Organic solvent exposure and hearing loss in a cohort of aluminium workers

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ABSTRACT

Objectives: Organic solvent exposure has been shown to cause hearing loss in animals and humans. Less is known about the risk of hearing loss due to solvent exposures typically found in US industry. The authors performed a retrospective cohort study to examine the relationship between solvent exposure and hearing loss in US aluminium industry workers.

Methods: A cohort of 1319 workers aged 35 years or less at inception was followed for 5 years. Linkage of employment, industrial hygiene and audiometric surveillance records allowed for estimation of noise and solvent exposures and hearing loss rates over the study period. Study subjects were classified as "solvent exposed" or not, on the basis of industrial hygiene records linked with individual job histories. High frequency hearing loss was modelled as both a continuous and a dichotomous outcome.

Results: Typical solvent exposures involved mixtures of xylene, toluene and/or methyl ethyl ketone (MEK). Recorded solvent exposure levels varied widely both within and between jobs. In a multivariate logistic model, risk factors for high frequency hearing loss included age (OR = 1.06, p = 0.004), hunting or shooting (OR = 1.35, p = 0.049), noisy hobbies (OR = 1.74, p = 0.01), baseline hearing level (OR = 1.04, p<0.001) and solvent exposure (OR = 1.87, p = 0.004). A multivariate linear regression analysis similarly found significant associations between high frequency hearing loss and age (p<0.001), hunting or shooting (p<0.001), noisy hobbies (p = 0.03), solvent exposure (p<0.001) and baseline hearing (p = 0.03).

Conclusion: These results suggest that occupational exposure to organic solvent mixtures is a risk factor for high frequency hearing loss, although the data do not allow conclusions about dose–response relationships. Industries with solvent-exposed workers should include such workers in hearing conservation programs.

Industrial hearing loss due to excessive noise exposure is one of the most prevalent occupational conditions. Since the 1983 Occupational Safety and Health Administration (OSHA) hearing conservation standard, industries where individuals are exposed to noise of at least 85 decibels (dBA) for an 8 h time-weighted average are required to implement hearing conservation programs that include noise controls, use of personal hearing protection, employee training and annual surveillance audiograms for noise-exposed workers.

While such measures are now part of routine industrial practice for noise-exposed employees, more recent evidence suggests that exposure to neurotoxic chemicals could be contributing to occupational hearing loss risk.[1] Attention has focused on certain organic solvents that are widespread in industry and which have been shown in animal studies to be capable of causing sensorineural hearing damage.[2–8] In addition to reports of individual solvents causing hearing loss, animal studies have suggested that mixtures of solvents may act synergistically to exert greater auditory damage than individual agents alone.[9 10]

A number of small-scale observational studies in humans have provided further evidence of solvent ototoxicity. Case reports of acute overexposure to organic solvents through "glue sniffing" have documented severe acute sensorineural hearing loss.[11] A longitudinal study of hearing loss among 319 workers in a Swedish factory found higher rates of hearing loss among workers in the chemical department (who presumably had solvent but not noise exposure) compared to workers in other departments exposed to noise but not to chemicals.[12] A cross-sectional survey of 124 printers working with toluene, ethyl alcohol and ethyl acetate[13] assessed solvent exposure both by air monitoring and testing of urinary levels of hippuric acid (a metabolite of toluene). Most air monitoring results for individual solvents did not exceed the threshold limit value (TLV) set by the American Conference of Governmental Industrial Hygienists (ACGIH). However, 8% of the 109 workers who had biological monitoring for toluene had urinary hippuric acid in excess of the biological exposure index (BEI) of 2.5 g/g creatinine. This suggested that dermal or other unassessed exposure routes and/or individual metabolic differences could result in significant solvent exposure even in the setting of reassuring air-monitoring results. In a multiple logistic regression model, the only predictors of hearing loss were age and hippuric acid levels. Risk for hearing loss was elevated even at the BEI for solvent metabolites, raising the possibility that exposures below current regulatory limits, including brief peak exposures, may be ototoxic. Other cross-sectional studies have found an association between chronic solvent exposures and hearing loss.[14] While some of these studies have been carried out in settings where average exposures were in excess of ACGIH limits,[15] others have suggested that exposure at levels below current regulatory limits could still cause ototoxicity.[16] There has been a lack of human studies to date that longitudinally assess the risk of hearing loss in workers exposed to low or intermittent levels of organic solvents. We therefore performed a longitudinal cohort analysis of workers exposed to low levels of solvent mixtures in the aluminium industry to test the hypothesis that workers in solvent exposure jobs would demonstrate greater hearing loss rates than workers without solvent exposure, after controlling for covariate risk factors.

