Occupational exposure to insecticides and their effects on the auditory system

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The objective of this investigation was to study the effects of occupational exposure to organophosphates and pyrethroid insecticides on the central auditory system. The study group consisted of 98 workers exposed to insecticides and 54 non-exposed workers. Data on work history, medical history, present diseases, occupational and non-occupational exposure to noise or chemicals and lifestyle factors were obtained through an interview. Central auditory system functions were assessed through frequency patterns and duration patterns testing. Fifty-six percent of the exposed workers had hearing dysfunction at the central level and its relative risk was 7.58 for the group with exposure to insecticides (95% CI 2.9- 19.8) when compared to the non-exposed group. The group exposed to insecticides and noise had a relative risk for central disorders of 6.5 (95% CI 2.2-20.0) when compared to the non-exposed group and 9.8 (95% CI 1.4-64.5) when compared to the group exposed only to noise. The finding suggests that exposure to organophosphates and pyrethroid products can induce damage to central auditory system. Further research is needed on the ototoxic mechanisms of these chemicals, and on hearing loss prevention measurements that are applicable and adequate to such risks and populations.

Keywords: organophosphates, pyrethroids, ototoxicity, hearing, insects' control.

Introduction

There are more than 750 different groups of chemicals that are considered potential neurotoxicants (Ahlstrom et al., 1986; Arlien-Soborg et al., 1981, 1998; Mergler, 1995) but, the majority of these chemicals have not been extensively tested. When there is a continuous interference by chemical substances on cellular and molecular processes, alterations will develop slowly, especially the ones related to the neuropsychological and psychological functions (Wesseling at al., 1997).

The first occupational studies demonstrating that occupational chemicals could have ototoxic effects were conducted more than 30 years ago. However, for the last 16 years, more systematic research has been conducted to explore the ototoxic effects of these chemicals (Abbate et al., 1993; Araki et al., 1992; Arlien-Soborg et al., 1981; Franks and Morata, 1996; Gregersen, 1988; Möller et al, 1989; Ödkvist et al., 1982; Otto et al., 1993; Jacobsen et al 1993; Morata et al, 1993; 1997). The auditory system has been shown to be vulnerable to a variety of chemicals (Mergler, 1995), including organic solvents. Their effect can be observed independently from exposure to noise (Franks and Morata, 1996; Hirata et al., 1992; Johnson and Nylon, 1995; Morata et al., 1993, 1997). Studies on the auditory effects of exposure to insecticides, however, are very rare.

The organophosphates and other organic compounds that are derived from phosphoric acid, inhibit cholinesterase, producing an accumulation of acetylcholine, which affects the peripheral nervous system (Hawkers et al., 1989), as well as the cognitive and sensory systems (Fornazzari et al, 1983; Mencher et al, 1996. Another class of insecticides, the pyrethroids, have low persistency in the environment and greater stability to degradation by light. Exposure to certain concentrations of organophosphates will produce effects on the nervous system that will show up later in life as a delayed neuropathology (Axelsson, 1996). Sensations of numbness and tingling, weakness and loss of equilibrium can occur after a few weeks of exposure. Exposures to certain neurotoxic chemicals can also be associated with an increase in the risk of neurodegenerative diseases (Mencher et al., 1996). A study comparing two groups exposed to organophosphates with different levels of pseudocolinesterase activity (N=34) reported peripheral neuropathies in the group with low values of pseudocolinesterase. Both groups had sensorineural hearing loss, ranging in severity from low to moderate (Ernest et al., 1995). Profound bilateral hearing loss, associated with residual peripheral neuropathy in the extremities was reported for a patient with acute poisoning from sprays containing a mixture of two organophosphates, 7.5% of malathion and 15% of metamidophos (Harell et al., 1987). Peripheral auditory disorders were also observed in a group of 98 farm workers free from noise exposure (ages ranging from 15 to 59 years old). The hearing losses were found to be associated with combined exposure to pesticides, organophosphates and pyrethroid insecticides. The audiometric screening revealed that 57.1% of the exposed had high frequency sensorioneural hearing losses (Teixeira and Brandão, 1998). More recently, in a source apportionment analysis (n=185, Beckett et al., 2000) in the New York Farm Family Health and Hazard Survey, hearing loss was found to be associated with a history of spraying crops with insecticides (including organophosphates and pyrethroid compounds). Other factors associated with hearing loss were: age, gender, high school education, firearms use, and grain dryer operation.

