Occupational Medicine 2005;**55:**48–53
doi:10.1093/occmed/kqi002

Joint effects of smoking, noise exposure and age on hearing loss

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Background Smoking has been shown to have adverse effects on hearing, but it's unclear whether smoking interacts with known causes of hearing loss such as noise exposure and ageing.

Aims To examine the hypothesis that smoking, noise and age jointly affect hearing acuity.

Methods This cross-sectional study was carried out in 535 male adult workers of a metal processing factory. Pure-tone audiometric tests were utilized to assess hearing loss. Noise exposure assessment was based on a job exposure matrix constructed with industrial hygienist scoring and job titles. Each participant answered questionnaires about socio-demographic, life-style, occupational and health-related data. Analysis of the possible underlying biological model was undertaken assessing departures from additivity using measures of the size of the interaction present.

Results Age and occupational noise exposures were, separately, positively associated with hearing loss. For all the factors combined the estimated effect on hearing loss was higher than the sum of the effects from each isolated variable, especially for smoking and noise among those 20–40 years of age, and for smoking and age among those non-exposed to occupational noise.

Conclusions The synergistic effect of smoking, noise exposure and age on hearing loss, found in this study, is consistent with the biological interaction. Furthermore, it is possible that distinct ototoxic substances in the chemical composition of mainstream smoke may synergistically affect hearing when in combination with noise exposure, which needs to be examined in future studies.

Key words Age; hearing loss; noise-induced hearing loss; occupational noise; smoking.

Introduction

Noise is considered the most common occupational exposure in the world. It is estimated that approximately 600 million workers are exposed to occupational noise [1]. Long-term exposure to noise is a cause of hearing loss, a disabling and irreversible disease. Although noise-induced hearing loss (NIHL) is a potentially preventable disease, it remains an important public health problem. The biological basis of NIHL is a combination of mechanical and metabolic factors [2]: chronic excessive noise exposure damages cochlear hair cells and metabolic changes result from hypoxia caused by noise-induced capillary vasoconstriction [3]. Another worldwide exposure is tobacco, consumed by approximately 1.3 billion of the global population [4]. Tobacco may also affect cochlear blood supply because it causes peripheral vascular changes, such as increased blood viscosity [5], and reduced available oxygen. These effects were identified in the aetiology of cochlear lesions in laboratory animals [6] and humans [7]. As the elderly population increases, age becomes a major risk for hearing loss. Ageing-related degenerative changes may affect neural fibres, stria vascularis, and inner and outer hair cells causing progressive hearing impairment [8]. Therefore, smoking, noise and ageing may act in common causal pathways for hearing loss, through the reduction on cochlear blood supply, which support the hypothesis that these factors interact under an additive model.

Although studies have reported positive association between smoking and hearing loss [9–13], the joint effects involving smoking and noise have rarely been assessed [14,15]. In one study, the combined effects of

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smoking and exposure to noise on hearing were estimated to be additive [14]. In contrast, based on experiments, smoking was described as having a possible hearing protective effect [15]. Previous studies among noise-exposed workers observed more adverse effects on hearing in smokers than in non-smokers [16–18]. The aim of this study is to examine the hypothesis that smoking, noise and age jointly affect hearing acuity, which may be of particular relevance in preventive programmes for workers or the general population.

Methods

This cross-sectional study was conducted in a large metal plant situated in northeast Brazil. Recently, anti-tobacco campaigns had taken place and, for safety reasons, smoking was forbidden in operational areas or any other closed environment. However, workers were allowed to smoke in open areas during breaks from work. Personal hearing protective equipment has been reported to be available for all workers since the plant started to operate. Except for noise, there were no other occupational agents hazardous to hearing.

The eligible population comprised all active male workers who participated in a hearing screening, and voluntarily joined a health promotion programme. Socio-demographic, life-style, occupational and health-related data were obtained using questionnaires administered by trained field workers in an isolated room. Smoking was ascertained based on the following questions: 'have you ever smoked?' and 'are you a current smoker?' Duration of smoking habit was registered in months. Smoking was categorized as non-smokers (never-smokers or less than 6 months) and ever-smokers (current or past smokers). Age was recorded in years and analysed as a dichotomous variable i.e. 20–40 years and 41–55 years of age.

Noise exposure assessment was based on a job exposure matrix that had job titles on one axis and chemical or physical hazards associated with the job on the other axis. Study participants were scored on their degree of exposure to each agent by industrial hygienists who worked in the plant, using four levels of exposure. These scores were assigned to each job in a worker's occupational history to develop an individual exposure profile. The four original exposure levels were combined to distinguish workers who were exposed, which correspond to work posts with noise exposure between 81 and 93 dBA, and non-exposed for those with levels below this range. Pre-employment noise exposure history was also assessed using a similar job exposure matrix based on the occupational profiles recorded in individual interviews. Duration of noise exposure was estimated as the sum of the years employed in exposed jobs. This variable was further categorized, i.e. $0 < 4$ years and ≥ 4 years of occupational noise exposure.

