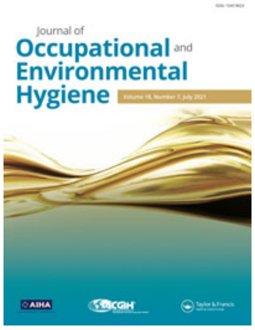

Journal of Occupational and Environmental Hygiene

ISSN: (Print) (Online) Journal homepage: https://oeh.tandfonline.com/loi/uoeh20

Effect of noise and ototoxicants on developing standard threshold shifts at a U.S. Air Force depot level maintenance facility

Marc Blair, Jeremy Slagley & N. Cody Schaal

To cite this article: Marc Blair, Jeremy Slagley & N. Cody Schaal (2021) Effect of noise and ototoxicants on developing standard threshold shifts at a U.S. Air Force depot level maintenance facility, Journal of Occupational and Environmental Hygiene, 18:7, 323-333, DOI: 10.1080/15459624.2021.1922693

To link to this article: https://doi.org/10.1080/15459624.2021.1922693

Published online: 08 Jun 2021.

JOURNAL OF OCCUPATIONAL AND ENVIRONMENTAL HYGIENE
2021, VOL. 18, NO. 7, 323–333
https://doi.org/10.1080/15459624.2021.1922693

Effect of noise and ototoxicants on developing standard threshold shifts at a U.S. Air Force depot level maintenance facility

Marc Blair[a], Jeremy Slagley[a], and N. Cody Schaal[a,b]

[a]Department of Systems Engineering and Management, Air Force Institute of Technology, Wright-Patterson AFB, Ohio;
[b]Environmental Health Effects Laboratory, Naval Medical Research Unit Dayton, Wright-Patterson AFB, Ohio

ABSTRACT

Noise exposure has traditionally been considered the primary risk factor for hearing loss. However, ototoxicants commonly found in occupational settings could affect hearing loss independently, additively, or synergistically when combined with noise exposures. The purpose of this investigation was to determine the combined effect of metal and solvent ototoxicants, continuous noise, and impulse noise on hearing loss. Noise and ototoxicant exposure and pure-tone audiometry results were analyzed for U.S. Air Force personnel ($n = 2,372$) at a depot-level aircraft maintenance activity at Tinker Air Force Base, Oklahoma. Eight similar exposure groups based on combinations of ototoxicant and noise exposure were created including: (1) Continuous noise (reference group); (2) Continuous noise + Impulse noise; (3) Metal exposures + Continuous noise; (4) Metal exposures + Continuous noise + Impulse noise; (5) Solvent exposure + Continuous noise; (6) Solvent exposures + Continuous noise + Impulse noise; (7) Metal exposure + Solvent exposures + Continuous noise; and (8) Metal exposure + Solvent exposures + Continuous noise + Impulse noise. Hearing loss was assessed at center octave band frequencies of 500–6,000 Hz and using National Institute for Occupational Safety and Health Standard Threshold Shift (STS) criteria. Hearing changes were significantly worse at 2,000 Hz in the Metal exposure + Solvent exposure + Continuous noise group compared to the Continuous noise only reference group ($p = 0.023$). The Metal exposure + Solvent exposure + Continuous noise group had a significantly greater relative risk (RR) of 2.44; 95% CI [1.24, 4.83] for developing an STS at 2,000 Hz. While not statistically significant, the Solvent exposure + Continuous noise group had a RR of 2.32; 95%CI [1.00, 5.34] for developing an STS at 1,000 Hz. These results indicate that noise exposure may dominate hearing loss at $\geq$3,000 Hz while combined effects of concomitant exposure to ototoxic substances and noise are only noticeable at $\leq$2,000 Hz. These results also suggest combined exposures to ototoxicants and noise presents a greater hearing loss risk than just noise.

KEYWORDS
Continuous noise; hearing loss; impulse noise; metal ototoxicant; solvent ototoxicant

Introduction

Background

Hearing loss can lead to increased disability costs and adverse effects on worker quality of life. In fiscal year (FY) 2019, the United States Department of Veterans Affairs (VA) reported tinnitus and hearing loss as the top two most prevalent service-connected disabilities of all compensation recipients representing 12.8% of all service-connected disabilities (Department of Veterans Affairs 2020). Tinnitus and hearing loss are also the first and third, respectively, most prevalent service-connected disabilities of new compensation recipients representing 17% of all new compensation disabilities (Department of Veterans Affairs 2020). The United States Centers for Disease Control (CDC 2016) estimates that occupational hearing loss is the most common work-related illness, and exposure to hazardous noise impacts approximately 22 million workers. Reduction in auditory disabilities could enable substantial cost savings for the U.S. government and industry. Mitigating auditory disabilities is not only a vital social responsibility to maintain worker health and quality of life but also will enhance force health performance of Department of Defense (DoD) personnel because auditory disabilities, such as tinnitus and hearing loss, are irreversible.

The purpose of the DoD hearing conservation program (HCP) is to protect all military personnel and noise-exposed civilian personnel from hearing loss

CONTACT N. Cody Schaal codyschaal@gmail.com Department of Systems Engineering and Management, Air Force Institute of Technology, 2950 Hobson Way, Wright-Patterson AFB, OH 45433-7765; Environmental Health Effects Laboratory, Naval Medical Research Unit Dayton, 2728 Q Street, Bldg 837, Area B Wright Patterson AFB, OH 45433-5707.

and reduce hazardous occupational and operational noise exposure to personnel to enhance mission readiness, communication, and safety. The DoD also considers hazardous noise control in military capabilities to support operational readiness, and integrates noise control into the design and development of defense systems and equipment (DoD 2019). HCP entry is triggered for workers exposed to sound pressure levels (SPL) above the 8-hr time-weighted average (TWA) of 85 decibels A-weighted (dBA) for continuous noise and 140 peak unweighted pressure (dBP) for impulse noise. Growing research indicates ototoxic substances, chemicals that impact the hearing organs, may have combined effects with continuous noise exposure (Campo et al. 2009). It is unknown if additional exposure to impulse noise, peak noises that are less than 1 second in duration (ACGIH 2020), may further increase these combined effects. Therefore, concomitant exposures to continuous noise, impulse noise, and ototoxic substances could potentially lead to increased incidence of auditory disability.