METHODS

Alcoa Inc. maintains a database of audiometric tests performed as part of company hearing conservation programs. Under the company's health and safety protocols, individuals working in jobs where the 95th percentile of measured noise levels (8-h time-weighted average) is 85 dBA or greater, undergo yearly surveillance audiometry, while individuals exposed to between 82 and 84 dBA have audiograms performed at least every 3 years. In general, hearing protection is required for all workers in areas where 5% of measured noise levels equals or exceeds 85 dBA. Pure tone audiograms are performed using sound booth environments that meet OSHA standards for audiometric testing. For the past 20 years, the centralised database of audiograms has been developed under the direction of a certified audiologist who directs the corporation's hearing conservation program, and who is also a certified industrial hygienist. There have been ongoing efforts to ensure the quality of the testing and data entry. An anonymous set of these audiograms has been assembled for research purposes with the approvals of the Human Investigation Committee and the company's Occupational and Environmental Health Advisory Committee.

In addition to audiometric records, the company also maintains a computerised database of industrial hygiene records (Hygenius) including, for many of their locations, all industrial hygiene exposure measurements performed since 1985, and human resource records (Peoplesoft) detailing job assignment for individuals employed for approximately the same period. An anonymous set of these data has also been created, with unique record numbers allowing for linkage with the audiometric files. Previous linkage of industrial hygiene measurements for noise exposure with audiometric results has demonstrated that in the Alcoa workforce hearing loss rates do not increase with ambient noise exposure levels, due perhaps to widespread use of hearing protection.[17]

Selection of study locations

Using the data from Hygenius, as well as audiometric records, we identified company locations where exposures to the organic solvents toluene, xylene and/or methyl ethyl ketone (MEK) had been recorded at levels of 5 ppm or more (8-h time-weighted average) for an individual personal sample in at least one job area, and if available, audiograms on workers as well as job history information from the human resource database dating back to at least 1990. Using these criteria, five plants in different geographical locations were selected for study, including both aluminium smelters and secondary aluminium processing facilities. Jobs where solvent measurements met the above criteria included those of coating operators on aluminium coating lines, maintenance workers who performed painting activities, and aluminium extrusion and foil operators.

The study cohort was comprised of hourly workers from five company locations who were 35 years of age or less at the time of their first recorded test subsequent to 1989, with a minimum of 4–6 years of audiometric follow-up, and at least three audiograms performed during that period. Individuals for whom job assignment in the human resources database was missing or who had jobs for which there were no matching industrial hygiene records were excluded, leaving 1319 in our study cohort.

Exposure assessment

Using data from the industrial hygiene database, median exposures to noise, and arithmetic mean exposures to carbon monoxide and the organic solvents xylene, toluene and MEK (the solvents most commonly sampled in the database) were calculated for specific jobs that could be matched to employment records. We used arithmetic means for chemical exposures to avoid artificially magnifying a possible dose–response effect. Time trend analysis was used to detect temporal trends for noise exposures within particular standardised job titles. If a significant trend was found we used the estimate from the specific year of exposure to calculate exposure levels for particular jobs.

These industrial hygiene job titles were then linked to the human resource database job titles using standardised linkage codes, in a process overseen by the company's industrial hygienist who was blinded to the results of the hearing outcome assessment. This process allowed estimation of solvent exposures and noise exposures for study individuals for each year worked.