Qualified audiologists assessed hearing ability using standardized audiometric examination procedures assuring at least 14 h of previous acoustic resting. The exams were conducted in an isolated acoustic room with a Siemens audiometer (Model SD 25). The pure-tone hearing thresholds were measured at frequencies of 0.25, 0.5, 1, 2, 3, 4, 6, 8 kHz for air-conduction, and for bone conduction corresponding to frequencies of 0.5, 1, 2, 4 kHz, respectively, for both ears. Hearing loss was defined based on hearing thresholds worse than 25 dBHL, at least in one of the following frequencies: 3, 4, 6, 8 kHz, bilaterally.

To assess the joint effects of the three variables, smoking, noise and age, prevalence ratios were estimated for each group of combined variables taking as the reference group non-smoker workers, aged 20–40 years and non-exposed to occupational noise. The Mantel–Haenszel 90% confidence interval (CI) was used to describe the precision of the estimates. An alpha of 0.10 was utilized because of the small sample size and the required examination of a three-way interaction. Confounding evaluation was not possible because data were sparse. Examination of a possible underlying biological model was conducted using synergistic departures of additive models based on excess prevalence ratio (EPR). In the case of two factors, if EPR_{11} is defined as the excess prevalence ratio when both factors are present and EPR_{01} and EPR_{10} when each factor is present in isolation, then $EPR_{11} > EPR_{01} + EPR_{10}$ means the observed combined effect of two factors is greater than either of them working alone. In other words, superadditivity occurs when the first term of this equation is greater than the second. Size measures of positive departures from the assumption of additivity was calculated as $[ERP_{11}/(ERP_{01} + ERP_{10})] - 1$ [19]. The formulae were adjusted to take account of a three-factor analysis. Data analysis was performed with SAS 8.11. The Internal Review Board of the Institute of Collective Health, Federal University of Bahia, approved the study protocol.

Results

There were 870 active workers in the plant, but only 732 (84%) voluntarily participated in the health programme. All 68 women were excluded from the study population because of their small number and concentration in non-exposed jobs. From the remaining 664 workers, an audiometric exam was available for 560 individuals, which corresponds to 104 (16%) with missing information for the referent study year. In addition, 16 (3%) presented hearing loss non-compatible with noise-induced damage. Nine (2%) individuals older than 55 years of age were also excluded because of the small number in the study population, resulting in a total of 535 individuals. Among them, 35% were smokers, 46% noise-exposed workers, and 39% over 40 years of age.

All these factors were independently associated with hearing loss in the study population, as shown in Table 1.

The prevalence of hearing loss varied widely across the combined variable categories (Table 2). The lowest estimate was found among the reference group of non-smokers, non-exposed to noise, aged 20–40 years (6.1%) and the highest prevalence estimated for smokers, noise-exposed who were older than 40 years of age (46.4%). When analysed alone or in combination, smoking, noise and age were also positively associated with hearing loss ($P < 0.10$), except for smoking alone (Table 2). For isolated factors, the largest estimate was found for age (PR = 4.02, 90% CI: 2.04–7.92), followed by noise (PR = 2.38, 90% CI: 1.26–4.51) and smoking (PR = 1.27, 90% CI: 0.37–4.32), respectively. However, no statistical differences were found between the prevalence ratios across the combined exposure groups overall.

Excess prevalence ratios for isolated and combined factors of smoking, noise and age on hearing loss are shown in Table 3. It was observed that for all combined factors, the estimated effect on hearing loss was higher than the sum of the effects from each isolated variable. Relative differences between these estimates also indicate that the largest departure occurs for the combination of smoking and noise (133%) in the young group, followed by the joint effect of smoking and being older than 40 years (98%) among workers non-exposed to noise. When the three factors were combined, the estimated departure was 42%, according to additive models. Apparently, larger superadditivity was estimated for smoking and old ages among workers non-exposed to noise, and for smoking and noise exposure, among those 20–40 years of age.

