Chemical-Induced Hearing Loss in Shipyard Workers

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Objective: The aim of this study was to determine the effect of lead, cadmium, arsenic, toluene, and xylene exposure on hearing compared with noise exposures alone. **Methods:** Personnel at a shipyard ($n = 1266$) were divided into four exposure groups on the basis of concentrations: low metals/low solvents/high noise (reference group), high metals/high solvents/low noise, high metals/low solvents/high noise, and high metals/high solvents/high noise. Hearing changes occurring from the years 2004 to 2015 were analyzed. **Results:** Hearing changes were significantly worse at 1000 Hz ($P = 0.007$), averaged across 2000 to 4000 Hz ($P = 0.014$), and averaged across 500 to 6000 Hz ($P = 0.014$) for the high metals/high solvent/high noise group compared with the low metals/low solvents/high noise only reference group. **Conclusion:** Simultaneous exposures classified as high for metals/solvents/noise appear to damage hearing more than exposure to noise alone. Hearing conservation programs should take into consideration combined exposures to metals, solvents, and noise, not simply exposure to noise.

Hearing loss may lead to a reduction in quality of life that includes reduced speech recognition, reduced perception of audible warnings, and adverse health function. Hearing loss and tinnitus were the most prevalent service connected disabilities among Department of Defense (DoD) personnel in FY 2015, consisting of nearly two million affected individuals.[1] Hearing loss is the third most prevalent chronic condition in the U.S., ahead of diabetes and cancer.[2] The cost for hearing loss treatment continues to grow nationally with projected growth from $8.2 billion in 2002 to $51.4 billion in 2030.[3]

Hearing loss may adversely affect work environments where accurate communication between coworkers, or awareness of audible warnings from equipment, may be necessary to prevent accidents that would otherwise lead to injury and property damage. The negative effects of hearing loss may also affect an individual's social environment leading to more depressive symptoms, more feelings of loneliness, and smaller social networks.[4] Environmental noise exposure has also been shown to increase the prevalence of coronary heart disease mortality.[5] Rate of hearing loss due to chronic noise exposure is greatest during the first 10 to 15 years of noise exposure and decreases as the hearing threshold increases.[6] Due to this characteristic, most workers are unaware that their hearing ability is decreasing, which poses additional challenges in preventing hearing loss or changing the exposure profile to limit further loss.

The most common auditory pattern in noisy occupations is hearing loss sloping toward high frequencies between 3000 and 6000 Hertz (Hz). A ''notch'' configuration is seen when hearing loss is greatest at 4000 Hz.[7] Specifically, receptor hair cells in the cochlea may become broken, collapsed, or fused, which has the ability to adversely affect hearing sensitivity, as well as inhibit neural transmission through the central auditory pathways.[8] Hearing loss at lower frequencies, such as the 500 and 1000 Hz octave bands, can be detrimental because of the adverse effects on speech perception and quality. Although noise exposure is considered the primary risk factor in the development of hearing loss, recent evidence has suggested that exposures to ototoxic substances may affect hearing alone or in combination with noise. The terms ''ototoxic'' and ''vestibulotoxic'' are used to define any substance, including drugs or industrial chemicals, toxic to the auditory or vestibular system and affects the senses of hearing and/or balance.[9] Noise exposure may damage the cochlea as a component of the peripheral auditory system; however, chemicals are believed to affect both the cochlea and central auditory system.[9] Solvents are expected to disrupt antioxidant defenses, making the ear more sensitive to the effects of noise when exposure occurs synergistically, or in combination.[9]

Vyskocil et al[10] evaluated weight of evidence for ototoxic potential of industrial chemicals by conducting a literature review of 224 ototoxic substances related to animal and human studies. Materials such as ethyl benzene, n-hexane, and xylene were classified as potentially ototoxic individually, while materials such as lead, styrene, toluene, and trichloroethylene were classified as ototoxic individually without consideration of combined noise exposure.[10] Noise and toluene in combination was classified as presenting evidence of interaction.[10]

An extensive review of literature, including epidemiological data, animal studies, and case reports, conducted by Campo et al[8] classified toluene, ethylbenzene, n-propyl benzene, styrene, trichloroethylene, xylene, n-hexane, carbon disulfide, carbon monoxide, hydrogen cyanide, acrylonitrile, lead, mercury, and tin as having a ''good'' weight of evidence for ototoxicity. Cadmium, arsenic,

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(3) Air Force Institute of Technology Occupational & Environmental Health Seminar, Dayton OH, April 2017.