The objective of this cross-sectional investigation was to study the effects of occupational exposure to organophosphate and pyrethroid insecticides on the central auditory system. Central audiologic tests were used to evaluate the occurrence of hearing disorders in workers exposed to organophosphate and pyrethroid insecticides because of their potential neurotoxicity, which can include effects on the sensory and cognitive systems. The confirmation of auditory effects of insecticides may impact current recommendations for health surveillance of exposed workers to monitor and prevent central audiologic damage.

Methods

In Brazil, the National Foundation of Health (FNS) develops programs to control tropical diseases such as Dengue, Malaria, Yellow Fever and Chagas Disease using organophosphate and pyrethroid compounds. In the past organochlorinated aromatics, such as DDT, and Benzene Hexachloride compounds, were used (see Table 1).

Study Population

The exposed group, Group A (n=98), consisted of ninety-eight male workers with a minimum of three years of insecticide exposure, who used organophosphate and pyrethroid compounds in their present job. Their mean age was 41.6 years (SD=6.9), and 86.7 % were younger than 50 years old. Their mean duration of chronic exposure to insecticides was 7.3 years (SD=4.5) and 31.6% had 10 or more years of exposure to it. These workers did not receive formal training on safety measures and/or personal protection equipment. Workers reported that incompatibilities between the different types of equipment that they are offered (respirators, glasses, hearing protectors and helmets) prevent them from using any of the equipment consistently. The non-exposed group, Group B (n=54) was comprised of workers in the administrative sector, matched by age, socio-economic group and educational level.

The workers were subdivided according to their past or current noise exposure. Subgroup A1 applied the insecticides through spray

Table 1. Distribution of exposed workers by insecticide class.

Pesticides	Class	Number	% Exposed
Malathion	Organophosphates	81	82.7
K-Otrin / Deltamethrin	Pyrethroid	72	73.5
Tmefós /Abate	Organophosphates	65	66.3
Fenitrothion / Sumithion	Organophosphates	63	64.3
Ripcord / Cipermethrin	Pyrethroid	45	45.9
DDT	Chlorinated ethane derivative	24	24.5
Benzene Hexachloride	Hexachlorocyclohexane	07	7.1

***** Individuals were exposed to more than one agent.

applicators that were not noisy. Subgroup A2 used motorized pumps, which weighed approximately 20 pounds when full, that produced noise levels above 90 dB (A); see exposure characteristics of the study groups in Table 2. Only 35.7% of the studied population were smokers and the majority (84.4%) did not frequently use alcoholic beverages.

Interview

A semi-structured questionnaire gathered data on: medical history; occupational history including full job description; history of occupational and non-occupational exposure to noise and chemicals; and current and previous hearing disorders as well as relevant symptoms. The results of audiological testing were added to each questionnaire after each worker was interviewed.

Testing Procedures

To assess the worker's hearing status, otoscopy, pure-tone audiometry and central auditory tests were performed by audiologists who did not have any knowledge of the subjects' exposure history. Workers were excluded from the study in case of obstructed external ear canal, perforated tympanic membrane, previously diagnosed non-occupational hearing loss, (conductive, mixed and sensorioneural), frequent use of ototoxic medications and any diagnosed degenerative diseases. In addition, subjects were excluded from participation in the non-exposed group (A) if they reported any kind of exposure to chemical substances, or to amplified musical instruments.

Pitch Pattern Sequence – PPS and Duration Pattern Sequence – DPS tests

The subjects were tested in a sound-insulated chamber, which met the requirements of ANSI S 3.1.1991 for audiometric testing environments. The audiometer used was a GSI model 1761 with TDH-59p headphones, calibrated following the ANSI S3.6, 1989 standard. Pitch Pattern Sequence (PPS) behavioural tests and duration pattern sequence (DPS), were selected because they offer information on the central auditory functions, can be easily administered in the time allowed and did not involve verbal stimuli, as speech tests would have been contaminated by different regional accents and educational level. For the PPS testing, 30 sequences of 3

Table 2. Distribution of the study population by their insecticide exposure, and by the noise exposure history (N=152).