Discussion

The findings of this study suggest that smokers, who were exposed to occupational noise or non-exposed but older than 40 years of age, have increased prevalence of hearing loss than the expected estimate based on the summation of each factor separately, although no evidence of statistical interaction was found. When smoking was considered, larger departures from additive models were also observed especially for combined effects of smoking and noise exposure among the youngest, and for smoking and older age among those non-exposed to noise. This may express synergism of these factors regarding biological additive models. One previous study reported a multiplicative effect from smoking and age on hearing loss [12], but no statistical inference results were provided. In another one, a positive association between smoking and NIHL was found after adjustment for age, but the possibility of combined effects were not explored [16]. Consistently, a dose–response gradient between the number of cigarettes and hearing impairment among noise-exposed workers was also observed [14,17]. The results of this study are in accordance with these research findings and add to the evidence for synergistic effects from smoking, noise and age on hearing loss, and also an estimation of direction and magnitude of each joint effect. Synergism from smoking and occupational noise exposure on hearing loss is a not-yet reported result. It is consistent with a potentiation of NIHL caused by simultaneous carbon monoxide exposure, observed in animal experiments [20]. Nevertheless, a simple additive effect from smoking and noise on hearing was once observed in humans [14]. In addition, in a human

Table 1. Crude and adjusted prevalence ratios and 95% confidence intervals for hearing loss according to smoking, noise exposure and age

Variables	Population $n = 535$	Number of cases $n = 120$	Prevalence (%)	Prevalence ratio			
				Crude		Adjusted[c]	
				PR[a]	95% CI[b]	PR	95% CI
Smoking							
Never smokers	349	50	14.3				
Ever smokers	186	70	37.6	2.63	1.91–3.60	1.55	1.12–2.14
Noise exposure							
No	289	48	16.6				
Yes	246	72	29.3	1.76	1.28–2.43	1.48	1.10–2.00
Age in years							
20–40	329	37	11.3				
41–55	206	83	40.3	3.58	2.53–5.06	2.66	1.84–3.84

[a] Prevalence ratio.

[b] 95% Mantel–Haenszel confidence intervals.

[c] Adjusted for the other variables.

Table 2. Prevalence, prevalence ratios and 90% confidence intervals for the joint effects of smoking, noise exposure and age on hearing loss

Variables[a]	$N = 535$	Prevalence (%)	Prevalence ratio	90% CI[b]
Referent				
Smoking = 0, noise = 0, age = 0	165	6.1	1.00	–
Isolated variables				
Smoking = 1, noise = 0, age = 0	26	7.7	1.27	0.37–4.32
Smoking = 0, noise = 1, age = 0	104	14.4	2.38	1.26–4.51
Smoking = 0, noise = 0, age = 1	41	24.4	4.02	2.04–7.92
Combined variables				
Smoking = 1, noise = 1, age = 0	34	29.4	4.85	2.49–9.46
Smoking = 0, noise = 1, age = 1	39	38.5	6.35	3.47–11.61
Smoking = 1, noise = 0, age = 1	57	45.6	7.53	4.31–13.14
Smoking = 1, noise = 1, age = 1	69	46.4	7.65	4.43–13.23

[a] Smoking: 0 = never smoker, 1 = ever smoker; occupational noise exposure: 0 = no, 1 = yes; age range: 0 = 20–40 years of age, 1 = 41–55 years of age.

[b] Mantel–Haenszel confidence intervals.

experiment, smoking was found to be negatively associated with temporary threshold shifts, suggestive of a possible protective effect from smoking to NIHL [15], which is biologically inconsistent.

Assuming that smoking, noise and age are not protective for hearing loss, and instead, they are separate causal factors, the estimated superadditivity found in this study may express a possible biological synergism [21]. The degree of interaction is dependent on underlying pathogenic mechanisms, but their nature cannot be fully understood by epidemiological data because distinct pathways may predict similar disease patterns [22]. In this study, a possible biological support for underlying pathogenic mechanisms is the well-known vascular changes and consequent cochlear hypoxia related to smoking and also to long-term intense noise exposure [3,5,6,23]. For example, carbon monoxide present in the mainstream smoke reduces cochlear blood oxygen levels as a result of capillary vasoconstriction, increased blood viscosity, reduction of transported oxygen and difficulties in oxyhaemoglobin dissociation. Noise exposure also induces hypoxia in the cochlea, causing direct lesions or interacting with mechanical noise-induced impairments [23]. Chronic hypoxia may result in cochlear lesions particularly in the basal, high frequency region, the most vulnerable part of the cochlea. Also, age-related degenerative changes may affect neural fibres and those parts of the cochlea, including vascular structures, which affect most pronouncedly the high frequencies [8].

Despite the low concentration, potentially ototoxic substances present in mainstream cigarette smoke may also interact with noise and/or age to cause hearing impairment. Complex mixtures of substances are difficult to analyse because their effects are entangled and sometimes modified in unexpected directions [24]. It is possible that toxic exposure within acceptable concentration levels may cause hearing impairment when associated with other toxic exposures, particularly when noise is present. Cigarette burning releases organic solvents, i.e. toluene, styrene, xylene, and also lead, mercury and carbon monoxide [25]. These substances have been described as independent factors and/or in potential interaction with noise exposure on hearing loss [26–28]. Synergisms were identified for the combined effects of noise and organic solvents [29]. They differ in relation to their ototoxic properties, and can affect sensorial or neural auditory structures [27,30]. The interaction mechanism of noise and chemical substances on hearing damage involves changes such as an increased cochlear vulnerability to noise and noise-related intensification of cochlear damage from chemical agents that have ototoxic effects [30]. Smoking may also strengthen these ototoxic effects by increasing their access to cochlear areas, where carbon monoxide is present in high concentrations, which leads to an elevated blood flow and vascular permeability as a response [31]. In this study, in order to observe possible synergistic effects even when noise is below action levels, workers exposed to an 81–84 dB range were also included as exposed.