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bromates, and halogenated hydrocarbons were classified as having a ''fair'' weight of evidence for ototoxicity.[8]

Voluntary agencies, such as the American Conference of Governmental Industrial Hygienists (ACGIH), recognize that some chemicals alone or in combination with noise may result in hearing loss. This recognition has led to the recommendation for obtaining audiograms in settings where there are exposures to noise and carbon monoxide, lead, manganese, styrene, toluene, or xylene.[11] Beyond the ACGIH recommendations, assessment of hearing loss risk may be problematic because there are no specific exposure limits established for lead, cadmium, arsenic, toluene, and xylene considering ototoxicity as an endpoint, with and without coexposure to noise. The level of hearing loss that is attributable to combinations of lead, cadmium, arsenic, toluene, and xylene with hazardous noise, compared with hazardous noise alone, is not known at this time. The purpose of the study was to determine whether high concentrations of heavy metals (consisting of lead, cadmium, and/or arsenic), high concentrations of solvents (consisting of toluene and/or xylene), and high noise levels modify the effect on hearing compared with noise exposure alone in a population of shipyard personnel.

METHODS

Data for this retrospective study were collected from several sources; pure tone audiometry records, industrial hygiene air sampling, and noise measurement records. Industrial hygiene sampling records were supplemented with documented workplace exposure assessments contained in written industrial hygiene survey reports. This study was designed to include an 11-year time frame because hearing change generally develops over the first 6 to 10 years of noise exposure and because research suggests hearing loss effects from solvents initially begin at 2 years postexposure, but may manifest as late as 5 years postexposure.[12]

Research Setting

Personnel employed by the Puget Sound Naval Shipyard (PSNS) in Bremerton, Washington, were targeted for investigation. Specific PSNS modernization/repair activities included maintenance on hulls, mechanical, electrical, electronics, and weapon systems in a heavy industry environment consisting of several workplaces. Workplaces including shops responsible for a variety of tasks, including ship fitting, metal forging, welding, ship-wrighting, fabric-working, woodworking, piping, electric installation, sheet metal fabrication, general maintenance, and quality assurance were specifically included in this study due to their wide-ranging noise, metal, and solvent exposure conditions. The research population consisted of male and female civilian personnel ranging in age from 24 up to 75 years and receiving audiometric evaluations during the study period of January 1, 2004, to March 30, 2015. The 2004 to 2015 timeframe was selected to assess effects of exposure across the hypothesized latency periods for metals, solvents, and noise and because exposure records were readily available beginning in the year 2004 through the investigation end date of April 1, 2015.

Exclusion Criteria

At the beginning of the study, the initial PSNS population was large including 103,612 audiogram records; however, several exclusion/inclusion criteria were applied to the data set. The data were originally collected for nonresearch purposes and, thus, some of the data contained inaccurate or incomplete information. The researchers made audiogram exclusion decisions in consultation with a licensed audiologist. Exclusion criteria are summarized here including the number of records removed.

(1) Audiograms for personnel assigned to workplaces with uncharacterized noise, metal, and solvent exposures or for personnel with noise exposures in excess of 95 dBA (36,388);
(2) Audiograms for personnel with less than 5 years of audiograms (20,908);
(3) Audiograms missing results in any of the 500 to 6000 Hz frequencies or workplace/shop assignment information (2737);
(4) Personnel with only low metals, solvents, and noise exposures (280);
(5) Personnel changing workplace/shop assignment during the study period and audiograms demonstrating unlikely values potentially indicating testing errors (276).

Audiometry

Audiogram results were retrieved from the Defense Occupational and Environmental Heath Readiness System-Hearing Conservation (DOEHRS-HC) program. Results were reported in 5 decibels Hearing Level (dBHL) increments at 500, 1000, 2000, 3000, 4000, and 6000 Hz octave bands for the left and right ears individually, and averaged across 2000 to 4000 and 500 to 6000 Hz. Hearing change was averaged across 2000 to 4000 Hz because these frequencies are used by the DoD and OSHA to determine Permanent Threshold Shifts. Hearing change was averaged across 500 to 6000 Hz to determine the potential for broadband systemic toxicity from ototoxic substance exposure and to determine if ototoxic substances are associated with hearing loss at other than Permanent Threshold Shift frequencies. Hearing change for each individual was recorded in dB by subtracting the reference (or first) audiogram conducted during the study time frame from the last audiogram conducted during the time frame.