Number of workers	Exposure conditions
	Group A - Insecticide Exposed Group
A_1 (n=41)	No previous or current exposure to excessive noise, neither at work nor off-work
A_2 (n=51)	Previous or current exposure to excessive noise, either at work or off-work
	Group B - Non-exposed Group
B_1 (n=36)	No previous or current exposure to excessive noise, neither at work nor off-work
B_2 (n=18)	Previous or current exposure to excessive noise, either at work or off-work

consecutive pure-tones of either 880 Hz or 1430 Hz, were presented at 50 dBSL, through a compact disk recording, as proposed by Noffsinger et al. (1994). The duration of each pure-tones was 150 ms, and there was an interval of 200 ms between each tone presentation. Subjects were asked to identify the pitch sequence heard (i.e. low, low, high). The test result is expressed in percentage of sequences correctly identified, and reflects the subject's perception of changes in pitch. In a study conducted with Brazilian adults with normal hearing, the author suggested that percentages of correctly identified sequences greater than 76% be considered in the normal range (Corazza, 1998).

The DPS test consisted of presenting a sequence of three consecutive tones of 1000Hz, with either a long duration, of 500 ms, or a short duration, of 250 ms, with a 300 ms interval between stimuli. Subjects were asked to identify the sequence heard (i.e. long, long, short). The test result is expressed in percentage of sequences correctly identified, and reflects the subject's perception of changes in stimulus duration. In a study reported previously, conducted with Brazilian adults with normal hearing, the author suggested that percentages of correctly identified sequences greater than 83% be considered in the normal range (Corazza, 1998).

Statistical Analysis

The statistic analyses were performed using the SAS software (Statistical Analysis System) version 6.12. Chi-square tests were used to compare groups and to determine if audiological test results were associated with duration of exposure.

Results

Few workers (34,7%) wore personal protection to limit exposure to insecticides, despite a high prevalence of health symptoms. The main health complaints in the exposed group were irritation of the eyes (54%), headaches (44.9%), dizziness (35.7%), nausea (16.3%), and torpor (16.3%). These symptoms, common in cases of neurotoxic intoxication, have been previously associated with exposures to organophosphates and pyrethroid substances (Augusto, 1995; WHO, 1990; Wesseling et al, 1997).

Pitch Pattern Sequence – PPS and Duration Pattern Sequence – DPS tests

Fifty-six percent (56.1%) of the exposed group (A), had altered results in the central tests performed (PPS and / or DPS). Only 4 subjects (7.4%) from the non-exposed group (B) had altered central test results, all of them in the DPS test (Table 3).

Statistically significant differences were observed among the A1 and B1 subgroups (p=0.001), among the A2 and B2 subgroups (p=0.001) and A2 and B1 (p=0.001) for the results of central tests PPS and DPS (see Table 4). This indicates that noise exposure did not play a role in the results of these central auditory tests. The relative risk for hearing dysfunction at the central level was 6.8 for the group exposed to insecticides, when compared to the group not exposed to insecticides or noise. It was 6.5 for the subjects with exposures to insecticides and noise, when compared to subjects not exposed to noise; and 9.8 for subjects with exposures to insecticides and noise, when compared to subjects exposed to noise only.

The results of the central test PPS and DPS, by subgroup, by ear and duration of exposure to insecticides is illustrated in Figure 1. It can be seen that for the subgroups, A1 and A2, there is no difference between the exposure times needed for the onset of the central auditory dysfunction.

To further explore the impact of the duration of exposure to pesticides on the auditory test results, we divided the exposed subjects from Group A, by their duration of exposure in two categories: those with more, or with less, than 6 years of exposure (Table 5). In Table 5 an increase in the occurrence of altered results can be noted for all the tests administered, as the duration of exposure increases. The difference was shown to be statistically significant for the results of the central auditory tests ($x^2 = 8.461$, $p < 0.004$,) and relative risk of 1.83.

Table 3. Distribution of the study population by the results in the tests Pitch Pattern Sequence (PPS) and Duration Pattern Sequence (DPS)

CENTRAL AUDITORY TEST	Results	GROUPS A		GROUPS B		Total	
		N	**%**	**N**	**%**	**N**	**%**
PPS and/or DPS	Altered	55	56.1	4	7.4	59	38.8
	Normal	43	43.9	50	92.6	93	61.2
TOTAL		**98**	**100.0**	**54**	**100.0**	**152**	**100.0**

Chi–square test, Yates correction: χ^2 = 32.769 $p < 0.001$ RR = 7.58 (2.90 <RR< 19.77)

Discussion

Organophosphate and pyrethroid insecticide use was found to be associated with the occurrence of central auditory disorders, independently of noise exposure. Noise and insecticide exposure might interact at the cochlear level, but due to the lack of historical exposure data, the kind of interaction that took place between noise and insecticide exposure was not examined in the present investigation. Interaction between noise and insecticides at a retrocochlear level can be ruled out in the studied groups, as noise did not seem to affect the results of the central auditory tests in any of the analysis performed.