Interactions are commonly ignored in epidemiological analysis and effect modifiers often mistakenly considered as confounders [32]. Interaction analysis requires specific and sometimes complex procedures, not yet popular, and a considerable sample size. In this investigation, the size of the study population was not an obstacle to performing appropriate analysis, although confidence intervals were quite large for some estimates. It is worth noting that there were only 26 in the group of non-smoker workers, aged 20–40 years and non-exposed to noise, which may account for the relative differences when smoking was considered. The main limit is its cross-sectional design,

Table 3. Excess prevalence ratio for isolated and combined effects of smoking, noise and age on hearing loss and corresponding percent estimated departure from additive models

Subgroups[a]	$n = 535$	Excess prevalence ratio (EPR = PR − 1)		Relative difference[c] [(A/B) − 1] (%)
		Observed for combined exposures (A)	Expected based on separated exposures[b] (B)	
Referent				
Smoking = 0, noise = 0, age = 0	165	–	–	
Isolated variables				
Smoking = 1, noise = 0, age = 0 (smoking)	26	0.27	–	
Smoking = 0, noise = 1, age = 0 (noise)	104	1.38	–	
Smoking = 0, noise = 0, age = 1 (age)	41	3.02	–	
Combined variables[d]				
Smoking = 1, noise = 1, age = 0 (smoking–noise)	34	3.85	1.65	133
Smoking = 0, noise = 1, age = 1 (noise–age)	39	5.35	4.40	22
Smoking = 1, noise = 0, age = 1 (smoking–age)	57	6.53	3.29	98
Smoking = 1, noise = 1, age = 1 (smoking–noise–age)	69	6.65	4.67	42

[a] Smoking: 0 = never smoker, 1 = ever smoker; occupational noise exposure: 0 = no, 1 = yes; age range: 0 = 20–40 years of age, 1 = 41–55 years of age.

[b] Excess prevalence ratio expected according to additive model ($EPR_{11} = EPR_{01} + EPR_{10}$) [19].

[c] Percent estimated departure of the prevalence ratio observed excess from the expected excess for combined exposures as $[EPR_{11}/(EPR_{01} + EPR_{10})] - 1$ [19].

[d] Calculations were adapted to analyse three-way interaction.

particularly to examine biological causal synergism. Another methodological limitation was the need to examine independent variables dichotomously. Therefore, gradients of intensity and duration could not be distinguished. Selection bias could also have occurred because of incomplete worker coverage by audiometry, particularly for non-noise-exposed workers whose audiometry was not mandatory. These workers could be more likely to volunteer for audiometry because of hearing complaints, hence increasing the prevalence in the reference group.

Non-occupational noise exposures are common in this study region, where loud electronic music is usually played in popular outdoor parties, but these data were not available. There is no reason to think that noise-exposed workers would be more exposed to non-occupational noise than those among the referent group. However, smokers' less careful life-style may increase exposure to non-occupational noise [14]. Survivor healthy worker effect could also have occurred because of extensive downsizing in the last decade. Although interviews were confidential and answers recorded anonymously, there may have been under-reporting of smoking. To reduce misclassification error, occupational noise exposure prior to employment at the plant was assessed. Longitudinal studies with improved assessment of smoking, time exposure and also the use of severity levels of auditory damage should be developed to overcome methodological limitations of this study.

Despite methodological limitations the results of the present study contribute to the knowledge about potentially preventable risk factors for hearing loss. The study provides evidence that joint effects of smoking, noise and ageing contribute to increased hearing impairment. This is the case especially when combined effects of smoking and noise exposure among the youngest are considered, and that of smoking and older age among those not exposed to noise. Moreover, the synergistic effects are consistent with the hypothesis that these factors may act in common pathogenic pathways. Because of the presence of an interaction between these factors, intervention programmes designed to reduce exposure to noise and smoking should result in a reduction in those suffering from hearing loss.

Acknowledgements

We are indebted to Dr Antonio Alberto Lopes, who carefully helped to edit an early version of the manuscript and also to the workers, administrators and the health staff of the metal plant, who made this research possible. Grant sponsor: CNPq/Ministry of Science and Technology of Brazil, Proc. No.522.621-96-1.

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