Calculation of time-weighted exposures

On an individual basis, 5-year time-weighted exposures to noise and organic solvents were calculated. The equivalent noise exposure (L_{eq}) during the study period for individuals was determined using previously described methods to integrate the noise exposures for each individual based on their job history, adjusted for the period of follow-up for each individual.[18] We used the following equation for equivalent noise exposure (L_{eq}):

$$L_{eq,T} = A \log [(1/T)*(t_1*10^{(L1/A)}+t_2*10^{(L2/A)}+\ldots+t_n*10^{(Ln/A)})]$$

where T is the time duration over which the equivalent level is being determined, A is the exchange rate selected (A = 10 for a 3 dB exchange rate) and L is the noise level for that time duration. For example, an individual who worked for 3 years at 90 dBA and for 2 years at 88 dBA would have a 5-year time-weighted noise exposure level ($L_{eq,5yr}$) = 10 log $[(1/5)*(3*10^{(90/10)}+2*10^{(88/10)})]$ = 89.3 dBA.

Time-weighted exposures to solvents were calculated as follows:

$$TWA = (1/T)*[(t_1*L1)+(t_2*L2)+\ldots+(t_n*L_n)]$$

where TWA is time-weighted average, T is the time duration over which the solvent exposure is being determined and L is the solvent level for that time duration. For example, an individual who was exposed to toluene for 3 years at a level of 46 ppm and for 2 years at 20 ppm would have a 5-year time-weighted toluene exposure level = (1/5)*[(3*46)+(2*20)] = 35.6 ppm.

Since many individuals with solvent exposures worked with multiple solvents, a value for "solvent index" was calculated as the sum of the mean time-weighted exposures to each of the three solvents studied divided by the ACGIH TLV for each solvent, expressed as a unit value. We classified individuals as "solvent exposed" if their time-weighted solvent index was greater than the 90th percentile. These 116 individuals comprised the top 10% of calculated average solvent exposures in the cohort, and had a mean time-weighted average solvent exposure index of 0.26 (range 0.01–1.34).

In a similar fashion, time-weighted averages were calculated for carbon monoxide exposure. We used the 90th percentile of time-weighted exposures (13.7 mm) to define "carbon monoxide-exposed" employees.

Hearing outcomes

Hearing levels were assessed using the results of pure tone audiometry. For each individual, the rate of change (decibels/

year) in the binaural average of hearing threshold levels at the noise-sensitive frequencies of 3, 4 and 6 kHz was determined over the follow-up period using linear regression. Hearing loss was defined either in terms of this continuous rate of change (dB/year) or dichotomously as an annual rate of change greater than 1 dB/year at these frequencies.

Other hearing loss risk factors

Data on age, gender and race/ethnicity were obtained from the human resources database. At the time of the audiograms, individuals completed questionnaires regarding non-occupational noise exposures and medical risk factors for hearing loss. These were coded as yes/no answers and stored in the audiometric database. If an individual had answered yes at least once to any one of these questions, the individual was assigned a "yes" value for that variable. For example, if an individual ever answered "yes" to the question "do you hunt or shoot", he or she was assigned that risk factor for the purpose of the analysis.

Analysis

Two metrics to measure hearing loss were constructed. In the first, hearing loss was defined dichotomously as a rate of change in excess of 1 dB/year for the average of hearing thresholds at 3, 4 and 6 kHz. In the second, hearing loss was defined as the rate of change of average hearing thresholds at 3, 4 and 6 kHz in dB/year (a continuous outcome). Both linear and logistic regression analyses were used to determine associations between individual risk factors and hearing outcomes (bivariate analysis). Multivariate linear and logistic regression models were then constructed and a backward elimination technique was used to select those risk factors remaining significant in the adjusted analysis, using a selection criteria of $p = 0.05$. We tested for possible interaction effects between age and solvent exposure, baseline hearing status and solvent exposure, shooting or hunting and baseline hearing status, noisy hobbies and baseline hearing status, shooting or hunting and solvent exposure, and noisy hobbies and solvent exposure. In addition, we stratified the multivariate analysis according to whether or not individuals reported either hunting or shooting, or noisy hobbies. To assess data heterogeneity and model stability, we searched for outliers among the solvent-exposed group, and performed subgroup analysis on individual plant locations.

RESULTS

Table 1 shows the demographics and risk factor information for the study population.

