Effects of Combined Exposure to Metals, Solvents, and Noise on Permanent Threshold Shifts

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Background *Studies suggest metal and solvent exposure may damage hearing. This study evaluated the association between exposures classified as high for metals, solvents, and noise on permanent threshold shift (PTS) development.*
Methods *A total of 1,546 personnel at an industrial shipyard were divided into five exposure groups based on level of concentration: high noise, high metals/solvents, high metals/noise, high metals/solvents/noise, and a low metals/solvents/noise reference group. Hearing threshold changes were analyzed to identify development of a PTS.*
Results *Logistic regression indicated high metals/solvents and high metals/solvent/noise groups had significantly greater odds ratios of 2.4; 95%CI [1.02, 2.85] and 1.7; 95%CI [1.46, 3.94], respectively, compared to a reference group. Both groups were associated with PTSs while controlling for age, gender, and exposure duration.*
Conclusions *Simultaneous exposures classified as high for metals and solvents may damage hearing. Results suggest the need for expanding hearing conservation programs to consider combinations of exposures to metals, solvents, and noise.* Am. J. Ind. Med.
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KEY WORDS:* *hearing-loss; chemicals; metals; solvents; noise; permanent threshold shift; shipyard

INTRODUCTION

Hearing loss affects 31 million Americans [Fausti et al., 2005]. Occupational hearing loss and tinnitus were the most frequently occurring service-connected disabilities among Department of Defense personnel as reported by the Veterans Benefits Administration for fiscal year 2013 [Department of Veteran's Affairs, 2014]. These disabilities combined to account for 1.7 million cases in fiscal year 2012 with a cost of $424.1 million in audiological services. The overall standard threshold shift rate, including U.S. Navy, Marine Corps, military and civilian subgroups for the Department of the Navy, was 11.4 percent in fiscal year 2014 [Navy and Marine Corps Public Health Center, 2014]. In the general population, hearing loss is the third-most common chronic health condition among older adults after hypertension and arthritis with an estimated hearing difficulty prevalence of 11% [Bogardus et al., 2003]. In addition to the 31 million Americans affected by hearing loss, an additional 9 million are estimated to be exposed to chemicals that may damage hearing [National Institute of Occupational Safety and Health (NIOSH), 2016].

The effects of chemical exposure on hearing loss is an understudied research area. While hearing loss is commonly associated with exposure to loud noise, research has been conducted suggesting exposure to chemicals such as solvents

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and metals in industrial settings in combination with noise or alone may be an additional contributor to hearing loss [Botelho et al., 2009]. Chemicals such as metals and solvents may damage hearing by cochlear hair cell and central nervous system impairment [Campo et al., 2009]. Specifically, solvents such as toluene inhibit the auditory efferent system by modifying the protective acoustic reflex response that is normally invoked with exposure to high intensity noise [Campo et al., 2009]. Multiple studies investigating the effect on hearing loss from co-exposure to noise and organic solvents found exposure to such chemicals as toluene, xylene, styrene, and methyl ethyl ketone to present an increased odds of hearing loss both alone and when combined with noise exposure [Morata et al., 1993; Śliwinska-Kowalska et al., 2004; Kim et al., 2005; Chang et al., 2006; Rabinowitz et al., 2008]. Some studies have found that personnel exposed to organic solvents at concentrations less than Occupational Safety and Health Administration (OSHA) permissible exposure limits (PELs) in combination with noise developed hearing loss earlier than personnel exposed only to noise [Metwally et al., 2012].

Metal exposure effects on hearing loss has been studied less extensively compared to solvent and noise exposures. Studies investigating the effect of metals, when measured biologically, on hearing loss found exposures to lead, cadmium, and arsenic were correlated with worse hearing thresholds, specifically resulting in an increased odds of hearing loss [Forst et al., 1997; Wu et al., 2000; Hwang et al., 2009; Prasher, 2009; Shargorodsky et al., 2011; Choi et al., 2012]. Similar results were reported during investigation of inhalation exposures of metals in combination with noise in industrial settings where cadmium and noise posed a greater risk of hearing loss than noise alone [Abreu and Suzuki, 2002]. A study investigating whether co-exposure to organic solvents and heavy metals in the workplace modified the risk of hearing loss in a background of hazardous noise exposure found the odds of hearing loss was 1.64-fold higher for the heavy metals exposed group while the odds of hearing loss was 2.15-fold higher in individuals exposed to organic solvents when compared to unexposed groups [Choi and Kim, 2014].

The American Conference of Governmental Industrial Hygienists [ACGIH] recognizes that some chemicals pose adverse health risks to hearing, recommending periodic hearing tests for personnel exposed to such chemicals as carbon monoxide, lead, manganese, styrene, toluene, or xylene [ACGIH, 2016]. Considering occupational chemicals could alter auditory function by either ototoxicity, neurotoxicity, or a combination of both processes, exposure to some chemicals at sufficient concentrations could affect hearing without occupational exposure to noise [Franks et al., 1996]. Additionally, it has been estimated that workers may be exposed to at least three hazardous agents simultaneously so it may be inappropriate to restrict occupational hearing loss to only a noise-induced origin [Franks et al., 1996]. The large opportunity for exposure to multiple stressors simultaneously presents challenges in studying the effects of each stressor alone and in combination due to difficulty in distinguishing between biological effects.