Stressor Data Collection

The DOEHRS-Industrial Hygiene (DOEHRS-IH) database was used to extract 8-hour TWA personal breathing zone air sampling and personal noise monitoring results. Exposure data in this study included noise, lead, cadmium, arsenic, toluene, and xylene due to their high exposure prevalence in the occupational environment.

Point estimates of the exceedance fraction, as described by Mulhausen and Milz,[13] were used to classify metal and solvent concentrations as ''high exposure'' or ''low exposure.'' The OSHA action levels for lead (0.03 mg/m^3; milligrams per cubic meter of air), cadmium (0.0025 mg/m^3), and arsenic (0.005 mg/m^3) were selected to replace the occupational exposure limit (OEL) when determining the exceedance fraction. Exposure profiles with exceedance fraction estimates at least 5% for each metal concentration within each similar exposure group (SEG) were classified as high exposures, while all other exposure profiles were classified as low exposure. Exceedance fraction, normality, and log-normality characteristics were calculated with the American Industrial Hygiene Association's (AIHA's) version 235 ''IHSTAT'' pre-programmed spreadsheet statistical package.[14] This process of assigning concentrations to high or low exposure profiles was also used for solvent concentration and noise dosimetry measurement classifications. However, 25 ppm (parts per million) of air for toluene and 3 ppm for xylene were used as the exceedance fraction thresholds consistent with a study conducted by Śliwinska-Kowalska,[15] which suggested adverse audiological effects beginning at these concentrations. Noise dosimetry data as 8-hour TWAs were compiled to an equivalent continuous level for each SEG. Consistent with the DoD 6055.12 Hearing Conservation Program instruction,[16] noise SEGs were classified as high exposure if at least 85 dBA.

Confirmed, suspected, or questionable ototoxic substances, including carbon monoxide, trichloroethylene, n-hexane, styrene, mercury, tin, and carbon disulfide, may have been present in the workplaces being studied. However, a review of IH survey reports and sample results for chemicals classified as ototoxins but not included in the study revealed that either the chemical was not present in the workplace or all exposures were less than their respective OSHA action levels.

After lead, cadmium, arsenic, toluene, and xylene concentrations were stratified according to high or low concentration, general groups of metals, solvents, and noise were classified as high or low exposure based on the individual contaminant. If at least one metal component or one solvent component was classified as ‘‘high’’ for each SEG, this would result in the entire group being classified as ‘‘high’’ exposure. Using low metals/low solvents/high noise exposure as the reference group, one-way statistical classification of exposures resulted in four exposure combinations: (1) low metals/low solvents/high noise (reference group), (2) high metals/high solvents/low noise, (3) high metals/low solvents/high noise, and (4) high metals/high solvents/high noise.

Descriptive statistic measures, Kruskal–Wallis nonparametric analysis of variance (ANOVA) test, and Mann–Whitney *U* pairwise comparison tests were conducted to determine whether there were significant differences in hearing acuity (measured in dBHL) across the frequency range of 500 to 6000 Hz according to exposure group. Statistical analyses were conducted with SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY) using an alpha level of 0.05. The study was approved by the Institutional Review Boards (IRBs) at all institutions associated with the project. Each IRB classified the study as ‘‘exempt from further review,’’ due to the retrospective nature of this research.

RESULTS

After implementation of the exclusion criteria, there were 1266 personnel included in the study who received audiograms from January 1, 2004, to March 30, 2015. Information regarding workplace, population, and industrial processes completed by the workers included in this investigation is presented in Table 1. Generally, hearing changes were greatest in the high frequency range, beginning at 2000 Hz and extending through 6000 Hz for both the left and right ears. The mean hearing change averaged over the 2000, 3000, and 4000 Hz frequencies for the left ear was 3.8 dB (SD = 6.1 dB). The mean hearing change for the right ear was 3.9 dB (SD = 6.1 dB). Hearing change was similar between left and right ears across all frequencies. However, while industrial exposures are not expected to target hearing in a specific ear, the left ear was slightly better and had smaller hearing changes. The ear with the smallest hearing change was used in all analysis as a conservative statistical approach. Mean hearing changes along with all other monitored frequencies are presented in Table 2.