Ototoxic substance exposure is a gap in the current evaluation of hearing-related hazards, and research has indicated that ototoxic substances could impact an individual's hearing thresholds (Campo et al. 2009). These ototoxic substances include solvents and metals, such as cadmium, lead, toluene, and xylene that DoD personnel are likely to encounter during operation and maintenance of equipment while performing such activities as paint removal (sanding and grinding primers and paints containing heavy metals), painting, and fuel system maintenance, among others. Previous DoD research (Schaal et al. 2017, 2018) supports this claim through the identification of increased hearing loss in shipyard workers associated with exposure to ototoxic metals and ototoxic solvents when compared both to workers exposed only to continuous noise exceeding 85 dBA and compared to workers exposed to less than 85 dBA. The Occupational Safety and Health Administration (OSHA) and American Conference of Governmental Industrial Hygienists (ACGIH®) have published ototoxic substance advisories (OSHA 2018) and the DoD has added ototoxic exposure evaluation and control requirements to HCP written plans and as an element for noise measurement and analysis (DoD 2019). However, current federal regulatory hearing conservation statutes in the U.S. do not include ototoxic substance monitoring or specific occupational exposure limits when considering ototoxic exposures.

Due to the prevalence of high levels of continuous noise in workplace environments, continuous noise above 85 dBA has been thoroughly researched and regulated. However, during a 40-year lifetime, exposure to 85 dBA may still result in an 8% excess risk of developing occupational Noise Induced Hearing Loss (NIHL) (NIOSH 1998).

NIHL is most prevalent in the 3,000, 4,000, and 6,000 Hz frequencies, referred to as the "noise notch," and then spreads to 1,000 and 2,000 Hz frequencies (Ackley et al. 2007). Since 1998, the National Institute for Occupational Safety and Health (NIOSH) has recommended more sensitive measures by defining significant threshold shifts as a 15 dB hearing threshold level (HTL) or higher at 500, 1,000, 2,000, 3,000, 4,000, or 6,000 Hz in either ear without age adjustments (NIOSH 1998).

Ototoxicants

Ototoxic substances are typically organized in the following classes: Pharmaceuticals, Solvents, Asphyxiants, Nitriles, and Metals (Campo et al. 2009; Johnson and Morata 2010; OSHA 2018). Ototoxicity literature has expanded substantially in the last 20 years, but ototoxic exposure limits, mechanisms of action, excess risk, and target frequencies of ototoxic substances are still unclear.

Metals

Ototoxic metals, such as cadmium and lead, have been identified as contributing to hearing loss (Roth and Salvi 2016). However, there is an unclear relationship between lead exposure and hearing loss when considering both animal and human studies (Carlson and Neitzel 2018). Recent animal studies found no cochlear damage and no statistical difference in Auditory Brainstem Response (ABR) tests between non-exposed groups and groups exposed to combinations of lead and cadmium above the OSHA Permissible Exposure Limit (Carlson et al. 2018). With noise added as an additional exposure factor, there continued to be no statistical difference between exposure groups, but all noise-exposed groups demonstrated cochlear outer hair cell damage implicating noise as the dominating factor in hearing loss compared to ototoxic metal exposure (Carlson et al. 2018). A study by Choi and Kim found that the likelihood of hearing loss in the 2,000 to 4,000 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. While lead is believed to be primarily neurotoxic and cadmium is primarily believed to be cochleotoxic (Campo et al. 2009), mechanism of action is not clear.

Solvents

The alkylbenzene family of solvents has been identified as one of the largest groups of ototoxic solvents impacting the auditory system (Johnson and Morata 2010). Ototoxic solvents, such as styrene, trichloroethylene, toluene, and xylene are all identified as being able to cause hearing loss in animal studies (Crofton et al. 1994). In addition to the typical cochlear damage from ototoxic solvents, another potential mechanism of action for ototoxic aromatic solvents is the disruption of the middle ear reflex that protects the inner ear (Wathier et al. 2019). Wathier et al. (2019) found that benzene and chlorobenzene had significant effects on the middle ear reflex but are typically not considered to target the cochlea. Conversely, solvents known to target the cochlea did not show effects on the middle ear response (Wathier et al. 2019). Ototoxic chemical associated reduction of the middle ear response could potentially make exposure to repetitive sources of impulse noise such as riveting and ratcheting a more significant contributor to hearing loss in workers compared to impulse noise exposure alone.

Some studies indicate exposure to solvents below Occupational Exposure Limits (OELs) could have an adverse effect on hearing. Among a population of paint manufacturing workers, there was a higher prevalence of pure-tone audiometry (PTA) hearing loss and increased auditory evoked potential latencies in workers exposed to noise below 85 dBA in combination with ototoxic substance exposure below OELs (Juárez-Pérez et al. 2014). In a population of workers at fiberglass product manufacturing plants, individuals exposed to styrene concentrations ranging from 10 ppm to 20 ppm in combination with noise levels below 85 dBA were identified as having significantly greater levels of hearing loss compared to a reference population (Morata et al. 2011). Chang et al. (2006) observed in a cross-sectional study of 58 workers that concurrent exposure to noise and toluene resulted in high decibel hearing level (dB HL) thresholds at 1,000 and 2,000 Hz compared to a noise only reference group. However, in the exposure groups where noise exposures exceeded 85 dBA, continuous noise became the primary significant factor in the outcome of hearing loss (Morata et al. 2011). These studies suggest continuous noise exposure damage may mask the potential effect ototoxic solvents have on hearing thresholds.

Dose response relationships of ototoxicants, duration of exposure, and multiple ototoxicant exposures have been investigated. A meta-analysis of 15 studies with 7,530 combined subjects indicated a dose-response relationship between different levels of exposure to organic solvent mixtures and noise (Hormozi et al. 2017). Compared to a non-exposed reference group, individuals with solvent exposures at half the OEL had an Odds Ratio (OR) of 1.37 95% CI [0.75–2.48] in developing hearing loss, and those exposed to levels higher than the OEL had an OR of 4.51 95% CI [3.46–5.90] (Hormozi et al. 2017). Increasing the duration of exposure and the number of solvents present had a similar increase in OR of developing hearing loss (Hormozi et al. 2017). In particular, exposures lasting less than 5 years resulted in an OR of 1.01 95% CI [0.92–1.10], indicating exposure durations less than this period may not be enough time for hearing loss to develop (Hormozi et al. 2017).