Additionally, there is little governmental guidance regulating chemical exposures for purposes of preventing hearing loss [Vyskocil et al., 2012]. Most ototoxic substances commonly found in industrial workplaces have established occupational exposure limits to avoid adverse health effects based on the primary target organ affected by the specific material and not combinations of target organs. Overall, it is not known if occupational exposure limits for materials such as lead, cadmium, arsenic, toluene, and xylene, among others, are adequate in preventing hearing loss, considering exposure occurring alone or in combination with noise. The few studies conducted have been designed to determine solvent and metal effects among exposed or non-exposed groups rather than determining the effect of high and low exposure concentration gradients on hearing loss. While many studies have found an association between metal and solvent exposed personnel and hearing loss, the specific concentrations at which adverse audiological effects begin are not known.

The present study aimed to fill a gap in research and investigate the effect of combined exposures to metals, solvents, and noise on hearing loss. Additionally, the purpose of the study was to determine if exposures classified as high for heavy metals such as lead, cadmium, and arsenic; exposures classified as high for solvents such as toluene and xylene; and exposures classified as high for noise modify the effect of permanent threshold shift (PTS) development among shipyard personnel.

MATERIALS AND METHODS

The purpose of this research was to determine if combined exposure to heavy metals, solvents, and noise was associated with development of hearing loss compared to a low concentration exposed reference group. Data were collected retrospectively from several sources including audiometric evaluations and industrial hygiene sampling records as the primary sources of data. Industrial hygiene sampling records were supplemented with documented workplace exposure assessments contained in written industrial hygiene survey reports.

Research Setting

Individuals assigned to workplaces in the Puget Sound Naval Shipyard (PSNS) in Bremerton, Washington, an industrial shipyard, were the focus of the research. Shops at the shipyard conducted a variety of tasks in support of ship fitting, metal forging, sheet metal fabrication, welding, electrical, shipwright, fabric-work, woodwork, piping, general maintenance, and quality assurance. The research population consisted of civilian personnel receiving audiograms during the study period of January 1, 2004 to March 30, 2015. Audiogram and sampling records for male and female personnel ranging in age from 18 up to 77 years old were included in the study.

Exclusion/Inclusion Criteria

Exclusion criteria were necessary because the data were originally collected for non-research purposes and, as a result, some of the data contained inaccurate or incomplete information. The researchers made audiogram exclusion decisions in consultation with a licensed audiologist. The following exclusion criteria were used for this study:

- Personnel assigned to workplaces with eight-hour time weighted average noise dosimetry exposures in excess of 95 decibels A weighted (dBA). The purpose of this exclusion factor was to avoid excessive noise exposure from potentially masking hearing loss effects that may have been otherwise identified from heavy metal and solvent exposures. Additionally, this exclusion factor was selected to be consistent with the noise levels found in past noise and ototoxic substance investigations;
- Audiograms missing:
    - threshold results in any of the 2,000–4,000Hz frequencies,
    - year of birth,
    - gender,
    - workplace/shop assignment information;
- Personnel with less than 5 years of audiograms;
- Personnel changing workplace/shop assignment during the study period;
- Personnel under 18 years of age;
- Personnel assigned to workplaces where noise and chemical stressors were present in the workplace but were not quantified with sampling;
- Audiograms demonstrating unlikely threshold values potentially indicating testing errors.

Audiometry

Pure tone audiograms analyzed during this study were originally administered by occupational medicine personnel and audiologists trained and certified by a Hearing Conservation course accredited by the Council for Accreditation in Occupational Hearing Conservation (CAOHC). Audiogram results were later retrieved from the Defense Occupational and Environmental Heath Readiness System-Hearing Conservation (DOEHRS-HC) program. DOEHRS-HC is the Department of Defense's (DoD's) repository for audiogram data. Auditory thresholds in the left and right ear across the 2,000, 3,000, and 4,000 Hz frequency bands were reported in 5 dB increments. Hearing change was considered the outcome measure during the study period and was assessed by subtracting the reference or first audiogram during the study time frame from the last audiogram conducted during the time frame for the respective individual. Presence of a PTS was determined by evaluating changes in hearing using the criteria defined by DoD Instruction 6055.12: Hearing Conservation Program [Department of Defense, 2010]. A PTS was defined as a hearing acuity change of $\geq$10 dB averaged over the 2,000, 3,000, and 4,000 Hz frequencies. Changes $\geq$10 dB at these frequencies were categorized as a PTS while changes $<$10 dB were categorized as non-PTS (dichotomous variable). After the comparison between each person's first and last audiogram and after the threshold change was calculated, only the last valid audiogram for the worker was retained in the analysis. Workplace information provided for each subject in the audiogram results was used to link the audiogram to the chemical and noise exposure data.