Exposure Group Characteristics

Initially, personnel were individually assigned to a high or low exposure profile for lead, cadmium, arsenic, toluene, xylene, and noise. When viewed independently, 76.8% of the study population was exposed to noise levels at least 85 dBA. A total of 97.1% of the population was exposed to high lead concentrations ($\geq$0.03 mg/m^3). Conversely, 28.4% of the population was exposed to high cadmium ($\geq$0.0025 mg/m^3) and high arsenic ($\geq$0.005 mg/m^3) concentrations individually. A total of 23% of the population was exposed to high concentrations of toluene ($\geq$25 ppm) and 23.2% was exposed to high concentrations of xylene (3 ppm). No subject was exposed to metals and solvents in isolation; however, a group of subjects were exposed only to noise. Table 3 details the individual group characteristics for lead, cadmium, arsenic, toluene, xylene, and noise without consideration for exposure combinations.

Considering exposure group combinations, the largest proportion of subjects had high metals/low solvents/high noise at 50.9% ($n = 644$). The group classified as low metals/low solvents/high noise contained the fewest subjects ($n = 37$), representing 2.9% of the full population. Due to the low exposure to metals and solvents, but high levels of noise, this group became the reference group. Table 4 describes the distribution of population by combined exposure groups.

TABLE 1. Distribution of Population by Shop and Process

Shop Number	Shop Title	Shop Population	Processes
6	Central Tool Issue	37	Tool repair Equipment Repair/Maintenance/Testing
11	Shipfitter	294	Metal machining Brazing/Soldering/Welding/Cutting Coating/Painting operations Coating/Painting removal Mechanical cleaning Equipment repair/Preventative maintenance
26	Welding	360	Metal machining Brazing/Soldering/Welding/Cutting Coating/Painting removal Nondestructive inspection/Testing
99	Facilities/Project Support	284	Electrical/Electronics Equipment repair/Preventative maintenance Hazardous material clean-up and handling Supplies/Materials handling Utility production/Distribution
64	Woodworking	291	Metal machining Brazing/Soldering/Welding/Cutting Coating/Painting operations Coating/Painting removal Mechanical cleaning Composite work Insulation Plastics/Rubber processing Woodworking

TABLE 2. Mean Threshold Change According to Frequency and Exposure Group

	Low Metals/Low Solvents/High Noise (Reference Group) ($n = 37$)		High Metals/High Solvents/Low Noise ($n = 294$)		High Metals/Low Solvents/High Noise ($n = 644$)		High Metals/High Solvents/High Noise ($n = 291$)	
Frequency, Hz	Mean, dB	SD, dB	Mean, dB	SD, dB	Mean, dB	SD, dB	Mean, dB	SD, dB
500	0.3	6.8	0.1	6.7	0.5	6.2	1.2	6.4
1,000	−1.6	6.4	−0.3	6.5	0.2	6.2	0.8	7.2
2,000	0.5	7.2	1.6	6.5	1.9	7.0	2.5	6.8
3,000	3.4	9.4	4.2	6.9	4.3	7.7	5.0	7.8
4,000	2.9	10.0	5.3	8.4	4.8	8.9	5.7	8.9
6,000	6.4	10.5	6.9	10.2	7.0	11.0	7.1	11.1
2,000–4,000 Mean	2.3	7.7	3.7	5.7	3.7	6.2	4.4	6.1
500–6,000 Mean	2.0	6.2	3.0	4.9	3.1	5.2	3.7	5.6

SD, standard deviation.

Mean age between exposure groups was approximately equal ranging from 48 to 51 years. The highest mean age was found in the noise-only group at 51 years. Mean years of audiogram follow-up was 6.7 years for the low metals/low solvents/high noise reference group, which was less than the mean years of audiograms for the other exposure groups, ranging from 7.6 to 8.2 years. Mean years of age, audiograms per subject, and years of audiograms per subject are summarized in Table 5.

Kruskal–Wallis Nonparametric Test

Because the data did not meet the assumptions of one-way ANOVA, Kruskal–Wallis, a nonparametric test, was used to determine whether there was a significant difference between hearing changes among the four exposure groups: (1) low metals/low solvents/high noise (reference group), (2) high metals/high solvents/low noise, (3) high metals/low solvents/high noise, and (4) high metals/high solvents/high noise.

Hearing outcome analysis included hearing changes in the left ear at (1) the individual frequencies of 500, 1000, 2000, 3000, 4000, and 6000 Hz, (2) the averaged frequencies across 2000, 3000, and 4000 Hz (the frequencies known to exhibit permanent threshold shifts from noise exposure), and (3) the averaged frequencies across the 500 to 6000 Hz frequency range. As described in Table 6, hearing changes between exposure groups were statistically significant at 1000 Hz ($P = 0.019$), across 2000, 3000, and 4000 Hz ($P = 0.032$), and across the 500 to 6000 Hz range ($P = 0.039$). No other individual frequency change was significantly different at the 0.05 alpha level.