Little has been published on the time necessary for occupational chemicals to affect the auditory system. Certainly, this issue is dependent on exposure parameters. Epidemiological studies on solvents have reported different exposure times as necessary to induce an effect to audition (Jacobsen et al, 1993; Morata et al, 1993, 1997). By stratifying this population into two subgroups, using duration of exposure of up to six years or greater, the difference observed between subgroups was statistically significant for the central auditory tests suggesting a positive correlation between the duration of exposure to these neurotoxic insecticides and the observed dysfunctions. It was also observed that central auditory dysfunction could be detected after 4 years of exposure, and that, the longer the duration of exposure, the greater the probability of central auditory alterations.

The evaluation of the central auditory system, through standardized behavioural tests, especially in individuals exposed to neurotoxic substances, is valuable in detecting auditory processing disorders (Dublin, 1976; Musiek et al., 1984). From the clinical and research point of view, the use of tests with non-verbal material can be advantageous, since the results can be directly related to behavioural studies in animals

Table 4. Results of the Pitch Pattern Sequence (PPS) and Duration Pattern Sequence (DPS) and Relative Risk of central auditory disorders, by exposure group.

Central Auditory Test	Results	Subgroup A_1		Subgroup A_2		Subgroup B_1		Subgroup B_2	
		N	%	N	%	N	%	N	%
PPS and/or DPS	Altered	27	57.4	28	54.9	3	8.3	1	5.6
	Normal	20	42.6	23	45.1	33	91.7	17	94.4
TOTAL		47	100.0	51	100.0	36	100.0	18	100.0

A_1 vs. A_2 = χ^2 = 0.020 and $p = 0.960$ RR= 0.88 (0.57 < RR < 1.35)
A_1 vs. B_1 = χ^2 = 19.230 and $p < 0.001$ RR= 6.89 (2.27 < RR < 20.93)
A_2 vs. B_2 = χ^2 = 11.239 and $p < 0.001$ RR= 9.88 (1.45 < RR < 64.47)
A_2 vs. B_1 = χ^2 = 17.975 and $p < 0.001$ RR= 6.59 (2.17 < RR < 20.02)
B_1 vs. B_2 = Fisher's exact test $p = 1.000$ RR= 0.67 (0.70 < RR < 5.96)