Stressor Data Collection

Exposure data were collected from the DOEHRS-Industrial Hygiene (DOEHRS-IH) database from personal breathing zone air sampling or personal noise monitoring compiled to eight-hour time weighted averages. Exposure data in this study included: (i) noise; (ii) lead, cadmium, and arsenic heavy metals; and (iii) toluene and xylene solvents. Specific information exported from DOEHRS-IH for each sample included unit identification code (description of the command), shop number, shop name, worksite assessment name and number (process name), similar exposure group (SEG) name, sampling identification number, date of monitoring, laboratory analytical number, chemical sampled, chemical concentration (reported in mg/m^3 or ppm), sampling length (reported in min), and eight-hour time weighted average (reported in mg/m^3 or ppm).

The metal, solvent, and noise measurements were assigned to personnel using the SEG method described by Mulhausen and Damiano [2015]. Establishing SEGS allows for grouping workers based on their general occupational exposure profile and considers similar job classifications, work teams, and industrial tasks performed for similar durations [Mulhausen and Damiano, 2015]. Metal, solvent, and noise measurements for specific industrial tasks, work teams, and job classifications were assigned to personnel performing similar duties in each shop. Any individual changing jobs during the 11-year study timeframe were excluded from analysis because the job change may have led to an inaccurate exposure concentration assignment.

Each metal sample result within each shipyard shop selected for study, as an eight-hour time weighted average, was compared to the respective OSHA action levels for lead (0.03 mg/m^3), cadmium (0.0025 mg/m^3), and arsenic (0.005 mg/m^3). Solvent sample results were compared to a threshold level of 25 ppm for toluene and 3 ppm for xylene, based on the results of a literature review of past ototoxic substance studies concluding that these were the threshold levels for potentially inducing hearing loss as a result of exposure to organic solvents [Śliwinska-Kowalska, 2007].

Similar to the exposure assessment criteria described by Mulhausen and Milz [2015], the point estimate of the exceedance fraction was used as the threshold for classifying lead, cadmium, and arsenic metal concentrations as high or low exposure. However, the action level for lead, cadmium, and arsenic were selected to replace the occupational exposure limit (OEL) when determining the exceedance fraction. Specifically, any exceedance fraction estimate where ≥5% of the exposure profile for each metal concentration within each similar exposure group exceeded the respective OSHA action level as an eight-hour time weighted average were classified as high exposures. All other exposure profiles were classified as low exposure. Exceedance fractions were calculated with American Industrial Hygiene Association's (AIHA's) version 235 "IHSTAT" pre-programmed spreadsheet statistical package [AIHA, 2015]. During this process, each exposure distribution was checked for normality and log-normality. A similar process was used to classify toluene and xylene solvent concentrations into high or low exposure groups. However, the toluene exceedance fraction threshold was established as 25 ppm while the xylene exceedance fraction threshold was established as 3 ppm.

Noise dosimetry measurements were exported from DOEHRS-IH as eight-hour time weighted averages to identify workplaces with average sound pressure levels equal to or greater than 85 dBA. These eight-hour time weighted average noise dosimetry data were compiled to an equivalent continuous level for each SEG which represents the log average of sound pressure levels as a function of time during the observation period [Earshen, 2003]. Consistent with the DoD 6055.12 Hearing Conservation Program Instruction [Department of Defense, 2010], noise was classified as high exposure if the eight-hour time weighted average noise dosimetry measurement was ≥85 dBA and low exposure if the eight-hour time weighted average noise dosimetry measurement was <85 dBA.

There may have been some situations where noise, metal, and solvent exposures may have been present in the workplace but exposure was not quantified. This may have been a result of a low exposure assessment or determination that the exposure did not present a substantial health risk. These qualitative exposure assessment decisions were documented in the industrial hygiene survey and considered such information as frequency and duration of exposure. Regarding situations where noise, metal, and solvent concentrations were not measured, industrial hygiene survey documentation was consulted to confirm the overall low exposure assessment.

There may have been other contaminants present suspected of causing audiological damage but were not included in this study. These contaminants included carbon monoxide, trichloroethylene, n-hexane, styrene, mercury, tin, and carbon disulfide. However, these chemicals were not as widely present in the shipyard compared to the study chemicals of interest, and were either not present in the workplace or all exposures were less than their respective action levels. The latter exposure situation would have led to a classification of low exposure if the chemicals were included in this study.

After classifying each individual chemical as a high or low exposure based on the respective OSHA action levels for lead (0.03 mg/m^3), cadmium (0.0025 mg/m^3), and arsenic (0.005 mg/m^3), and literature derived levels for toluene (25 ppm) and xylene (3 ppm), the general groups of metals, solvents, and noise were classified as high or low exposure based on the individual lead, cadmium, arsenic, toluene, and xylene exposure classifications. At least one metal component and at least one solvent classified as high for each SEG would result in the entire group being classified as high exposure. Based on the exposure distribution found in this study population, subject exposure combinations were described as five groups: (i) high noise/low metals/low solvents; (ii) high metals/high solvents/low noise; (iii) high metals/high noise/low solvents; (d) high metals/high solvents/high noise; and (e) low metals/low solvents/low noise (reference group). Examination of a high solvent/high noise/low metals group was not conducted because after applying all classification and exclusion criteria, no individuals met the characteristics for the group.