TABLE 3. Distribution of Population by Individual Stressor Groups

Stressor	Number	Percent
Noise		
Low (<85 dBA)	294	23.2
High (≥85 dBA)	972	76.8
Lead		
Low (<0.03 mg/m^3)	37	2.9
High (≥0.03 mg/m^3)	1229	97.1
Cadmium		
Low (<0.0025 mg/m^3)	906	71.6
High (≥0.0025 mg/m^3)	360	28.4
Arsenic		
Low (<0.005 mg/m^3)	906	71.6
High (≥0.005 mg/m^3)	360	28.4
Toluene		
Low (<25 ppm)	975	77.0
High (≥25 ppm)	291	23.0
Xylene		
Low (<3 ppm)	972	76.8
High (≥3 ppm)	294	23.2

Mann–Whitney *U* Post Hoc Nonparametric Tests

A Mann–Whitney *U* test was conducted for the frequency of 1000 Hz, across the frequencies of 2000, 3000, and 4000 Hz, and across the frequencies of 500 to 6000 Hz (as previously identified during the Kruskal–Wallis test) to determine which specific exposure group combinations had significantly different hearing changes. Although these pairwise comparisons indicated statistically different hearing changes between some of the exposed groups, a Bonferroni adjustment consistent with the procedures detailed by Pallant[17] was needed to avoid expanding the type I error associated with multiple statistical tests while making multiple pairwise comparisons between groups. Bonferroni adjustment resulted in a new alpha value of 0.017 (0.05/3). Full analyses for 1000, 2000 to 4000, and 500 to 6000 Hz are summarized in Table 7.

The Mann–Whitney *U* test revealed that hearing was worse for all personnel exposed to (1) high metals/high solvents/low noise, (2) high metals/low solvents/high noise, and (3) high metals/high solvents/high noise when compared with personnel exposed only to (4) low metals/low solvents/high noise (reference group). Specifically, at 1000 Hz, hearing change in the high metals/high solvents/low noise group was not significantly worse than the low metals/low solvents/high noise reference group ($P = 0.07$). However, the high metals/low solvents/high noise group ($P = 0.012$) and the high metals/high solvents/high noise group ($P = 0.007$) had significantly worse hearing change compared with subjects with low metals/low solvents/high noise exposure. Both groups recorded an increase (change) of 5 dB over the noise group at 1000 Hz. The high metals/

TABLE 4. Distribution of Population by Combined Metal, Solvent, and Noise Groups

Stressor Group	Number	Percent
Low metals/Low solvents/High noise (reference group)	37	2.9
High metals/High solvents/Low noise	294	23.2
High metals/Low solvents/High noise	644	50.9
High metals/High solvents/High noise	291	23.0

TABLE 5. Means and Standard Deviations for Years of Age, Audiograms per Subject, and Years of Audiograms by Exposure Group

	Exposure Group							
	Low Metals/Low Solvents/High Noise (Reference Group) ($n = 37$)		High Metals/High Solvents/Low Noise ($n = 294$)		High Metals/Low Solvents/High Noise ($n = 644$)		High Metals/High Solvents/High Noise ($n = 291$)	
Component	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Years of age	51.1	11.7	48.2	12.5	47.4	12.4	48.1	12.2
Audiogram/subject	7.7	3.0	10.0	2.9	9.5	2.9	10.2	2.9
Years of audiograms	6.7	1.7	8.2	1.9	7.6	1.9	8.1	1.9

SD, standard deviation.

low solvents/high noise group was comprised primarily of workers assigned to shop 26 welding shop and shop 99 Facilities and Project Support. The high metals/high solvents/high noise group was comprised primarily of workers assigned to shop 64 woodworking shop.

