damage. Therefore age-related hearing loss can be reduced by treatment with antioxidants.

Coenzyme Q10 is one of the antioxidants and vitamin-like substance. the reagent is used for the treatment of disorders of oxidative injury, such as Parkinson fs disease, stroke, and ischemic heart disease. in the ear, we reported coenzyme Q10 could protect cochlear from acoustic trauma.

in the present study, we investigated the effect of coenzyme Q10 on acoustic age-related hearing loss in DBA/2J and C57/B6 mouse. the DBA/2J mouse is known as one of the elderly hard hearing model animals because it gets hard hearing at the early stage. Actually, it is reported for hearing to decrease gradually from three weeks. Also C57/B6 are model of aging hearing loss, but more slowly than DBA/2J.

Animals were divided into the three groups: group 1, coenzyme Q10 200mg/day; group 2, coenzyme Q10 20mg/day; group 3,control, mixed into water and given from 4weeks old. We assessed auditory brainstem response (ABR) threshold every 4week in DBA/2J mouse and 8week in C57/B6 mouse. in addition we observed the cochlear hair cell damages.

153 Mefloquine-Induced Changes in Apoptotic Gene Expression in Cochlear Basilar Membrane and Spiral Ganglion Neurons

Haiyan Jiang[1], Dalian Ding[1], Richard Salvi[1]

[1]*University at Buffalo*

in previous studies, we showed that mefloquine damages the cochlear hair cells and auditory nerve fibers in the inner ear by apoptosis; however, the signaling pathways involved are poorly understood. to address this issue, we used quantitative RT-PCR apoptosis-focused gene arrays (96 genes) to assess the changes in gene expression in the basilar membrane (hair cells-supporting cells) and spiral ganglion regions of rat cochlear organotypic cultures treated with 100 µM of mefloquine for 3 h. in the basilar membrane, 13 genes increased expression and 13 gene decreased expressions. of these 26 genes, 11 were classified as anti-apoptotic and 15 genes as apoptotic. in spiral ganglion neurons, 21 genes changed significantly; 18 genes showed increased expression and 3 gene showed reduced expression. the apoptotic and anti-apoptotic genes in both basilar membrane and spiral ganglion tissues mainly involved gene associated with p53 signaling, TNF ligand family, CARD family, TNF receptor family, death domain family, and lactate dehydrogenase A. While the gene expression changes in basilar membrane and spiral ganglion tissues showed considerable, some differences were observed which may reflect the unique response of each tissue. These results indicate that mefloquine induces a wide range of apoptotic and anti-apoptotic signals during the early states of ototoxicity. Supported in part by NIH grant R01 DC06630.

154 Ototoxicity of Mefloquine in Vestibular organotypic Cultures

Dongzhen Yu[1], **Dalian Ding**[1], Richard Salvi[1]

[1]*University at Buffalo*

Mefloquine is an effective and widely used anti-malaria drug; however there are clinical reports suggesting that mefloquine may be neurotoxic and ototoxic. in previous studies, we showed that mefloquine damaged hair cells and neurons in cochlear organ cultures in a dose-dependent manner. Since dizziness and loss of balance are listed as common side effects of mefloquine, we hypothesized the mefloquine might damage the vestibular epithelium. to test this hypothesis, we applied mefloquine to organotypic cultures from postnatal day 3 rat utricles. the macula of the utricle was carefully dissected out, mounted as a flat surface preparation and cultured overnight in serum free medium. Utricular explants were treated with 10, 50, 100, or 200 µM mefloquine for 24 h. Some utricles were cultured for 24 h with 50 µM mefloquine and the activity of caspase-3, -6, -8, or -9 was evaluated with these fluorogenic caspase inhibitors. Specimens were stained with rhodamine conjugated phalloidin to label the actin in the stereocilia and Topro-3 to visualize the nuclei. Mean vestibular hair cell density was 65.2± 4.9 per 0.01 mm2 in controls. Mefloquine caused a dose-dependent loss of utricular hair cells. Treatment with 10 µM caused a slight reduction to 58 per 0.1 mm2; 50 µM caused a significant decline to 28.3±13.4 per 0.01mm2 and 200 µM destroyed nearly all the hair cells (5.2±3.6 per 0.01 mm2). These results indicate that 10µM of mefloquine is the approximate “threshold” for inducing hair cell loss in postnatal utricular cultures. Hair cell nuclei from mefloquine treated utricles were condensed and fragmented and hair cells were positive for initiator caspases-8, -9 and executioner caspase-3, -6. These results indicate that mefloquine-induced hair cell degeneration in the postnatal rat utricle occurs by apoptosis and is initiated by both membrane and mitochondrial cell death pathways.

Supported in part by NIH grant R01 DC06630-01

155 Styrene Ototoxic Effect Depends Mainly On the Exposure Level

Chiemi Tanaka[1], Guang-Di Chen[1], Donald Henderson[1]

[1]*SUNY at Buffalo*

Campo and colleagues (Campo et al., Hear. Res., 154, 170-180, 2001) reported that styrene-induced hearing loss did not increase with exposure duration. in this experiment, the issue of whether the total dose or the distribution is a key for determining extent of hearing loss was evaluated. Experimental animals (Long-Evans rats) were divided into 4 groups (n=6 rats in each group) to be exposed by gavage to styrene at a dose of 800 mg/kg once a day for 5 days per week for 3 weeks (3w-800 group), at 400 mg/kg for 6 weeks (6w-400 group), at 200 mg/kg for 12 weeks (12w-200 group), and at 100 mg/kg for 24 weeks (24w-100 group). the 3w-800-mg-group developed an up to 35-dB permanent threshold shift (PTS) and an up to 60% OHC loss in the middle turn. the 6w-400 group showed an up to 15-dB PTS and an up to 40% OHC loss, which were

slightly higher than those induced by a 3-week-exposure at a dose of 400 mg/kg. the 12w-200 group showed less than 10% OHC loss and less than 10-dB PTS. the 24w-100 did not show significant damage, although the animals received the same amount of styrene as the other animals. the data indicate that exposure level is critical for styrene ototoxicity and that the ear fs propensity to accumulate the toxic styrene is limited. a clinical implication of this research is that short, transient, high-level styrene exposure can be ototoxic.