Jobs with significant organic solvent exposures

Table 2 shows the job titles for which the industrial hygiene database had recorded at least one measurement of exposure to either toluene, MEK or xylene in excess of 5 ppm. The table also shows the number of samples performed in each of these job categories for these substances and the mean level of solvent measured. As table 2 demonstrates, solvent exposures of more than a trivial level were recorded for only a small number of jobs. For the majority of the jobs where there was non-trivial solvent exposures, the mean of the exposure measurements was below the TLV for that solvent. Within each of these jobs, the recorded levels varied over a range as wide as two orders of magnitude, even within a single location and over a short time period. Most of the jobs also involved solvent mixtures rather than single solvent exposures.

Table 3 shows the mean 5-year time-weighted average solvent exposures for the subset of individuals who were classified as "solvent exposed", since their mixed "solvent index" was greater than 1% (a value corresponding to the top 10% of solvent exposures in the study population). As table 3 demonstrates, the mean exposure levels for individual agents was usually well below the TLV values, yet the range was wide and some workers had time-weighted exposures in excess of the TLV for specific agents, as well as solvent index values in excess of 100%.

Tables 4 and 5 show the bivariate and multivariate models for prediction of high-frequency hearing loss. Table 4 shows the results of model one, where hearing loss was assessed as a dichotomous outcome (defined in this case as an average loss at 3, 4 and 6 kHz (both ears) in excess of 1 dB per year over the 5-year period). In this model, a number of variables demonstrated a bivariate association with an increased rate of hearing loss, including age, male gender, a certain study location, reported shooting or hunting, noisy hobbies, previous noisy job and baseline hearing status. Neither noise level nor carbon monoxide exposure significantly correlated with hearing loss, while being in the "solvent-exposed" group (highest decile of solvent index values) was associated with statistically significant increased risk. African-American race showed a protective effect on hearing loss. In the multivariate analysis of model one, risk factors remaining significant for hearing loss included age, reported shooting or hunting, noisy hobbies, solvent exposure and baseline hearing status. A significant interaction was detected between noisy hobbies and baseline hearing level, as the risk associated with baseline hearing was less for employees with noisy hobbies. The overall explanatory power of model one, as measured by a c statistic, was good (0.66).

Table 5 shows similar bivariate and multivariate analysis of risk factors for model two, defining hearing loss as a continuous outcome. Risk factors showing significant bivariate association with this outcome included age, African-American race (again showing a protective effect), a certain study location, hunting or shooting, previous noisy job, noisy hobbies, solvent exposure and baseline hearing status. In the multivariate analysis of model two, the factors remaining significant included age, shooting or hunting, noisy hobbies, solvent exposure and baseline hearing status. A significant interaction was detected between shooting or hunting and solvent exposure, as the risk associated with solvent exposure was less for employees who reported shooting or hunting.

Several analyses were performed to look for data heterogeneity. The authors reviewed individual audiograms of the subjects who were classified as solvent exposed. One individual had a particularly large slope of hearing loss over the 5 years (10 dB per year). We tested the stability of the models by excluding this outlier data point and re-running the models. For model one, deleting this individual did not have a significant effect on the measured association between solvent exposure and hearing loss. For model two, the effect of "solvent exposure" appeared somewhat unstable, with the p value increasing to 0.01. Since there was some indication of a location effect in the bivariate model, we performed analyses for both models using only the subjects in the largest location (location one). The results were similar to those found in the entire cohort, with significant predictors of increased hearing loss being age, reported shooting or hunting, and solvent exposure. For the dichotomous analysis (model one), the magnitude of the solvent effect was similar ($OR = 2.0$, 95% CI 1.02 to 4.0, $p = 0.05$), and the p value for solvent exposure in the continuous model (model two) remained significant

Table 1 Demographic and risk factor characteristics of 1319 hourly workers under 35 years of age at first audiogram

Characteristic	n (%)
Mean age (SD)	30.4 (3.7)
African-American	62 (4.7)
Male	1167 (88.5)
Location	
Location 1	743 (56.3)
Location 2	72 (5.5)
Location 3	22 (1.7)
Location 4	114 (8.6)
Location 5	368 (27.9)
Risk factors	
Ear infections	283 (21.5)
Shooting or hunting	757 (57.4)
Noisy hobbies	665 (50.4)
Previous noisy job	830 (62.9)
History of hearing loss in family	256 (19.4)
Noise exposure category (dBA)	
<82	129 (9.8)
82–84	593 (45)
85–87	510 (38.7)
⩾88	87 (6.6)
Carbon monoxide exposure (highest decile)	140 (10.6)
Solvent exposure	
Solvent index >1%	116 (8.8)
Mean number of hearing tests during study (SD)	5.7 (1.4)
Mean baseline hearing status (SD)	
Binaural average at 3, 4 and 6 KHz	13.3 (11.3)