Mixtures and co-exposures

A study of aircraft maintenance personnel exposed to jet fuel, a complex organic solvent mixture of n-hexane, n-heptane, toluene, and xylene, revealed 70% increased odds of hearing loss at 1,000 to 4,000 Hz when exposure occurred in combination with noise (Kaufman et al. 2005). Exposure duration was at least 3 years and jet fuel concentrations were below each chemical's respective OEL (Kaufman et al. 2005). A study by Choi and Kim found that the likelihood of hearing loss in the 2,000 to 4,000 Hz 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 (Choi and Kim 2014). In an industrial shipyard, Schaal et al. (2018) assessed 1,266 personnel exposed to combinations of noise >85 dBA, ototoxic solvents beginning at sub-OEL concentrations, and ototoxic metals beginning at OSHA action levels (ALs). Results identified statistically higher levels of hearing loss at 1,000 Hz for both the metal + noise and metal + solvent + noise groups compared to groups exposed only to noise >85 dBA. Similar results were found for the metal + solvent + noise group when averaged across 2,000 to 4,000 Hz, and hearing loss averaged across 500 to 6,000 Hz (Schaal et al. 2018).

Impulse noise

Studies of exposure to impulse noise and ototoxic substances have revealed higher risks for hearing loss compared to groups exposed to continuous noise and ototoxic substances. In an animal study, Lund and Kristiansen (2008) identified impulse noise exposure in combination with toluene exposure resulted in a broader range of center frequency band shifts, from 4,000 to 24,000 Hz when tested by otoacoustic emissions. Carreres Pons et al. (2017) also conducted an animal study with carbon disulfide and found impulse noise with ototoxic exposure was significantly more damaging than continuous noise of the same energy with ototoxic exposures. Fuente et al. (2018) used the kurtosis metric to determine the significance of impulse noise and ototoxic solvents exposure in furniture factories. Worker PTA threshold shift results remained the same for impulse noise-exposed and solvent/impulse noise-exposed groups below 4,000 Hz, but there was a significant difference in shifts at 6,000 Hz (Fuente et al. 2018). Integration of the kurtosis metric in cumulative noise exposure calculations was found to describe this interaction best and suggests the equal energy rule does not adequately reflect hearing loss risks when impulse noise and ototoxic solvents are present (Fuente et al. 2018).

The purpose of this investigation was to determine the risk of developing hearing loss based on individual exposure to combinations of ototoxic substances, continuous noise, and impulse noise. Additionally, we sought to determine if threshold shifts across 500 to 6,000 Hz were significantly different according to exposure group.

Methods

Research design

The two data systems used in this investigation were the Defense Occupational and Environmental Health Readiness System–Industrial Hygiene (DOEHRS–IH) and Defense Occupational and Environmental Health Readiness System–Hearing Conservation (DOEHRS–HC). DOEHRS–IH is used to manage occupational and environmental health risk data and actively track biological, chemical, and physical health hazards and engineered nano-object processes to service members worldwide (Defense Health Agency 2018). DOEHRS–HC is used to collect, maintain, compare, and report hearing conservation, hearing readiness and deployment data for DoD personnel (Defense Health Agency 2019). DOEHRS–IH and DOEHRS–HC systems are not directly connected except via an individual's social security number (SSN). Joining the data from these systems required establishing a unique personal identifier combined with assigned unique Similar Exposure Group (SEG) identifiers (SEGID) to create individual exposure records for assessment and build exposure groups of interest for the study. Following connecting audiogram records with exposure records, researchers conducted a quantitative assessment of individual longitudinal exposure records for hearing threshold shifts across all center-band frequencies 500–6,000 Hz, unadjusted for age. Individual records were assigned to study exposure groups by evaluating exposure to ototoxic substances, continuous noise, and impulse noise.

Population and sample

Data was extracted from DOEHRS–HC and DOEHRS–IH for personnel employed at Tinker Air Force Base (AFB), near Oklahoma City, Oklahoma. Tinker AFB is the site of the largest of three depot installations within the United States Air Force (USAF) Material Command (AFMC) and is the location of an extensive maintenance activity for C/KC-135, B-1B, B-52, and E-3 airframes (USAF 2020a). This depot level maintenance includes full overhaul maintenance, aircraft repairs, engineering services, aircraft modifications, depaint and paint services, and flight testing (USAF 2020b). Ototoxic solvents and metals, such as cadmium, lead, toluene, and xylene, are likely to be encountered during the operation and maintenance of equipment while performing such activities as paint removal (sanding and grinding primers and paints containing heavy metals), painting, and fuel system maintenance, among others. These attributes made Tinker AFB highly likely to have a significant number of employees with occupational exposure to the physical and chemical hazards of interest in this study.

DOEHRS–HC data collection

PTA results were assessed for civilian personnel employed by Tinker AFB from January 2005 to July 2019. The year 2005 was selected as the beginning date to align with a previous USAF cross-sectional study of threshold shifts in audiometric data (Soderlund et al. 2016). The basic methodology for using DOEHRS-HC data was to establish a baseline record by identifying an individual's oldest recorded audiogram and comparing it to an individual's most recent recorded audiogram. Either a reference or annual audiogram was used as a baseline record in this research by identifying the oldest audiogram in the study timeframe. An individual's final audiogram record was selected by identifying the most recent annual, follow-up, termination, or reference audiogram. Following the selection of a qualifying baseline and final record, threshold shifts at each center frequency were calculated to create an individual's threshold shift record by subtracting the baseline audiogram thresholds from the final audiogram thresholds at each frequency. Exclusion criteria and excluded personnel groups included: any audiogram records with missing hearing test data (at any frequency), personnel with multiple birthdates, declared ear nose throat (ENT) problems, values < -10 or >100 dB HL, <3 years difference between baseline and final audiogram, and military service members (due to short duration exposures).