This study was supported by NIOSH grant 1R01OH008113-01A1.

156 Ototoxic Effects of Styrene Exposure During Gestation and Lactation in Rats

Manna Li [1], Guang-Di Chen[1], Chiemi Tanaka[1], Eric Bielefeld[1], Donald Henderson[1]

[1]SUNY at Buffalo

Styrene is extensively used in industries and many workers, including women, are exposed to styrene. Styrene ototoxicity has been well documented. However, the impact of styrene ototoxicity during gestation and lactation is still unclear. We hypothesize that styrene may induce less ototoxic effect on pregnant rats because of high estrogen levels, but may induce significant ototoxic effects on the development of the babies' auditory system. Five pregnant rats were exposed to styrene by gavage at a dose of 400 mg/kg/day starting from the fourth day of gestation for 5 days per week for 6 weeks. Six male rats were exposed at the same dosage for the same period for comparison. Two pregnant rats were unexposed and their offspring were used as controls. Three days after the last gavage of the 6-week styrene exposure, threshold shift in the mother rats and the male rats was assessed using compound action potential (CAP) recording, and their auditory hair cells were counted. the styrene exposure caused an about 15-20-dB threshold shift and 30-40% outer hair cell (OHC) loss in the mid-frequency region in both groups of the pregnant rats and the males rats. Threshold shifts of the baby rats were measured 2 months after birth by recording of both auditory brainstem response (ABR) and CAP. Significant CAP threshold shift was only observed in those rats from one mother but not the other four mothers. Interestingly, ABR threshold shift was observed in all of the 5 families. Almost all of the baby rats have normal cochlear anatomy, i.e.: no hair cells loss. the mechanism for the hearing loss in the mother rats and the pups is discussed.

This study was supported by NIOSH grant 1R01OH008113-01A1.

157 Functional and Structural Changes in the Chinchilla Cochlea and Vestibular System Following Round Window Application of Carboplatin

Yide Zhou[1], Dalian Ding[1], Suzanne Kraus[1], Richard Salvi[1]

[1]University at Buffalo

Carboplatin, a second-generation anticancer drug, has a low level of ototoxicity in most species; however, in chinchillas carboplatin preferentially destroys inner hair cells (IHC) and type I vestibular hair cells at moderate doses while at higher doses it destroys both IHC and outer hair cells (OHC) and type I and type II vestibular hair cells. to better understand the time course and mechanisms of carboplatin toxicity, carboplatin was applied to the round window membrane (5mg/ml, 50¡Ìl) of the right ear and the functional and anatomical consequences were examined at 1, 3, 7, 14 and 30 days post-treatment. Carboplatin caused a significant reduction in distortion product otoacoustic emissions (DPOAE) at all frequencies 3 d post-treatment. the threshold of the compound action potential (CAP) increased significantly from 3 to 7 d post-treatment and after 14 d the CAP was absent. Carboplatin treatment induced spontaneous nystagmus 1 d after carboplatin treatment which disappeared 2-3 d later. Cold caloric stimulation evoked a robust nystagmus response in untreated ears, but the nystagmus response disappeared approximately 3 d after carboplatin treatment. Vestibular dysfunction was associated with a significant reduction of vestibular hair cell density 3 d post-treatment. the early stages of cochlear and vestibular hair cell degeneration were associated with nuclear shrinkage and fragmentation, morphologic features of apoptosis, upregulation of initiator caspase 8 and executioner caspase 3, but absence of caspase 9 labeling. These results indicate that carboplatin rapidly penetrates the round window leading to severe functional deficits arising from programmed hair cell death initiated from the cell death receptors on the surface of cell membrane. Supported by NIH grant R01 DC06630-01

158 Effects of Cisplatin-Ethacrynic Acid Cochlear Pathology On DPOAE

Withdrawn

159 Selective Damage of Murine Cochlear Cell Types by Varying Concentrations of Ouabain

Osamu Adachi[1], Konstantina M. Stankovic[1], Arthur G. Kristiansen[1], Joe C. Adams[1], Michael J. McKenna[1]

[1]Massachusetts Eye & Ear Infirmary

Ouabain is a cardiac glycoside that specifically binds to Na/K-ATPase and inhibits its activity. Other authors have established that ouabain induces selective degeneration of spiral ganglion neurons when applied to the round window of gerbils. We wanted to determine whether ouabain can similarly cause selective damage in the murine cochlea. to minimize variability inherent in intratympanic application of pharmacologic agents, we used intralabyrinthine approach to delivered ouabain. a total of 10 µl of ouabain at the concentrations 1.0, 0.1 or 0.05mM was injected through a small fenestra in the posterior semicircular canal of 6 week old male CBA/CaJ mice at the volume ratio of 1µl/min after making a release fenestra in the lateral semicircular canal. Mice were sacrificed 10 days after treatment (3 mice for each concentration of ouabain) and their cochleae analyzes histologically using Azure stain, and

ABSTRACTS OF THE THIRTY-FIRST ANNUAL MIDWINTER RESEARCH MEETING OF THE

Association for Research in Otolaryngology

February 16-21, 2008

Phoenix, Arizona, USA

Peter A. Santi, PhD
Editor

Association for Research in Otolaryngology
19 Mantua Road, Mt. Royal, NJ 08061 USA