(p = 0.002). For other locations, with smaller numbers of solvent-exposed individuals, the β value and p values for solvent exposure showed some variability and were not always significant. We performed stratified subanalyses for individuals with either reported noisy hobbies or shooting or hunting versus those reporting neither of these two risk factors, and found that the effect of solvent exposure remained statistically significant in both groups (data not shown).

DISCUSSION

The results of this longitudinal study of 1319 hourly industrial workers aged 35 years or less at the beginning of follow-up indicate a significant deleterious effect of mixed solvent exposure on 5-year hearing loss risk. While solvent-exposed individuals constituted only a small part of the workforce, the observed effect remained highly statistically significant in a multivariate model that adjusted for demographic factors and for exposure to non-occupational and occupational noise. Analysis for data heterogeneity and possible statistical confounding or interaction did not alter this conclusion. This study is therefore in agreement with previous human studies that have detected a deleterious effect of organic solvents on hearing.

Table 3 Time-weighted 5-year solvent exposure estimates for "solvent-exposed" individuals*

Solvent	Concentration Mean (SD)	Concentration Range
Toluene	4.0 (5.9)	0–28.8
Methyl ethyl ketone (MEK)	21.4 (35.7)	0–255.3
Xylene	7.6 (13.4)	0–64.0
Solvent summation index†	0.26 (0.26)	0.01–1.34

*Individuals in the highest decile of solvent exposure.
†Solvent summation index = toluene exposure/TLV+MEK exposure/TLV+xylene exposure/TLV (TLV for toluene = 50 ppm, for MEK = 200 ppm, and for xylene = 100 ppm).

The study was conducted in an industry where solvents were not in widespread use. Most solvent measurements were actually well below the TLV values. A small number of jobs had exposure measurements indicating mixed solvent exposures that showed significant variation in levels between samples, with a few sample results in excess of the TLV values. Only air samples were recorded, and no assessment of dermal exposures was available. Information on the frequency and duration of "peaks" in solvent exposures was also not available but could be biologically significant. It therefore seems likely that individual exposures in "solvent-exposed" jobs varied. Moreover, some dermal exposure is also likely but was not incorporated into our exposure metric. Therefore, while our belief is that these findings indicate that organic solvent exposures are associated with an increased risk of high-frequency hearing loss, it is not possible to make extrapolations from this study about dose–response relationships or speculate about the "safe" levels of solvent exposure to prevent hearing loss. Furthermore, it is not possible, given the diversity of the solvent mixtures encountered, to attribute greater ototoxicity to particular solvents or mixtures based on these results.

Alternatively, it is possible that the observed effect of solvent exposure on hearing loss is a spurious one due to exposure misclassification, confounding or both. Some degree of misclassification of exposures is inevitable in an epidemiological

Table 2 Jobs with solvent exposures >5 ppm for specific job titles in a cohort of aluminium workers from five locations

Job title	Toluene Obs (n)	Toluene Concentration (ppm) Mean (SD)	Toluene Concentration (ppm) Range	Methyl ethyl ketone Obs (n)	MEK Concentration (ppm) Mean (SD)	MEK Concentration (ppm) Range	Xylene Obs (n)	Xylene Concentration (ppm) Mean (SD)	Xylene Concentration (ppm) Range
Caster furnace operator	9	0	0–0	0			11	14 (46.4)	0–153.9
Coater operator	17	46.9 (108.7)	0.1–342.8	21	34.5 (82.8)	0.1–318.9	10	11.5 (22.9)	0–62.4
Extruder operator	13	43.8 (155.1)	0–559.8	9	13 (9.8)	1–30.1	0		
Facilities/grounds operator	18	3.2 (3.4)	0–10.3	10	128.5 (158.4)	0.3–433.5	20	15.9 (33)	0–113.5
Foil mill operator	8	3 (3.5)	0–8.2	3	1.7 (1.9)	0.1–3.9	0		
Laboratory operator	19	0.8 (0.6)	0.1–2.1	20	6.2 (10.9)	0.2–50	0		
Laminator operator	7	1.7 (1.8)	0–3.9	4	1.9 (2.3)	0.1–5.1	0		
Mixer operator	5	354 (488.4)	0.1–978.2	7	7.7 (9.3)	0.2–27	0		
Pack/ship operator	15	0.1 (0.2)	0–0.7	1	6.6	6.6–6.6	14	0 (0)	0–0.1
Sheet/plate mill operator	0			11	1.9 (2.5)	0.1–7.6	0		
Tube press operator	73	4 (27.5)	0–232.7	3	55 (21.6)	30.5–71.4	73	9.9 (81.9)	0–699.7