DOEHRS–IH data collection

DOEHRS–IH noise and chemical exposure data was collected from January 2005 to October 2019, using database queries. The basic methodology for creating an individual exposure record was derived from assessments and evaluations of occupational hazards of interest assigned to a SEG. After removing any records marked invalid, researchers determined SEG exposure to ototoxic metals in the study population included cadmium and lead while ototoxic solvents included benzene, ethyl benzene, toluene, and p-xylene.

Data for individual noise equipment was assessed at a location by Sound Level Meter (SLM) with dBA measurements and qualitative classification of the source as "continuous," "impact/impulse," or "intermittent." Because noise exposures were not always quantified, SEG exposure to continuous and impulse noise sources was based on the presence of keywords in the IH survey's qualitative description. Researchers used the description keywords "rivet," "shear," and "impact" to determine exposure to impulse/impact noise since these sources were commonly found at this maintenance facility.

DOEHRS–IH includes an exposure assessment strategy that groups workers in exposure profiles, called SEGs, with similar tasks, processes, materials, and time parameters similar to the process described by Mulhausen and Damiano (2015). SEG evaluations included professional judgment and sampling-based assessments thus dichotomous (presence or absence) exposure criteria to at least one substance per category were used to determine exposure classification. In workplaces where ototoxicants and noise sources were determined to be present, the industrial hygienist may have chosen to quantify exposures with air sampling and noise measurements. However, there may have been situations where noise and ototoxicant exposures were present in the workplace, but exposure was not quantified. This may have been a result of a determination that the exposure did not present a substantial health risk. These qualitative exposure assessment decisions were documented in DOEHRS-IH and considered such information as frequency and duration of exposure.

Multiple SEG exposure estimates and qualitative data were used for categorizing according to ototoxic metals, ototoxic solvents, continuous noise, and impulse noise to account for an individual's exposures being associated with several SEGS. As an example, it was possible for a single person to be assigned to multiple SEGs simultaneously and at different times during the current study's time period. Dichotomous exposure criteria to at least one substance per category and for at least 3 years were used to place personnel in an exposure category. If SEG assignment did not meet these criteria, then personnel were classified as not being exposed. The combination of DOEHRS-IH data enabled the creation of an individual exposure record that accounted for ototoxic substances, continuous noise, and impulse noise exposures that may have occurred from multiple SEG assignments during the study period. Everyone's exposure record was then joined to the individual's threshold shift audiogram. Using a unique identification number allowed for analyzing combinations of exposures and subsequent hearing threshold shift outcomes to determine potential synergistic or additive relationships.

Data analysis

Microsoft Access (Microsoft, Redmond, WA) was used to count unique entries that met PTA test conditions and to organize the results into a standard 2×2 format for Relative Risk (RR) and 95% confidence intervals calculation. Study exposure group data was then exported for statistical analysis using the Python programming language (Python Software Foundation, Fredericksburg, VA). Hearing loss was determined with NIOSH STS criteria of $>/=15$ dB HTL at any frequency: 500, 1,000, 2,000, 3,000, 4,000, and 6,000 Hz. Because the data did not meet the assumption of normality, Kruskal-Wallis nonparametric analysis of variance (ANOVA) and Mann-Whitney U pairwise comparison tests were conducted, with an alpha level of 0.05, to determine if there were

Table 1. Relative risk of NIOSH significant threshold shift.

Exposure	Yes STS	No STS	n	RR	CI 95 Lower	CI 95 Upper
Continuous (reference)	173	137	310	1.0	N/A	N/A
Continuous + Impulse noise	9	12	21	0.77	0.46	1.27
Metal + Continuous noise	154	112	266	1.04	0.9	1.2
Metal + Continuous noise + Impulse noise	6	6	12	0.9	0.5	1.59
Solvent + Continuous noise	281	210	491	1.03	0.9	1.16
Solvent + Continuous noise + Impulse noise	29	19	48	1.08	0.84	1.39
Metal + Solvent + Continuous noise	493	379	872	1.01	0.9	1.14
Metal + Solvent + Continuous noise + Impulse noise	220	132	352	1.12	0.99	1.27

RR: Relative Risk, CI95L/U: Confidence Interval 95% Lower/Upper.

significant differences in hearing threshold changes between the continuous noise only reference group and other exposure groups. Further exploration of the significant differences between exposure groups were assessed using a Mann–Whitney U post hoc pairwise test to determine which exposure groups were significantly different than the continuous noise only group. A Bonferroni adjustment was used to remove the potential for identifying significant errors by chance when conducting multiple statistical comparisons (Rosner 1995). Air Force Institute of Technology's Human Research Protection Program (HRPP) classified the study as exempt from further review due to the retrospective nature of this research (use of archival data).

Results

Study population and exposure group characteristics

A total of 2,372 personnel were organized into 8 groups composed of various combinations of exposure to ototoxic substances, impulse noise, and continuous noise: (1) Continuous noise (reference group), (2) Continuous noise + Impulse noise, (3) Metal exposures + Continuous noise, (4) Metal exposures + Continuous noise + Impulse noise, (5) Solvent exposure + Continuous noise, (6) Solvent exposures + Continuous noise + Impulse noise, (7) Metal exposure + Solvent exposures + Continuous noise, and (8) Metal exposure + Solvent exposures + Continuous noise + Impulse noise. The size of each exposure group ranged from 12 to 872 personnel, with the majority of smaller exposure groups, n < 50, containing impulse noise conditions (Table 1). The largest exposure group containing 872 personnel was the combination of ototoxic metals, ototoxic solvents, and continuous noise exposures. Individuals exposed to ototoxic substances totaled 2,041 (of the 2,373 individuals in the study population) and constituted approximately 86% of the study population. These results indicate that ototoxic substance exposure is highly prevalent in the civilian employee population assigned to the HCP at Tinker AFB.

The average duration in years between the established baseline audiogram and the final audiogram was approximately 8.7 years (standard deviation 3.1) for the study population. Further analysis of audiogram duration by study exposure groups indicated means and standard deviations were approximately equal (Table 2). Therefore, exposure duration was likely sufficient to demonstrate the gradual hearing loss that occurs within the first 10 years of exposure to occupational noise (Ackley et al. 2007) and the hearing loss that occurs within the first 3–5 years for ototoxicants (Kaufman et al. 2005; Hormozi et al. 2017).