The Mann–Whitney test results for the 2000 to 4000 Hz range of frequencies and the 500 to 6000 Hz range of frequencies revealed a significant decrease in hearing for the high metals/high solvents/high noise exposure group when compared with hearing for the low metals/low solvents/high noise reference group ($P = 0.014$). Overall, the (1) high metals/high solvents/high noise, (2) high metals/low solvents/high noise, and (3) high metals/high solvents/low noise groups exhibited hearing that was, on average, 3.3 dB worse than hearing for the (4) low metals/low solvents/high noise reference group across the 2000, 3000, and 4000 Hz range. The high metals/high solvents/low noise group was comprised primarily of workers assigned to shop 11 welding shop, while the low metals/low solvents/high noise reference group was comprised primarily of the workers assigned to shop 6 central tool Issue shop. Across the 500 to 6000 Hz frequencies, the high metals/high solvents/high noise group recorded a hearing change of 2.1 dB higher than the low metals/low solvents/high noise reference group. The high metals/high solvents/low noise group and high metals/low solvents/high noise group both exhibited a 1.7 dB higher hearing change than the low metals/low solvents/high noise reference group.

DISCUSSION

Effect of Metals, Solvents, and Noise on Hearing Loss

Because noise-induced hearing loss typically affects the outer hair cells of the cochlea first, and decreases hearing between 2000 and 4000 Hz, hearing loss at 1000 Hz suggests that the addition of high concentrations of metals in combination with noise, and high concentrations of metals and solvents in combination with noise, may target the outer hair cells in a more uniform manner across the entire basilar membrane. That is, while the outer hair cells in the basal portion of the basilar membrane (specifically between 2000 and 4000 Hz) are damaged physically by the pressure exertion of the stapes footplate pivoting in and out of the oval window, the outer hair cells in the medial portion of the basilar membrane (around 1000 Hz) appear to be damaged by the ototoxic concentration of metals and solvents in the tissues, or the effects that these metals and solvents have on the neural substrate within the cochlea.

This finding is similar to findings from our previous research.[18] When analyzing the same data set for associations between Permanent Threshold Shifts and metals, solvents, and noise exposures, Schaal et al[18] found that personnel exposed to high concentrations of noise and metals in combination had a, nonstatistically significant, 30% increased odds of developing permanent thresholds shifts in the 2000 to 4000 Hz range. Results of the present investigation in the 2000 to 4000 Hz range and when averaged across the 500 to 6000 Hz range are also consistent with the findings from a study investigating the effects of noise and cadmium fumes on hearing impairment.[19] These researchers found more auditory damage (primarily at 4000 and 6000 Hz) in a group of metallurgical industrial employees exposed to cadmium and noise when compared with a group of employees from the same factory exposed only to noise. A study by Choi and Kim[20] found that the likelihood of hearing loss in the 2000 to 4000 Hz range was 1.64-fold higher for a group of employees exposed to metals (lead, cadmium, mercury, chromium, and manganese) than in unexposed individuals. In addition, the likelihood for hearing loss in this same frequency range was 2.15-fold higher for a group of employees exposed to a mixture of solvents in the presence of noise than an unexposed group.[20]

Schaal et al[18] found that personnel with high exposures to metals and solvents in combination had 2.4 times the odds of developing a Permanent Threshold Shift compared with a low exposed metals/solvents/noise group. However, the present study did not find significant hearing loss differences in the high metals/high solvent/low noise group when compared with a group with only

TABLE 6. Kruskal–Wallis Test for Hearing Threshold Change Differences Between Exposure Group According to Frequency

Frequency, Hz	Chi-Square	df	*P*
500	4.587	3	0.205
1,000	9.980	3	**0.019**
2,000	4.894	3	0.180
3,000	6.781	3	0.079
4,000	5.077	3	0.166
6,000	0.267	3	0.966
2,000–4,000 average	8.796	3	**0.032**
500–6,000 average	8.381	3	**0.039**

P values in bold are statistically significant results at α level of 0.05.

TABLE 7. Mann–Whitney *U* Pairwise Comparisons According to Exposure Group

Exposure Group Comparison	*n*	Mean Rank	Sum of Ranks	*P*	Hearing Change, dB
1000 Hz					
Low metals/Low solvents/High noise	37	140.86	5,212.00	0.077	0
High metals/High solvents/Low noise	294	169.16	49,734.00		
Low metals/Low solvents/High noise	37	265.76	9,833.00	**0.012**	5
High metals/Low solvents/High noise	644	345.32	222,388.00		
Low metals/Low solvents/High noise	37	126.74	4,689.50	**0.007**	5
High metals/High solvents/High noise	291	169.30	49,266.50		
2000–4000 Hz					
Low metals/Low solvents/High noise	37	138.58	5,127.50	0.063	3.3
High metals/High solvents/Low noise	294	169.45	49,818.50		
Low metals/Low solvents/High noise	37	284.12	10,512.50	0.069	3.3
High metals/Low solvents/High noise	644	344.27	221,708.50		
Low metals/Low solvents/High noise	37	128.64	4,759.50	**0.014**	3.3
High metals/High solvents/High noise	291	169.06	49,196.50		
500–6000 Hz					
Low metals/Low solvents/High noise	37	139.51	5,162.00	0.074	1.7
High metals/High solvents/Low noise	294	169.33	49,784.00		
Low metals/Low solvents/High noise	37	281.74	10,424.50	0.059	1.7
High metals/Low solvents/High noise	644	344.40	221,796.50		
Low metals/Low solvents/High noise	37	128.47	4,753.50	**0.014**	2.1
High metals/High solvents/High noise	291	169.08	49,202.50		