Obs, observations.

Table 4 Model one: bivariate and multivariate predictors of high frequency hearing loss† (dichotomous outcome) over 5 years in a cohort of aluminium workers

Bivariate			Multivariate		
Characteristic	OR (95% CI)	p Value†	Characteristic	OR (95% CI)	p Value†
Age	1.08 (1.04 to 1.12)	<0.001	Age	1.06 (1.02 to 1.10)	0.004
African-American	0.38 (0.16 to 0.90)	0.03			
Male	1.59 (1.00 to 2.53)	0.05			
Location					
Location 1	1.03 (0.75 to 1.41)	0.85			
Location 2	1.9 (1.09 to 3.31)	0.02			
Location 3	1.19 (0.42 to 3.33)	0.74			
Location 4	1.38 (0.84 to 2.26)	0.2			
Location 5	Reference				
Median noise level in dBA					
<82	Reference				
82–84	1.17 (0.72 to 1.88)	0.52			
85–87	1.09 (0.67 to 1.77)	0.72			
⩾88	1.24 (0.64 to 2.41)	0.52			
Risk factors			Risk factors		
Ear infections	1.16 (0.85 to 1.59)	0.35			
Shooting or hunting	1.63 (1.24 to 2.15)	<0.001	Shooting or hunting	1.35 (1.00 to 1.80)	0.049
Noisy hobbies	1.42 (1.09 to 1.85)	0.01	Noisy hobbies	1.74 (1.12 to 2.70)	0.01
Previous noisy job	1.35 (1.02 to 1.79)	0.03			
History of hearing loss in family	1.3 (0.94 to 1.78)	0.11			
Carbon monoxide exposure	0.92 (0.59 to 1.42)	0.69			
Solvent exposure	1.84 (1.22 to 2.79)	0.004	Solvent exposure	1.87 (1.22 to 2.89)	0.004
Mean baseline hearing status (SD)			Mean baseline hearing status (SD)		
Binaural average at 3, 4 and 6 kHz	1.04 (1.02 to 1.05)	<0.001	Binaural average at 3, 4 and 6 kHz	1.04 (1.03 to 1.06)	<0.001
			Interactions		
			Noisy hobbies*baseline hearing status	0.98 (0.96 to 0.999)	0.04

†High frequency hearing loss: rate of loss for the average of hearing thresholds at 3, 4 and 6 kHz >1 dB/year (dichotomous outcome). Logistic regression was used to calculate the odds ratios, 95% confidence intervals and p values.

Table 5 Model two: bivariate and multivariate predictors of high frequency hearing loss† (continuous outcome) over 5 years in a cohort of aluminium workers

Bivariate			Multivariate		
Characteristic	β Coefficients	p Value	Characteristic	β Coefficients	p Value
Age	0.03	<0.001	Age	0.03	<0.001
African-American	0.32	0.01			
Male	0.14	0.08			
Location					
Location 1	0.04	0.45			
Location 2	0.28	0.03			
Location 3	0.32	0.1			
Location 4	0.17	0.08			
Location 5	Reference				
Median noise level in dBA					
<82	Reference				
82–84	−0.05	0.54			
85–87	−0.03	0.73			
⩾88	−0.06	0.64			
Risk factors			Risk factors		
Ear infections	−0.01	0.91			
Shooting or hunting	0.2	<0.001	Shooting or hunting	0.18	<0.001
Noisy hobbies	0.17	<0.001	Noisy hobbies	0.11	0.03
Previous noisy job	0.11	0.03			
History of hearing loss in family	0.05	0.41			
Carbon monoxide exposure	−0.05	0.55			
Solvent exposure	0.03	<0.001	Solvent exposure	0.58	<0.001
Mean baseline hearing status (SD)			Mean baseline hearing status (SD)		
Binaural average at 3, 4 and 6 kHz	0.01	<0.001	Binaural average at 3, 4 and 6 kHz	0.005	0.03
			Interactions		
			Shooting or hunting*solvent exposure	−0.43	0.02