DoD individual audiogram data is likely only available due to HCP enrollment criteria, and therefore continuous noise exposure is the only common shared exposure variable between study exposure groups. The average duration in years of exposure to continuous noise for the study population was 7.4 years (standard deviation 3.4), and exposure groups' mean values ranged from approximately 6 to 9 years (Table 2).

Exposure group hearing loss relative risk

The Metal + Solvent + Continuous noise + Impulse noise exposure group had the highest RR of 1.12, 95% CI [0.99, 1.27] for development of an STS compared to the continuous noise only reference group (Table 1). Further RR assessments were limited to exposure groups with >50 people. An assessment of the RR for NIOSH STS development by independent frequency of both the left and right ear (Table 3) revealed a general trend of RR > 1 at 1,000, 2,000, and 6,000 Hz. These combined effects for each exposure group were highest, RR > 1.75, in the left ear at 2,000 Hz and the right ear at 1,000 and 2,000 Hz frequencies. The observed higher RRs suggest continuous noise exposures dominate hearing loss in the higher frequencies from 3,000 to 6,000 Hz while ototoxic substances with

Table 2. Exposure duration.

SEG	Mean (Years)	Standard Deviation
Exposure duration from baseline to final audiogram by exposure group		
Continuous	8.3	3.3
Continuous + Impulse	8.4	3.1
Metal + Continuous	8.6	3.1
Metal + Continuous + Impulse	10.2	3.9
Solvent + Continuous	8.4	3
Solvent + Continuous + Impulse	8.1	3
Metal + Solvent + Continuous	8.7	3
Metal + Solvent + Continuous + Impulse	9.5	2.8
Exposure duration to continuous noise		
Continuous	6.1	3
Continuous + Impulse	6.3	2.1
Metal + Continuous	7	3.1
Metal + Continuous + Impulse	9.4	5.7
Solvent + Continuous	6.9	3
Solvent + Continuous + Impulse	7	3
Metal + Solvent + Continuous	7.8	3.6
Metal + Solvent + Continuous + Impulse	8.6	3.3

Table 3. Relative risk of NIOSH STS by frequency.

SEG	500	1,000	2,000	3,000	4,000	6,000
Left Ear	Frequency (Hz)					
Continuous noise	Ref	Ref	Ref	Ref	Ref	Ref
Metal + Continuous noise	0.87	0.83	1.75	1.21	0.84	0.91
Solvent + Continuous noise	0.91	1.44	1.97	1.17	0.97	1.21
Metal + Solvent + Continuous noise	0.91	1.27	2.44	0.89	0.93	1.10
Metal + Solvent + Continuous noise + Impulse noise	0.72	1.38	2.09	1.42	1.09	1.21
Right Ear						
Continuous noise	Ref	Ref	Ref	Ref	Ref	Ref
Metal + Continuous noise	1.17	1.36	0.87	0.83	0.94	1.02
Solvent + Continuous noise	1.49	2.32	1.10	0.92	0.92	1.05
Metal + Solvent + Continuous noise	1.42	1.48	1.21	0.86	0.90	0.83
Metal + Solvent + Continuous noise + Impulse noise	1.45	2.20	1.76	0.97	0.90	1.07

concurrent noise exposure lead to hearing shifts at 1,000 and 2,000 Hz.

Because 1,000 and 2,000 Hz had the highest RRs, further exploration was accomplished to determine if there was a statistically significant difference between hearing changes compared to the continuous noise alone group. This assessment indicated the Metals + Solvents + Continuous noise group had a RR of 2.4, 95% CI [1.24, 4.83] of developing an STS at 2,000 Hz compared to the noise only reference group (Table 4). Additionally, while not significantly different than the reference group, an increased RR of 2.09, 95% CI [0.97, 4.51] at 2,000 Hz and a RR of 2.2, 95% CI [0.91, 5.32] at 1,000 Hz was observed in the Metals + Solvents + Continuous noise + Impulse noise group. This suggests additional effects from impulse noise is possible, especially with a larger sample size in this group. The Solvent + Continuous noise group also had an elevated RR of 2.32 95% CI [1.00, 5.34] for STS development at 1000 Hz despite not being statistically different than the continuous noise only reference group.

Table 4. Selected relative risk of NIOSH STS with confidence intervals.

SEG	RR	CI 95 Lower	CI 95 Upper
Left Ear 2,000 Hz			
Metal + Continuous noise	1.75	0.75	4.05
Solvent + Continuous noise	1.97	0.94	4.13
Metal + Solvent + Continuous noise	**2.44**	**1.24**	**4.83**
Metal + Solvent + Continuous noise + Impulse noise	2.09	0.97	4.51
Right Ear 1,000 Hz			
Metal + Continuous noise	1.36	0.48	3.82
Solvent + Continuous noise	2.32	1.00	5.34
Metal + Solvent + Continuous noise	1.48	0.65	3.38
Metal + Solvent + Continuous noise + Impulse noise	2.20	0.91	5.32

Bold denotes significantly higher RR compared to noise only reference group.

Table 5. Kruskal–Wallis Test for hearing threshold change differences between exposure group according to frequency.

Frequency	*p*-value
500	0.243
1,000	0.300
2,000	**0.047**
3,000	0.912
4,000	0.839
6,000	0.990
Average 2,000–4,000 Hz	0.969
Average 500–6,000 Hz	0.894

Bold denotes significant p-values, $\alpha = 0.05$.

Exposure group inferential statistical analysis by frequency

As shown in Table 5, when assessing differences in overall dB HL, the Kruskal–Wallis non-parametric test revealed the only statistically significant difference between exposed groups was at 2,000 Hz ($p = 0.047$). This result is similar to the previously observed elevated RR for developing a NIOSH STS at 2,000 Hz. Further exploration for hearing differences at 2,000 Hz revealed Mann-Whitney U test p-values ranging from 0.001 to 0.972 with only the Metal + Solvent + Continuous noise group having statistically significant different threshold shifts (p-value adjusted = 0.023) compared to the continuous noise only reference group (Table 6).

Discussion

The overall sample size for the study was large but some exposure group combinations were too small in size to allow for confidence in data interpretation as indicated by some exposure groups having broad range confidence intervals. Wide ranging confidence

Table 6. Mann–Whitney U pairwise comparisons of exposure group for left ear at 2,000 Hz.

