ability against damage by traumatic noise. In particular, a method called forward sound conditioning (i.e., prior exposure to moderate levels of sound) has been shown to reduce noise-induced hearing impairment in a number of mammalian species, including humans.

Interestingly, recent report has suggested that low-level sound conditioning also reduces free radical-induced damage to hair cells, increases antioxidant enzyme activity, and reduces Cox-2 expression in cochlea, and can enhance cochlear sensitivity. Specifically, increased cochlear sensitivity was observed when distortion product otoacoustic emissions (DPOAEs) and compound action potentials (CAPs) were measured.

In addition to forward sound conditioning, backward sound conditioning (i.e., the use of acoustic stimuli after exposure to a traumatic noise) has been shown to protect hearing ability against acoustic trauma and to prevent the cortical map reorganization induced by traumatic noise.

In this study, the investigators examine the effect of sound stimulation on hearing ability in human subjects.

**The Effect of Sound Stimulation on Pure-tone Hearing Threshold**

This study has been completed.
Information Provided by (Responsible Party): Earlogic Korea, Inc.
Study Start Date: May 2010
First Received on August 16, 2010
The purpose of this study is to investigate if sound stimulation could improve pure-tone hearing threshold.

In the late 1990s, researchers discovered that acoustic stimuli slow progressive sensorineural hearing loss and exposure to a moderately augmented acoustic environment can delay the loss of auditory function. In addition, prolonged exposure to an augmented acoustic environment could improve age-related auditory changes. These ameliorative effects were shown in several types of mouse strains, as long as the acoustic environment was provided prior to the occurrence of severe hearing loss.

In addition to delaying progressive hearing loss, acoustic stimuli could also protect hearing ability against damage by traumatic noise. In particular, a method called forward sound conditioning (i.e., prior exposure to moderate levels of sound) has been shown to reduce noise-induced hearing impairment in a number of mammalian species, including humans.

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In addition to forward sound conditioning, backward sound conditioning (i.e., the use of acoustic stimuli after exposure to a traumatic noise) has been shown to protect hearing ability against acoustic trauma and to prevent the cortical map reorganization induced by traumatic noise.

Based on the results of animal studies, the investigators conducted a human study in 2007 and observed that sound stimulation could improve hearing ability. On average, the pure-tone hearing threshold decreased by 8.91 dB after sound stimulation for 2 weeks. In that study, however, the investigators observed only the hearing threshold changes by sound stimulation.

To verify the previous ameliorative effect of sound stimulation, the investigators included a control period in this study.

http://hearing.health.mil/EducationAdvocacy/Newsletters.aspx