Descriptive statistics, logistic regression, odds ratios, and 95% confidence intervals were calculated with SPSS version 23, using an alpha level of 0.05. The study was approved by the Naval Medical Center San Diego and Indiana University of Pennsylvania Institutional Review Boards (IRBs). Each IRB classified the study as exempt from further review.

RESULTS

The initial study population consisted of 103,612 audiogram records for 20,238 personnel receiving audiograms from January 1, 2004 to March 30, 2015. However, implementation of exclusion criteria limited the final number of people to 1,546 personnel representing 14,791 audiograms.

TABLE I. Demographic Characteristics of Study Population

Component	Number	Percent
Gender		
Male	1,360	88
Female	186	12
Age (years)		
18–27	43	2.8
28–37	384	24.8
38–47	302	19.5
48–57	355	23.0
58–67	423	27.4
68–77	39	2.5
Hearing loss		
PTS prevalence	228	14.7
Stressor group		
High noise/low metals/low solvents	37	2.4
High metals//high solvents/low noise	294	19
High metals/high noise/low solvents	644	41.7
High metals/high solvents/high noise	291	18.8
Low metals/low solvents/low noise (reference group)	280	18.1

PTS, permanent threshold shift.

The majority of subjects were male (88%) with the remaining female (12%). The average age of all subjects was 48 years old. Personnel involved in the study ranged from 18 to 77 years of age. However, the mean years of age was approximately equal across exposure groups ranging from 47.4 years of age to 51.1 years. Demographic characteristics of the full study population are provided in Table I while exposure group specific characteristics are described in Table II.

Distribution of the population by overall high or low metals, solvent, and noise group are shown in Table I. The largest proportion of subjects had high exposures to metals and noise at 41.7% (644). The high metals and solvents group, high metals, solvents, and noise group, and the reference group all were approximately equal in size. The group classified as high noise but low metals and solvents contained the least number of subjects (n = 37), representing 2.4% of the full population.

Information regarding the average number of audiograms per person and years of audiograms per person was collected as a surrogate for employment duration. Each subject was required to have at least two audiograms so that a comparison could be made between the first audiogram within the study time frame and the final audiogram during the study. Beyond this minimum of two audiograms, at least three audiograms would have been conducted per person if a PTS was exhibited. Each subject averaged nearly 10 audiograms over the 11-year study time-frame. Additionally, each subject averaged nearly 8 years of audiograms during the study. Audiogram demographics according to exposure group are provided in Table II.

Gender characteristics among the exposure groups were nearly equal for the high metals/solvent, high noise/metals, and high noise/metals/solvents groups ranging from 88.3 to 89.9% male. The lowest proportion of males was found in the high noise group at 73%. The minor differences in proportion of males for each exposure group were not expected to have confounded results because the unique contribution of exposure was assessed by controlling for the effects of gender among other demographic characteristics. Gender characteristics according to exposure group are presented in Table III.

PTS prevalence according to exposure group ranged from 10.4 to 24.6%. The highest prevalence was found in the high noise group (24.6%) and the lowest prevalence was found in the low metals, solvent, and noise reference group (10.4%). PTS prevalence according to exposure group is visually depicted as Figure 1.

Logistic Regression

Logistic regression was performed to assess the likelihood of subjects developing a PTS as a result of exposures to chemicals while controlling for demographic variables. Specifically, each of the five exposure groups, age, gender, and exposure duration were assessed collectively to determine their ability to predict development of a PTS. The risk factors were also individually assessed, while controlling for the

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

	Exposure group									
	High noise (n = 37)		High metals/solvents (n = 294)		High noise/metals (n = 644)		High noise/metals/solvents (n = 291)		Low noise/metals/solvents (n = 280)	
Component	Mean	SD	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	48.8	12.5
Audiogram/subject	7.7	3.0	10.0	2.9	9.5	2.9	10.2	2.9	8.9	3.0
Years of audiograms	6.7	1.7	8.2	1.9	7.6	1.9	8.1	1.9	7.5	1.9

SD, standard deviation.

TABLE III. Gender Characteristics According to Exposure Group

Characteristic	High noise (n = 37)	High metals, solvents (n = 294)	High noise, metals (n = 644)	High noise, metals, solvents (n = 291)	Low noise, metals, solvents (n = 280)
Male	73%	89.5%	89.9%	88.3%	83.6%
Female	27%	10.5%	10.1%	11.7%	16.4%

effects of all other variables, to determine their unique contribution in the development of a PTS. Interaction analysis was not conducted because three of the eight possible exposure combinations (cells) had zero subjects. As described by Searle [1978], for data with empty cells not all interactions are estimable and the traditional test for interaction does not test the hypothesis of all interactions equal to zero. We chose to analyze the data using a one-way classification of exposures to facilitate ease of result interpretation. Based on the composition of the exposure categories for personnel included in this investigation, the following exposure combinations, described as five groups, were analyzed: (i) high noise, low metals, low solvent group; (ii) high metals, high solvent, and low noise group; (iii) high metals, high noise, low solvents group; (iv) high metals, high solvents, high noise group, with (v) the reference group being low metals, low solvents, and low noise.