Exposure Group	*p*-value	p-value adjusted
Continuous noise + Impulse noise	0.824	1
Metal + Continuous noise	0.141	1
Metal + Continuous noise + Impulse noise	0.570	1
Metal + Solvent + Continuous noise	**0.001**	**0.023**
Metal + Solvent + Continuous noise + Impulse noise	0.062	1
Solvent + Continuous noise	0.088	1
Solvent + Continuous noise + Impulse noise	0.093	1

Bold denotes significant *p*-values, $\alpha = 0.05$.

intervals are also anticipated to be a result of low rates of hearing loss development. Additionally, researchers sought to use impulse noise as an exposure group variable, but very small group sizes with this exposure classification limit the conclusions that can be made.

While not always significantly different than the continuous noise group, researchers observed potentially ototoxic effects for all ototoxic exposure combinations using the NIOSH STS method. Further exploration of the NIOSH STS method by individual frequency revealed the RR for some ototoxic exposure groups was more than double the reference group at 1,000 and 2,000 Hz frequencies. In particular, the Metal + Solvent + Continuous noise exposure group displayed the highest combined effects with an RR 2.44 95% CI [1.24–4.83] at 2,000 Hz supporting the observed shifts from ototoxic substances at ≤2,000 Hz identified by Chang et al. (2006) and Schaal et al. (2018). These results indicate that continuous noise exposure may dominate hearing loss at ≥3,000 Hz, and therefore the combined effects of concomitant exposure to ototoxic substances to continuous noise are only noticeable at ≤2,000 Hz.

Analysis of dB HL across all frequencies for each exposure group revealed the characteristic noise notch at 3,000, 4,000, and 6,000 Hz in both ears. The range of hearing loss between exposure groups at each frequency was slight, with values approximately within 2 dB HL for most exposure groups. Despite this small hearing threshold change, detecting these changes earlier will allow for removing workers from hazardous environments sooner. As noticed in the NIOSH STS model, broader mean threshold shifts were observed at 1,000 and 2,000 Hz for ototoxic exposure groups. The significant difference in hearing loss observed in the Metal + Solvent + Continuous noise exposure group as compared to the continuous noise only reference group was similar to the results of Schaal et al. (2018) where a significant difference, p-value = 0.007, at 1,000 Hz was observed for a Metals + Solvents + Noise compared to a noise only exposure group in an industrial shipyard population. These results suggest continuous noise is predominantly responsible for hearing changes at 3,000–6,000 Hz and apparent ototoxic effects begin at 1,000–2,000 Hz. Results also suggest the addition of solvent exposure, regardless of other exposure combinations is important in realizing elevated STS risk beyond only continuous noise exposure.

Researchers postulated the RRs determined by the NIOSH STS determination method are potentially more sensitive in the evaluation of ototoxic effects because of the inclusion of the 500, 1,000, and 6,000 Hz frequencies and because the usage of absolute shifts by independent frequency instead of averaging values that is applicable to other STS determination methods. For example, Chang et al. (2006) identified concomitant exposure to toluene and noise increased hearing thresholds at the 1,000 and 2,000 Hz frequencies, and Fuente et al. (2018) observed significant changes at 6,000 Hz for concomitant exposure to impulse and solvent-exposed workers.

It is possible that PTA is not able to detect all associated adverse auditory effects from ototoxicants. An animal study by Fechter et al. (2012) found significant concentration-related impairment of auditory function when measuring distortion product otoacoustic emissions (DPOAE) after exposure to JP-8 jet fuel concentrations beginning at 750 mg/m^3 and noise at 95 dB. JP-8 jet fuel alone did not exert significant effects on auditory function (Fechter et al. 2012). An animal investigation by Guthrie et al. (2015) evaluated neurotransmission in both peripheral and central auditory pathways to differentiate between peripheral and central dysfunctions associated with noise and JP-8 jet fuel. There were no detectable effects on peripheral functions but brain responsiveness was significantly depressed and neural transmission time was delayed (Guthrie et al. 2015). Similarly, in an investigation by Guthrie et al. (2016) to determine if repeated exposure to low intensity noise with and without exposure to a blend of organic solvents would alter brain activity, subtoxic solvent exposure alone had no statistically significant effects. However, background noise significantly suppressed brain activity and slowed neurotransmission which was exacerbated with solvent exposure. These abnormal neurophysiologic findings occurred in the absence of hearing loss and detectable damage to sensory cells.

Limitations

Resource limitations make sampling every potential occupational hazard infeasible. Expansion of assessment types in the current investigation ensured the inclusion of potential hazards below OSHA action levels. The principal data quality limitation encountered in this research was the lack of measured chemical concentration and measured noise levels for all assessed hazards, particularly for impulse noise. This information gap required researchers to deviate from the original intention of creating hazard-specific time-weighted averages and, instead, required the creation of dichotomous exposure variables. This limitation also prevented determining specific contributions of each respective ototoxic metal and solvent in contributing to the RR of STS development and dB HL overall. Limiting the determination of hazard exposure only using air sampling and noise measurements would have likely underestimated the quantity of SEGs with ototoxicant and noise exposures of interest.

The lack of integration between DOEHRS–IH and DOEHRS–HC generated numerous study limitations during data processing. Researchers used baseline and final audiogram records from DOEHRS–HC to "fence" SEG exposures which required excluding SEG assignments outside the selected period. In this process, individuals may have had ototoxicant exposures that only occurred before the study time frame and not within the study time frame. This challenge was mitigated by screening individuals to ensure they possessed normal hearing at the selected baseline audiogram.

Another limitation encountered during data processing was overlapping unique SEGs. Researchers were unable to differentiate which SEGs dominated an individual's work schedule. The methodology in this research considered all SEG assignments equal in magnitude.

Data availability limited the analysis and control of confounding factors. Because DOEHRS–IH and DOEHRS–HC were not originally intended for research purposes, the only demographic data available for researchers in this study were age and gender. Therefore, this investigation was unable to account for confounding factors of hearing loss that could include personal usage of firearms, recreational activities involving ototoxicant and noise exposures, smoking, alcohol usage, or ototoxic pharmaceutical usage. Each of these factors could contribute to the indicators of hearing loss observed in the study. However, this potential confounding was expected to be non-differential between exposure groups.