†High frequency hearing loss: annual rate of loss for the average of hearing thresholds at 3, 4 and 6 kHz (continuous outcome). Linear regression was used to calculate the β coefficients and p values.

Main messages

- This study found that workers in solvent-exposed jobs had an increased risk of high frequency hearing loss, even after adjusting for demographic risk factors and noise exposure.
- These findings indicate that organic solvent exposures, perhaps related to dermal or intermittent peak exposure scenarios, are associated with an increased risk of high-frequency hearing loss.
- It is not possible, however, to make extrapolations from this study about dose–response relationships or to speculate about the ''safe'' levels of solvent exposure to prevent hearing loss.

Policy implications

- Workers in solvent-exposed jobs should be assessed for possible over-exposure due to intermittent peak exposures and dermal exposure.
- Given the ubiquitous use of organic solvents in industry, these results support the inclusion of solvent-exposed individuals in hearing conservation programs, including periodic monitoring of hearing status, until the dose–response relationships between solvent exposure and hearing loss are better clarified.

study where estimations of mean solvent exposures for a particular job are applied to individuals in order to estimate personal exposure over the study period. This can result in either over- or underestimation of the true values for individual exposures. Such misclassification, however, tends to be non-differential, biasing results toward the null.

Another possible explanation for our findings is confounding, whereby the designation of individuals as ''solvent-exposed'' was linked to other risk factors (such as age, gender, etc) that were actually responsible for the observed effect of solvent exposure on hearing loss risk. The fact that the effect of solvent exposure persisted in the multivariate model after adjusting for known confounding covariates makes this possibility less likely. Since the number of solvent-exposed employees varied between locations, it is possible that a location effect (such as a superior hearing conservation program in one facility) could be a hidden confounder. However, location did not remain as a significant risk factor in the multivariate model, and in addition, a stratified analysis of only the workers in the largest facility showed that the adverse association of solvent exposure and hearing outcomes remained significant. Analysis of locations two through five showed variation in the direction and magnitude of the solvent effect, but the numbers of solvent-exposed individuals in some plants was quite small.

Our search for possible outliers and data heterogeneity to explain the observed effect of solvent exposure on hearing loss revealed that when we removed the solvent-exposed individual with the greatest degree of hearing loss from analysis, the risk estimates for solvent exposure in model one (dichotomous outcome) remained relatively stable, while the risk estimate showed some instability in model two (continuous outcome). Therefore, while heterogeneity was found to exist, we do not believe it can account for all of the findings of an increased risk of hearing loss with solvent exposure.

We did find some evidence for statistical interaction among the risk factors in the model, particularly interaction between noisy hobbies and baseline hearing status (dichotomous model) and shooting and hunting with solvent exposure (continuous model). In each case, these interaction terms did not significantly alter the effect of other variables in the model.

The lack of a strong effect of noise level on hearing may seem surprising, since occupational noise is a recognised cause of high frequency hearing loss. However, previous analysis of the company's worker cohort has demonstrated a similar lack of increasing hearing loss risk with increasing ambient noise level.[18] Since the use of hearing protection is compulsory across company facilities at noise levels lower than required by OSHA mandate, the lack of a typical dose–response effect between ambient noise level and hearing loss rates is due, we believe, to effective use of hearing protection in the highest ambient noise exposure areas.

These limitations notwithstanding, we conclude that workers in solvent-exposed jobs should be assessed for possible over-exposure, due to variable exposure scenarios depending on job task, intermittent peak exposures and dermal exposure. We also believe that due to the ubiquitous use of organic solvents in industry, these results support the inclusion of solvent-exposed individuals in hearing conservation programs, including periodic monitoring of hearing status, until the dose–response relationships between solvent exposure and hearing loss are better clarified.

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