P values in bold are statistically significant results at α level of 0.017.

high noise exposures (low metals/low solvents/high noise). This finding is counterintuitive but may be explained because the former study compared a group with high metals and solvents exposures to a group with low exposures to metals, solvents, and noise. In contrast, the present study compared groups with high metal/high solvent exposures to groups with high noise exposures alone. The primary goal of the present study was to determine the additional contribution of high metal and solvent concentrations in the presence of noise, rather than determining the hearing loss compared with a low exposed group. The results of the current investigation suggest that exposure to high concentrations of metals and solvents combined with noise plays a major role in eliciting hearing loss compared with noise exposure alone.

Results of the present study are similar to results reported in previous studies for metals exposures in the presence of noise. Hearing loss was found between 2000 and 8000 Hz for workers exposed to lead in isolation.[21,22] Other investigators identified hearing loss between 500 and 4000 Hz from lead and cadmium exposure,[23,24] as well as from lead exposure in combination with noise.[25] The present study results of significant hearing loss occurring at 1000 Hz were similar to the results reported by Park et al[26] where lead exposures, measured biologically in bone, were positively associated with hearing changes at 1000, 2000, and 8000 Hz.

Hearing changes of 5 dBHL are generally considered to be normal test/retest variability. Computerized pure tone audiometry, such as the method used by the DoD, has been determined to have test and retest differences ranging from 3.3 to 3.6 dB,[27] while manual audiometry with over-the-ear (supra-aural) headphones showed similar test/retest variability of up to 5 dB.[28] Aside from these variabilities explained by testing and mechanical techniques, employees enrolled in a Hearing Conservation Program may not report noticing differences in their communication abilities or abilities to detect alarms or other signals for hearing loss of 1.7 to 5 dB. However, if monitoring these hearing threshold changes allows the CAOHC-trained personnel to detect changes in hearing earlier, it may allow workers to be removed from environments in which synergistic exposures occur in order to prevent hearing loss.

Worse hearing loss in the high metals/high solvents/high noise group may be partially explained by longer exposure duration (8.1 years) compared with the low metals/low solvents/high noise reference group (6.7 years). However, Schaal et al[18] found increased odds of developing decreased hearing due to exposure to high concentrations of metals and solvents while controlling for the effects of other cofactors, such as high noise levels, gender, age, and years of audiograms. The increased odds of exhibiting a permanent threshold shift after controlling for other demographic characteristics suggests that the exposure to high concentrations of metals and solvents could cause the greater levels of hearing change.

Strengths and Limitations

Strengths of the present study include a large population size (personnel) and long duration of employment. Other strengths include the stability and low turnover rate of this population. Choosing a population with low turnover was important because long-term employment ensured that multiple audiograms could be obtained and, as a result, hearing changes could be detected during the investigation timeframe. Long-term employment was evidenced by subjects averaging 9.6 audiograms during the January 1, 2004, to March 30, 2015, study period.

Substantial quality assurance measures were used to ensure accuracy of audiometric and exposure data. The inclusion of personnel having 5 or more years of audiometric data allowed for proper comparison of unequal exposure duration and allowed focus to be placed on hearing losses occurring during the study period, rather than from unquantified chemical exposures occurring outside the study's timeframe.