The logistic regression model containing exposure combination, age, gender, and years of audiograms significantly predicted PTS development ($\chi^2 = 145.27, P < 0.05$). The model explained 9–15.8% of PTS variance. Six of the seven predictor variables made a statistically significant contribution to the predictive model (i.e., the ability of exposure level and personnel demographic information to predict PTS development) including high metals/solvents, high metals/solvents/noise, high noise, age, years of audiograms, and gender (male).

The strongest predictor of development of a PTS after adjusting for all exposure levels, age, years of audiograms, and gender in the model was high exposures to noise with an adjusted OR of 2.65, 95%CI [1.05, 6.68]. The next strongest exposure related predictors of PTS development were high metals and solvents with an adjusted OR of 2.4, 95%CI [1.46, 3.94] followed by high metals, solvents, and noise exposures with an adjusted OR of 1.70, 95%CI [1.02, 2.84]. Subjects with high exposure to metals and noise in combination had an adjusted OR of 1.32, 95%CI [0.83, 2.11] indicating increased odds of developing a PTS by 32%. However, the high metals and noise group was not a statistically significant predictor in the logistic regression model when compared to the reference group. Overall, subjects with high exposures to noise and high exposure to metals and solvents had approximately 2.5 times the odds of developing a PTS compared to the reference group while high exposures to metals, solvents, and noise were nearly twice as likely to have a PTS while controlling for age, gender, years of audiograms, and the other exposure groups in the model. The primary objective of the present investigation was to determine the effects of metals, solvents, and noise exposure on development of a PTS. However, despite mean gender, age, and years of audiograms per subject being similar between each exposure group, the effects of these variables were controlled for in the

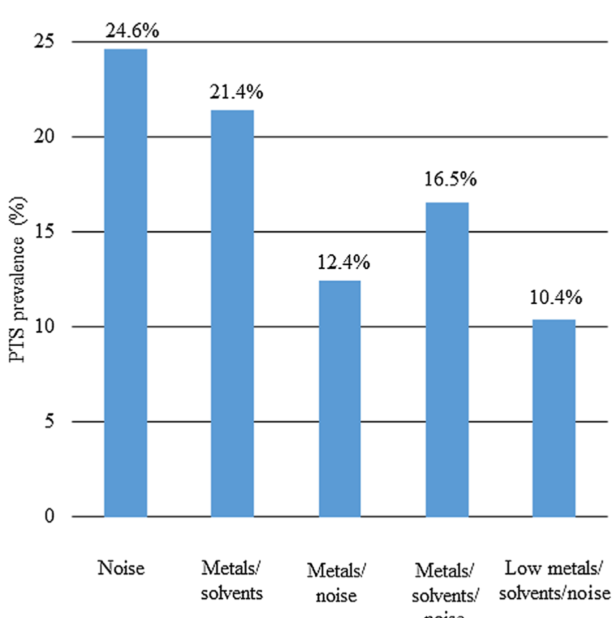

FIGURE 1. Permanent threshold shift (PTS) prevalence according to exposure group.

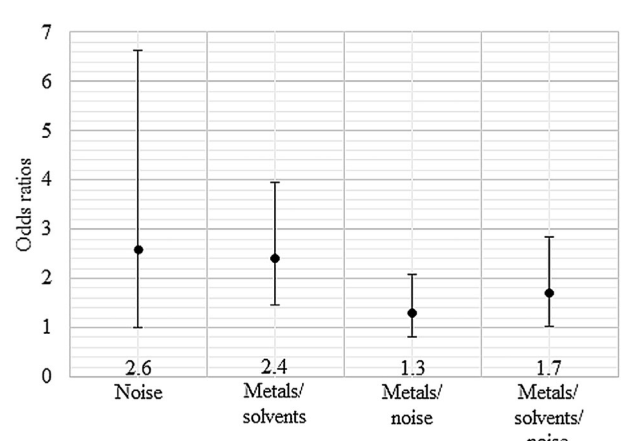

FIGURE 2. Odds ratios of exposure groups with 95% confidence intervals (CIs). Reference group: low metals/solvents/noise.