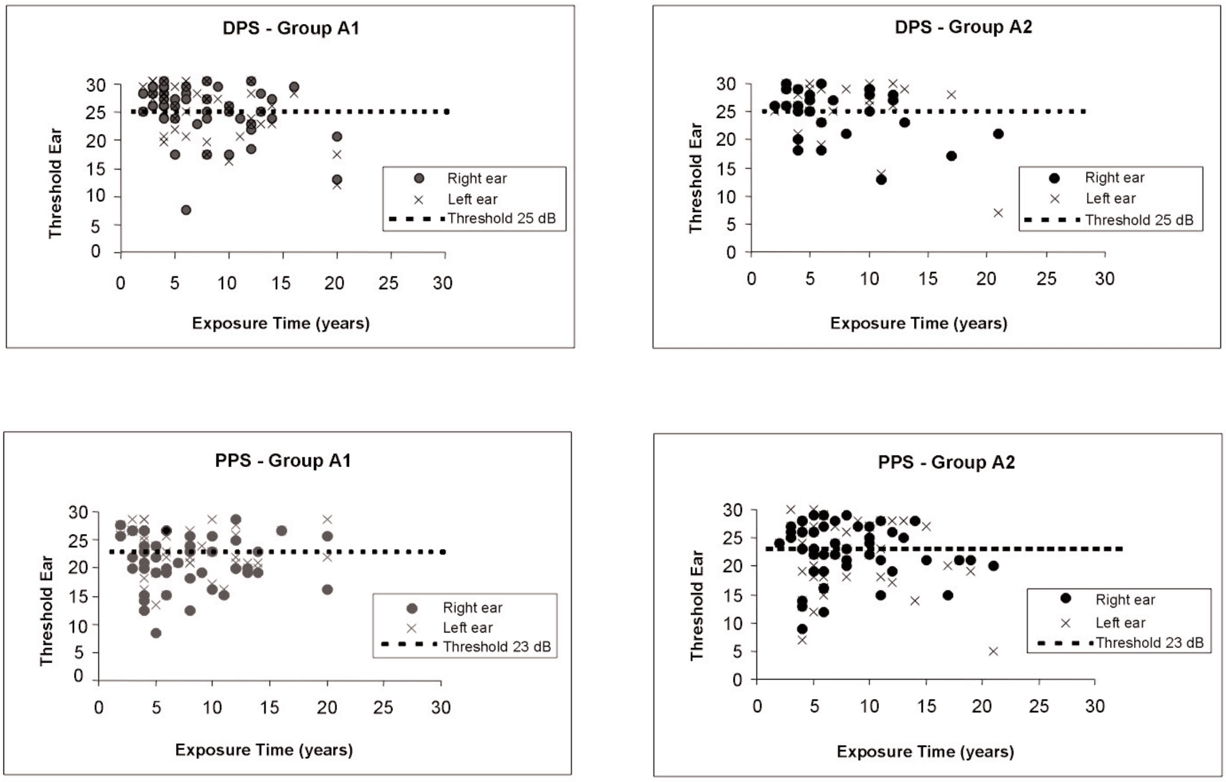

Figure 1. Distribution of the central tests PPS and PDS results of the groups exposed to insecticides, by their noise exposure history (non-exposed to noise A1, n =47; and exposed to noise, A2, n = 51).

(Neff et al, 1999). Moreover, linguistic knowledge, educational level and regional differences will not influence test performance (Keith, 1989). Central auditory tests involving verbal responses require a number of neural functions such as attention, intensity or pitch discrimination, recognition, immediate memory, and memory for sounds in sequence. In order that the sequential auditory stimuli be correctly identified, it is necessary that both the hemispheres interact adequately, independently of the side of stimulation (Pinheiro et al., 1985; Musiek et al., 1980).

The alterations observed in the present study offer clues to the type of the damage incurred in the individuals exposed to insecticides. However, despite the high sensitivity (PPS=83%, DPS=86%) and specificity (PPS=82%, DPS=92%) of the selected tests, they would not be able to detect all possible cortical damage if it has occurred. The standard duration and frequency tests seem to involve different processes of the highest auditory functions (Musiek et al., 1994, Musiek, 1994). This justifies the application of the two procedures in this type of evaluation, since they

Table 5. Results of the Pitch Pattern Sequence (PPS) and Duration Pattern Sequence (DPS) tests for the group exposed to insecticides (n=98), by duration of exposure.

		Duration of exposure					
Tests	Results	Up to 6 years		More than 6 years		Total	
		N	%	N	%	N	%
PPS and/or DPS	Altered	16	38.1	39	69.6	55	56.1
	Normal	26	61.9	17	30.4	43	43.9
	Total	42	100.0	56	100.0	98	100.0

Duration exposure: PPS and/or DPS: $p < 0.004$ $\chi^2 = 8.461$ RR = 1.83 (1.20<RR<2.79) seem to be complementary (Musiek et al, 1987). The results of the frequency patterns (PPS) and of duration patterns (DPS) tests, which evaluate the functional features of several structures of the central auditory system (Musiek et al, 1987, 1990) suggest central auditory dysfunction as a consequence of the neurotoxic exposure, as well as for other exposures, as suggested by Musiek et al, 1987; Ödkvist et al, 1982; and Pinheiro, 1976. Moreover, it is conceivable that the cortical area that supports language ability in the temporal-parietal region of the left hemisphere may be affected, as has been previously suggested in the literature (Efrom, 1963; Musiek et al., 1980, 1990; Phillips, 1993). However, these tests do not give information on which hemisphere was affected. Thus, the issue of site of lesion remains open for future studies.

Conclusions

Chronic exposure to pyrethroid and organophosphate insecticides seem to affect the central auditory functions. Exposure to noise did not modify the prevalence of alterations determined by the exposure to insecticides. Data from this study and other recent publications indicate that chemical exposures should be monitored and controlled as a part of the efforts to prevent hearing loss and other auditory dysfunctions. The inclusion of workers exposed to neurotoxic chemicals in hearing loss prevention programs, regardless of their noise exposure, is recommended.

The results of the central tests (PPS and DPS) were sensitive to the dysfunction of the central auditory pathways. Therefore the inclusion of central auditory tests in the audiological evaluation is justified for those exposed to chemical substances considered neurotoxic, such as pyrethroid and organophosphate insecticides. Traditional pure-tone and speech audiometry tests are not adequate for the detection of these alterations. Evidence from the present study shows that the evaluation of the neurotoxic effects of insecticides on the auditory system requires tests that assess the central part of the auditory system, in order to complement the information from pure-tone audiometry, the test routinely used in occupational surveillance.

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