Despite these limitations, this study contributed to an understudied area by targeting combinations of metals, solvents, and noise exposures on hearing loss. Accuracy of hearing loss determinations was greatly improved by analyzing audiometric records rather than assessing subjective personnel responses of hearing loss. Accuracy of exposure determinations was greatly improved by analyzing workplace exposure assessment records rather than assessing subjective personnel responses of workplace exposures. Extraction of data from the DOEHRS–IH and DOEHRS–HC repositories allowed for detailed analysis of a robust sample size during a lengthy 14-year duration while also maintaining personnel anonymity. The long duration is consistent with the chronic nature of exposure effects associated with solvents, metals, and noise.

Recommended future actions and study

As previously described, complete exposure value data was unavailable which limited the ability to create time-weighted average exposures for ototoxic and noise hazards. This challenge could be addressed by adopting an exposure assessment process that assigns an interim exposure value for each hazard that cannot be immediately sampled. These interim values could adopt the American Industrial Hygiene Association (AIHA®) SEG exposure control category paradigm that classifies hazards in stratified groups according to specific percentages of the OEL (Mulhausen et al. 2015). Additionally, developing time-weighted averages with available data would allow for determining dose response relationships by grouping personnel according to concentration.

Conclusions

A central theme in all current ototoxic reviews is concentrations eliciting adverse audiological outcomes may be less than current OELs, and the mechanisms of action for hearing damage are unclear. This investigation indicated combined exposures to Metals + Solvent + Continuous noise increase the risk of developing hearing loss at 1,000 and 2,000 Hz in a depot level aircraft maintenance workforce beyond the hearing loss incurred by personnel only exposed to continuous noise. This elevated hearing loss risk raises serious concerns. While the scientific community has recognized the risks of noise exposure, there has historically been little research on chemical exposure effects on hearing and less research on chemical and noise combinations. There is a lack of regulation in this area and few OELs for chemicals based on their adverse hearing effects have been established. Also, combined noise and ototoxicant health effects may be hidden by noise effects alone at high frequencies most commonly measured with PTA. 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. These findings provide information to support and drive hearing conservation policy decisions. While exposure to continuous and impulse noise exceeding OELs may warrant inclusion to HCPs, the addition of ototoxicants may further increase the hearing loss risk.

Acknowledgments

We would like to thank USAF School of Aerospace Medicine (USAFSAM) Epidemiology Consult Service Division for providing the PTA results and USAFSAM's Occupational and Environmental Health Operations Division (OET) DOEHRS Support Office for chemical and noise stressor information. We wish to thank the 72d Medical Group Bioenvironmental Engineering Flight at Tinker Air Force Base, Oklahoma, for their consultation.

Funding

Financial support was provided by 711th Human Performance Wing, Research, Studies, Analysis, and Assessments Council (RSAAC) project #18-015. The sponsor did not influence the study design, collection, analysis, or interpretation of the data.

Disclaimer

The authors do not have any financial or personal relationships with organizations that could inappropriately influence the work in this study. The views expressed in this article reflect the results of research conducted by the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of the Air Force, Department of Defense, nor the United States Government.

ORCID

Marc Blair http://orcid.org/0000-0003-4532-1660
Jeremy Slagley http://orcid.org/0000-0001-6696-4257
N. Cody Schaal http://orcid.org/0000-0002-3794-1600

References

ACGIH. 2020. TLVs and BEIs based on the documentation of the threshold limit values for chemical substances and physical agents & biological exposure indices. Cincinnati (OH): ACGIH Signature Publications.

Ackley R, Decker T, Limb C. 2007. An essential guide to hearing and balance disorders. New York (NY): Lawrence Erlbaum Associates.

Campo P, Maguin K, Gabriel S, Moller A, Dolores M, Toppila E. 2009. Combined exposure to noise and ototoxic substances. European Agency for Safety and Health at Work. [accessed 2020 Nov 21]. https://osha.europa.eu/en/publications/literature_reviews/combined-exposure-to-noise-and-ototoxic-substances.

Carlson K, Neitzel RL. 2018. Hearing loss, lead (Pb) exposure, and noise: a sound approach to ototoxicity exploration. J Toxicol Environ Heal B. 21(5):335–355. doi:10.1080/10937404.2018.1562391

Carlson K, Schacht J, Neitzel RL. 2018. Assessing ototoxicity due to chronic lead and cadmium intake with and without noise exposure in the mature mouse. J Toxicol Environ Heal A. 81(20):1041–1057. doi:10.1080/15287394.2018.1521320

Carreres Pons M, Chalansonnet M, Venet T, Thomas A, Nunge H, Merlen L, Cosnier F, Llorens J, Campo P. 2017. Carbon disulfide potentiates the effects of impulse noise on the organ of Corti. Neurotoxicology. 59:79–87. doi:10.1016/j.neuro.2017.02.003

CDC. 2016. Hearing impairment among noise-exposed workers United States. MMWR Morb Mortal Wkly Rep. 65(15):290–300. doi:10.1002/ajim.22565/epdf

Chang S, Chen C, Lien C, Sung F. 2006. Hearing loss in workers exposed to toluene and noise. Environ Health Persp. 114(8):1283–1286. doi:10.1289/ehp.8959

Choi Y, Kim K. 2014. Noise-induced hearing loss in Korean workers: co-exposure to organic solvents and heavy metals in nationwide industries. PLOS One. 9(5):e97538. doi:10.1371/journal.pone.0097538

Crofton K, Lassiter T, Rebert C. 1994. Solvent-induced ototoxicity in rats: an atypical selective mid-frequency hearing deficit. Hear Res. 80(1):25–30. doi:10.1016/0378-5955(94)90005-1

Defense Health Agency. 2018. DOEHRS-IH [fact sheet]. [accessed 2020 Nov 21]. https://www.health.mil/Reference-Center/Fact-Sheets/2019/04/05/DOEHRS-IH.

Defense Health Agency. 2019. DOEHRS-HC [fact sheet]. [accessed 2020 Nov 21]. https://health.mil/Reference-Center/Fact-Sheets/2019/06/17/DOEHRS-HC.