TABLE IV. Logistic Regression Predicting Likelihood of Developing a Permanent Threshold Shift

	Values*	B	S.E.	Wald statistic	df	P-value	Odds ratio	95%CI for odds ratio
All exposure groups				16.55	4	**0.002**		
High noise	1	0.97	0.47	4.27	1	**0.039**	2.65	1.05–6.68
High metals/solvents	2	00.88	0.25	11.96	1	**0.001**	2.40	1.46–3.94
High metals/noise	3	0.28	0.24	1.36	1	0.243	1.32	0.83–2.11
High metals/solvents/noise	4	0.53	0.26	4.08	1	**0.043**	1.70	1.02–2.85
Years of audiograms	5–11	0.14	0.04	12.65	1	**0.000**	1.15	1.07–1.25
Gender	Female = 0 Male = 1	0.63	0.31	4.19	1	**0.041**	1.87	1.03–3.42
Age (years)	18–77	0.07	0.01	82.68	1	**0.000**	1.07	1.05–1.08
Constant		−7.30	0.61	142.31	1	0.000	0.00	

CI, confidence interval; B, beta value; S.E., standard error.
*Exposure groups entered as dummy variables.
P values in bold are statistically significant results.

multivariate logistic model to prevent result confounding. All logistic regression results are presented in Table IV while Figure 2 provides a visual depiction of each exposure group's OR with 95 percent confidence intervals compared to the low metals, solvents, and noise reference group.

DISCUSSION

Noise has been a well-studied risk factor for hearing loss; however, hearing loss resulting from heavy metal exposures in combination with solvent and noise exposures is an issue requiring further investigation. This study was conducted to determine the combined effect of heavy metal, solvent, and noise exposures on hearing loss among a population of shipyard personnel while controlling for gender, age, and years of audiograms. This study found high exposures for metals which were defined as exposures exceeding OSHA action levels for lead 0.03 mg/m^3, cadmium 0.0025 mg/m^3, and arsenic 0.01 mg/m^3 in combination with high exposures to solvents which were defined as toluene exposures exceeding 25 ppm, and xylene exposures exceeding 3 ppm pose significantly greater odds of developing a PTS than a low exposed reference group.

Effect of Metals, Solvents, and Noise on Hearing Loss

Exposure to metals and solvents

Exposure to metal and solvents without the influence of noise was nearly equal to the odds of developing a PTS across the 2,000, 3,000, and 4,000 Hz frequencies as the high noise exposure group. These results were similar to a study by Choi and Kim [2014] that found the odds of hearing loss was 1.64-fold higher for a heavy metals exposed group while the odds of hearing loss were 2.15-fold higher in individuals exposed to organic solvents when compared to unexposed groups. The current study's results are also similar to those of previous studies that found elevated and statistically significant increased odds of hearing loss from metal and solvent exposures when measured biologically [Morata et al., 1997; Hwang et al., 2009; Park et al., 2010; Choi et al., 2012].

Regarding solvent concentrations, the results of the present study were consistent with a study by Morata et al. [1993] which showed a higher risk of hearing loss for personnel exposed to concentrations of toluene ranging from 10 to 70 ppm and for xylene ranging from 12 to 40 ppm. Chang et al. [2006] found exposure to toluene as low as 33 ppm was enough to result in a 10.9 times higher estimated risk of hearing loss from exposure to toluene and noise combined compared to a noise only group. Elevated odds of developing hearing loss in subjects exposed to xylene in concentrations as low as 3 ppm and ranging from 3 to 6 ppm was found during the present investigation. The combined exposure of metals and noise may be a potential explanation for adverse effects on hearing at lower toluene and xylene concentrations in the current study compared to previous studies. Previous studies have generally focused on solvent and noise exposures without the influence of metals.

Exposure to metals and noise

Despite personnel categorized with high metals and noise exposure being 32% more likely to develop a PTS, it was the only exposure group not significantly different from the reference group, a finding which conflicts with those of past studies. A study investigating the effects of noise and cadmium fumes on hearing impairment found significantly worse hearing at the 4,000 and 6,000 Hz frequencies in a group exposed to cadmium welding fumes and noise compared to a group only exposed to noise [Abreu and Suzuki, 2002]. A study by Choi and Kim [2014] found the likelihood of hearing loss was 1.64-fold higher for a heavy metals exposed group in the presence of noise compared to an unexposed group.

Results of the high metals and noise category were unexpected considering the group had the greatest number of subjects ($n = 644$) and had the greatest noise level of all groups ranging from 87.8 to 95 dBA. The lack of a high solvent exposure component in the high metal and noise group suggests high exposure to solvents composed of at least toluene and xylene in combination with metals and noise have a critical role in the development of hearing loss at the 2,000, 3,000, and 4,000 Hz frequencies. This is supported by several studies where solvent exposures were the focus of the study which identified an increased risk of hearing loss associated with solvent exposures such as toluene and xylene [Morata et al., 1993; Morata et al., 1997; Śliwinska-Kowalska et al., 2004; Gagnaire and Langlais, 2005; Kim et al., 2005; Chang et al., 2006; Śliwinska-Kowalska, 2007; Rabinowitz et al., 2008; Campo et al., 2009; Fuente et al., 2009; Johnson and Morata, 2009; Vyskocil et al., 2012].