Information on all potential risk factors associated with hearing loss was not available for analysis in the current study is a limitation of the study. Factors not investigated include health-related characteristics such as body mass index,[29] systolic blood pressure,[30] cardiac function and cholesterol,[31] cigarette smoking,[32] and ototoxic medication use.[33] In addition, demographic characteristics (eg, social/ethnic status and gender) and exposure-related risk factors (eg, off-duty noise and chemical exposures and whole body vibration) were not investigated in this study.[26,34–36] Medical histories related to ear surgeries were also not obtained due to the reported low risk of developing sensorineural hearing loss after surgery.[37,38] Although these factors have been shown to affect hearing in certain populations, this information is not routinely collected for day-to-day management of hearing conservation programs by the DoD or other federal regulatory bodies, such as OSHA. As a result, review of personnel medical records to retrieve this information was not included within the scope of this study's IRB and would have been time- and cost-prohibitive to collect.

Use of hearing protection and respiratory protection was not evaluated during this investigation due to lack of information availability and because compliance with personal protective equipment (PPE) requirements was anticipated. PPE, when used properly, would have reduced at-ear noise exposures and inhalation exposures that would have not otherwise been apparent because noise, metal, and solvent exposures were measured outside of PPE. Because this investigation found statistically significant differences between chemical and noise exposure and hearing loss, absence of PPE may have led to an even greater level of hearing loss.

Consistent with the National Institute of Occupational Safety and Health's (NIOSH's) recommendations[39] and DoD policy,[16] audiogram results were not age adjusted. Age was approximately equal across exposure groups averaging 47 to 51 years old with the oldest average age of 51 represented by the high noise reference group. Because significantly worse hearing was identified in the metals, solvents, and noise combined exposure groups, age adjusting the audiograms would have likely led to even greater levels of hearing loss. The American Academy of Audiology[40] has stated that people up to 60 years of age are expected to have normal hearing if their unprotected ears are not exposed to noise levels at least 85 dBA. Overall, adverse study effects potentially associated with prevalence of presbycusis from failing to adjust hearing change were not anticipated.

Recommendations for Future Research

It remains unknown what concentrations of lead, cadmium, arsenic, toluene, and xylene may be considered safe to the auditory system alone and in combination with noise. Magnitude of exceedance within each stressor's respective exceedance fraction was unable to be evaluated during this study. Although a minimum 5% exceedance fraction was used to distinguish between high and low exposures, exceedance fraction for lead was as high as 37.6% in some exposure combination groups and 9% in other exposure combination groups.

Interaction analysis was not conducted because some of the possible exposure combinations had no subjects. Searle[41] indicated that not all interactions are estimable for data with empty cells and, thus, the traditional test for interaction does not test the hypothesis of all interactions being equal to zero. We chose to analyze the data using a one-way classification of exposures to facilitate ease of result interpretation. Future research necessary to address these issues should include designing studies in which groups are isolated for exposure to lead, cadmium, arsenic, toluene, and xylene allowing investigators to determine main order, second-order, and third-order effects. However, identifying isolated groups exposed to single stressors may be challenging, as industrial workplaces commonly include multiple hazardous agents.[39]

Future studies should consider using other forms of audiological testing to replace or supplement pure tone audiometry. Auditory evoked response measurements, transient evoked otoacoustic emissions, distortion product otoacoustic emissions, and speech recognition tests (in quiet and in noise) may be more sensitive to cochlear changes and more capable of detecting adverse auditory effects from metal and solvent exposure.[42,43] Auditory evoked response measurements (ie, Auditory Brainstem Response, Middle Latency Response), which measure brain activity associated with the central auditory nervous system, may identify central auditory disorders resulting from ototoxic substances earlier than pure tone audiometry would identify peripheral hearing loss.[25,42]

CONCLUSION

Hearing loss resulting from the combination of lead, cadmium, arsenic, toluene, xylene, and noise exposure introduces potentially serious concerns. Historically, hazardous noise exposure has been considered the primary risk factor for hearing loss in occupational environments. The U.S. Navy requires personnel to be managed in a hearing conservation program when personal exposure to noise reaches 85 dBA as an 8-hour TWA. However, results from the current investigation revealed that exposure concentrations of less than OSHA action levels for lead, cadmium, arsenic, toluene, and xylene as 8-hour TWAs when combined with noise exposures at least 85 dBA as 8-hour TWAs led to greater levels of hearing change than noise exposure alone. These relationships were found at frequencies forming the basis of permanent threshold shift determinations and at lower frequencies. These findings could suggest adverse effects on quality of life measures, such as speech intelligibility, and could lead to earlier detection of hearing loss caused by synergistic effects from noise and other ototoxic agents. Although additional investigation continues to be needed, workplace interventions should target exposure reductions for multiple occupational stressors, not just noise, to reduce the risk of adverse workplace and social outcomes.

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