Department of Defense (DoD). 2019. DoD instruction 6055.12 hearing conservation program. [accessed 2020 Nov 21]. https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/605512p.pdf.

Department of Veterans Affairs. 2020. Veterans benefits administration annual benefits report fiscal year 2019. [accessed 2020 Nov 21]. https://www.benefits.va.gov/REPORTS/abr/docs/2019-compensation.pdf.

Fechter LD, Fisher JW, Chapman GD, Mokashi VP, Ortiz PA, Reboulet JE, Stubbs JE, Lear AM, McInturf SM, Prues SL, et al. 2012. Subchronic JP-8 jet fuel exposure enhances vulnerability to noise-induced hearing loss in rats. J Toxicol Environ Heal A. 75(5):299–317. doi:10.1080/15287394.2012.652060

Fuente A, Qiu W, Zhang M, Xie H, Kardous CA, Campo P, Morata T. 2018. Use of the kurtosis statistic in an evaluation of the effects of noise and solvent exposures on the hearing thresholds of workers: an exploratory study. J Acoust Soc A. 143(3):1704–1710. doi:10.1121/1.5028368

Guthrie O, Wong B, McInturf S, Reboulet J, Ortiz P, Mattie D. 2015. Inhalation of hydrocarbon jet fuel suppress central auditory nervous system function. J Toxicol Environ Heal A. 78(18):1154–1169. doi:10.1080/15287394.2015.1070389

Guthrie O, Wong B, McInturf S, Reboulet J, Ortiz P, Mattie D. 2016. Background noise contributes to organic solvent induced brain dysfunction. Neural Plast. 2016:1–11. doi:10.1155/2016/8742725

Hormozi M, Ansari-Moghaddam A, Mirzaei R, Dehghan Haghighi J, Eftekharian F. 2017. The risk of hearing loss associated with occupational exposure to organic solvents mixture with and without concurrent noise exposure: a systematic review and meta-analysis. Int J Occup Med Environ. 30(4):521–535. doi:10.13075/ijomeh.1896.01024

Johnson A, Morata T. 2010. Occupational exposure to chemicals and hearing impairment. [accessed 2020 Nov 21]. https://www.cdc.gov/niosh/nioshtic-2/20037156.html.

Juárez-Pérez C, Torres-Valenzuela A, Haro-García L, Borja-Aburto V, Aguilar-Madrid G. 2014. Ototoxicity effects of low exposure to solvent mixture among paint manufacturing workers. Int J Audiol. 53(6):370–376. doi:10.3109/14992027.2014.888597

Kaufman L, Lemasters G, Olsen D, Succop P. 2005. Effects of concurrent noise and jet fuel exposure on hearing loss. J Occup Environ Med. 47(3):212–218. doi:10.1097/01.jom.0000155710.28289.0e

Lund S, Kristiansen G. 2008. Hazards to hearing from combined exposure to toluene and noise in rats. Int J Occup Med Environ. 21(1):47–57. doi:10.2478/v10001-008-0008-x

Morata TC, Sliwinska-Kowalska M, Johnson A-C, Starck J, Pawlas K, Zamyslowska-Szmytke E, Nylen P, Toppila E, Krieg E, Pawlas N, et al. 2011. A multicenter study on the audiometric findings of styrene-exposed workers. Int J Audiol. 50(10):652–660. doi:10.3109/14992027.2011.588965

Mulhausen J, Damiano J. 2015. Establishing similar exposure groups. In: Jahn S, Bullock W, Ignacio J, editors. A strategy for assessing and managing occupational exposures. 4th ed. Falls Church (VA): American Industrial Hygiene Association. p. 36–50.

Mulhausen J, Damiano J, Pullen E. 2015. Defining and judging exposure profiles. In: Jahn S, Bullock W, Ignacio J, editors. A strategy for assessing and managing occupational exposures. 4th ed. Falls Church (VA): American Industrial Hygiene Association. p. 52–77.

NIOSH. 1998. Occupational noise exposure. National Institute for Occupational Health and Safety. [accessed 2020 Nov 21]. https://www.cdc.gov/niosh/docs/98-126/pdfs/98-126.pdf?id=10.26616/NIOSHPUB98126.

OSHA. 2018. Preventing hearing loss caused by chemical (ototoxicity) and noise exposure (DHHS NIOSH Publication Number 2018-124). [accessed 2020 Nov 21]. https://www.cdc.gov/niosh/docs/2018-124/pdfs/2018-24.pdf?id=10.26616/NIOSHPUB2018124.

Rosner B. 1995. Fundamentals of Biostatistics. 4th ed. Belmont (CA): Duxbury Press.

Roth J, Salvi R. 2016. Ototoxicity of divalent metals. Neurotox Res. 30(2):268–282. doi:10.1007/s12640-016-9627-3

Schaal N, Slagley J, Richburg C, Zreiqat M, Paschold H. 2018. Chemical-induced hearing loss in shipyard workers. J Occup Environ Med. 60(1):55–62. doi:10.1097/JOM.0000000000001186

Schaal N, Slagley J, Zreiqat M, Paschold H. 2017. Effects of combined exposure to metals, solvents, and noise on permanent threshold shifts. Am J Ind Med. 60(3):227–238. doi:10.1002/ajim.22690

Soderlund L, Mckenna E, Tastad K, Paul M. 2016. Prevalence of permanent threshold shifts in the United States Air Force hearing conservation program by career field, 2005 – 2011. J Occup Environ Hyg. 13(5):383–392. doi:10.1080/15459624.2015.1123814

USAF. 2020a. Tinker Air Force Base. [accessed 2020 Nov 21]. https://www.tinker.af.mil/Home/Welcome/.

USAF. 2020b. Oklahoma City air logistics complex fact sheet. [accessed 2021 Feb 13]. https://www.tinker.af.mil/About-Us/Fact-Sheets/Display/Article/384764/oklahoma-city-air-logistics-complex/.

Wathier L, Venet T, Bonfanti E, Nunge H, Cosnier F, Parietti-Winkler C, Campo P, Pouyatos B. 2019. Measuring the middle-ear reflex: a quantitative method to assess effects of industrial solvents on central auditory pathways. Neurotoxicology. 74:58–66. doi:10.1016/j.neuro.2019.05.007