Exposures to metals, solvents, and noise

Subjects classified as having high exposure to metals (lead, cadmium, and arsenic), solvents (toluene and xylene), and noise in combination had increased odds of developing a PTS but the odds was lower than the high metals and solvent group. Considering hazardous noise is a well-known risk factor for hearing loss, it was anticipated that the addition of high noise exposures to the high metals and solvents exposure group would further increase the likelihood of hearing loss compared to high metals and solvents exposure alone. A more detailed investigation of the metal and solvent content in the high metals and solvents group revealed an exceedance fraction (percentage of cases exceeding the OSHA action level) of 37.6% (31.8–37.6%) for lead and 2.7% (0–2.7%) for arsenic while the solvent exceedance fractions (percentage of cases exceeding 25 ppm for toluene and 3 ppm for xylene) were as high as 12.2% (3.7–12.2%) for xylene and 0% for toluene. Conversely, the high metals, solvents, and noise group had lower exceedance fractions for metals such as 9% (6.3–9%) for lead and 0% for arsenic and differing exceedance fractions for solvents such as 17.8% (12.5–17.8%) for toluene and 0% for xylene. The increased exceedance fraction of lead, the presence of arsenic, and the presence of xylene in the high metals and solvents group compared to the high metals, solvents, and noise group may indicate lead and arsenic's substantial contribution to the resulting hearing loss. This assertion is consistent with other studies demonstrating the ototoxic effects of lead when measured biologically [Forst et al., 1997; Wu et al., 2000; Counter and Buchanan, 2002; Campo et al., 2009; Hwang et al., 2009; Shargorodsky et al., 2011; Choi et al., 2012; Choi and Kim, 2014]. While both toluene and xylene exposure are suspected of resulting in hearing loss, several studies have found xylene may pose a greater hearing loss risk than toluene [Gagnaire and Langlais, 2005; Śliwinska-Kowalska, 2007].

Despite the effects of noise exposure being controlled for during the logistic regression analysis, assessment of absolute noise levels was necessary to determine if noise exposure between the groups accounted for the observed differences. Groups with a high noise exposure component had similar mean noise levels. Specifically, mean noise levels for each group was 85.3 dBA for the high noise group, 86.7 dBA for the high metals and noise group, and 86.3 dBA for the high metals, solvents, and noise group. In contrast, the mean noise level was 74.6 dBA for the high metals and solvent group and 79.6 dBA for the low metals, solvents, and noise reference group. The similarity of noise levels between the groups with a high noise exposure component suggests the observed differences were due to the combination of metal, solvent, and noise rather than noise alone.

Strengths and Limitations

This study had several limitations. Because exposures were classified as high for noise and metals (lead, cadmium, and arsenic) if exceeding OSHA action levels, true exposure may have been less than the measured concentration after considering use of hearing protection or respiratory protection. Hearing protection and respiratory protection, when used properly, would have reduced at-ear noise exposures and inhalation exposures that would have not otherwise been apparent because exposures were measured outside of personal protective equipment (PPE). The use of hearing protection and respiratory protection was not evaluated during this investigation due to lack of information availability and because compliance with PPE requirements was anticipated. Any potential for exposure misclassification was expected to be non-differential and not expected to bias toward any individual exposure group because personal exposure across all groups were assigned without consideration of PPE use. Because this investigation found statistically significant associations between chemical and noise exposure and hearing loss, absence of PPE may have led to an even greater association.

Information for all potential risk factors associated with hearing loss was not available for analysis in this study. Results of this study found up to 15.9% of the variance in hearing loss was explained by metals, solvents, and noise exposure, age, gender, and years of audiograms (as a surrogate for exposure duration). This indicates 84% of the variance was explained by other factors in the study population. Some studies have focused on such hearing loss cofactors as: body mass index, systolic blood pressure, cholesterol, alcohol drinking status, social class, ethnic status, family history of hearing loss, off-duty noise and chemical exposures (personal stereo use, firearm use, and hobbies), use of ototoxic medications (antibiotics and chemotherapy drugs), and whole body vibration [Toppila et al., 2000; Ecob et al., 2008; Park et al., 2010; Medeiros et al., 2015]. The widespread use of such potential risk factors as personal stereo use and ototoxic medication use were assumed to be non-differential between exposure groups.

Other important variables potentially impacting hearing loss include cigarette smoking, presbycusis, and a history of ear surgery/ear infections. Information for these risk factors, among others potentially responsible for hearing loss are not usually collected because the information is not mandated by the DOEHRS-HC program, DoD hearing conservation program instructions, and federal regulatory bodies. Review of individual medical records to retrieve this information was not included within the scope of this study's IRB approval and would have been cost prohibitive. Despite being unable to collect additional information on these factors, several studies have shown distribution of cigarette smoking is similar within occupationally exposed groups [Kim et al., 2005; Ecob et al., 2008; Park et al., 2010]. Some studies investigating the effects of organic solvents on hearing loss revealed smoking was not a statistically significant predictor of hearing loss [Morata et al., 1997; Kim et al., 2005]. Cigarette smoking was expected to be non-differential and not anticipated to influence hearing loss in favor of one exposure group over any other.

Audiogram results were not age adjusted in the investigation consistent with the National Institute of Occupational Safety and Health's (NIOSH) recommendations [NIOSH, 1998]. Age-related hearing loss develops differently across individuals in a population and not all members of a population suffer a clinically measureable decrease in hearing acuity with age. Applying population statistics to an individual was not appropriate because correcting for age would overestimate hearing loss in some subjects while underestimating it in other subjects [NIOSH, 1998; Kirchner et al., 2012; Campo et al., 2013]. Additionally, the American Academy of Audiology [2003] has stated that an otherwise healthy person is expected to have normal hearing through at least 60 years of age if their unprotected ears are not exposed to noise levels >85 dBA. The effects of presbycusis in the population is not expected to have affected the results of the investigation because of the small proportion by the oldest age group compared to others and because age was controlled for as a cofactor during the logistic regression analysis. As a result, adverse study effects potentially associated with prevalence of presbycusis from failing to adjust hearing thresholds were not anticipated.

It is also possible that workers with a history of ear surgery could have confounded this investigation's results. Past investigations have reported a low risk of developing sensorineural hearing loss after surgery for patients with chronic otitis. Prevalence of hearing loss after surgery ranged from 1.2 to 1.3% [Tos et al., 1984; Volter et al., 2000]. The low prevalence of ear surgery induced hearing loss is not expected to affect hearing loss in the population studied during this investigation.

Because the data used during this investigation was originally collected for purposes other than research, subjects classified as having high noise exposure alone numbered only 37 while all other exposure groups contained at least 280 subjects. Analyzing exposure effects for each individual by matching specific chemical and noise sampling results for each person to their associated personal audiogram results may have more accurately represented the effects of chemicals and noise on hearing loss for each individual. However, similar to traditional IH practice, discrete noise, solvent, and metal measurements were not available for each person in this data set so analyzing metal, solvent, and noise exposures at the individual level was not possible. Utilizing a SEG framework to assess exposures is a commonly accepted practice in the IH field when measuring exposure for every subject is impractical.

Despite these minor limitations, this study contributed to an understudied area by targeting combinations of metals, solvents, and noise exposures on hearing loss. Additionally, this study used a novel method of analyzing exposure to specific metals such as lead, cadmium, and arsenic and specific solvents such as toluene and xylene according to an exposure concentration gradient beginning at levels less than OSHA action levels. The approach allowed accounting for exposure concentration variability typical of most industrial environments rather than assessing metal, solvent, and noise as exposed or not-exposed groups.

Accuracy of exposure and hearing loss determinations was greatly improved by analyzing actual personal air sampling results as eight-hour time weighted averages, personal noise dosimetry measurements as eight-hour time weighted averages, and audiometric records rather than utilizing subjective personnel responses. Extraction of data from the DOEHRS-IH and DOEHRS-HC repositories allowed for detailed analysis of a robust sample size during a lengthy 11-year duration while also maintaining personnel anonymity. The long duration is consistent with the chronic nature of exposure effects associated with solvents and metals [Wu et al., 2000; Fuente and McPherson, 2006].

CONCLUSIONS

The positive association between occupational exposure to metals, solvents, and noise and hearing disorders found in this investigation raises serious concerns. While the scientific community has recognized the risks of noise exposure, there has historically been less research on chemical exposure effects on hearing. There is a lack of regulation in this area and exposure limits for chemicals based on their adverse hearing effects have not been established in regulatory practice. Specifically, occupational hearing conservation programs may not be taking chemical exposures into consideration and as a result there may be numerous workers with unmet hearing conservation needs. For this reason, it is important that all at-risk workers are identified so interventions can occur to prevent more severe losses in hearing.

Findings provide information to support and drive hearing conservation policy decisions not only for the Department of Defense but throughout private and public industry. These results suggest it may be beneficial to include metal and solvent exposed workers in hearing loss prevention programs even when chemical exposures are less than OSHA regulatory levels. Particularly, employers should continue to implement multi-faceted hearing conservation programs to protect against hearing loss among those who are routinely exposed to occupational hazardous noise while also utilizing engineering, administrative, and personal protective equipment controls to reduce chemical exposures.

AUTHORS' CONTRIBUTIONS

All authors participated in study design, analysis, and interpretation of the data. All authors approved the final version to be published and agreed to be accountable for all aspects of the work and ensuring questions related to the accuracy of any part of the work are appropriately investigated and resolved.

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The U.S. Navy's Naval Medical Center San Diego Department of Clinical Investigation Institutional Review Board (IRB) exempted the study from IRB review under protocol number NHBR.2015.0029. Additionally, Indiana University of Pennsylvania's Institutional Review Board for Protection of Human Subjects approved the research project and exempted the project from continuing review under IRB Protocol number 15-183. Informed consent was not sought since personnel data for the study was retrieved from a database of historical records. Additionally, personally identifiable information for each record was de-identified.

DISCLOSURE (AUTHORS)

The authors report no conflicts of interest.

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