CENTRAL AUDITORY PROCESSING EFFECTS INDUCED BY SOLVENT EXPOSURE

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Abstract
Objectives: Various studies have demonstrated that organic solvent exposure may induce auditory damage. Studies conducted in workers occupationally exposed to solvents suggest, on the one hand, poorer hearing thresholds than in matched non-exposed workers, and on the other hand, central auditory damage due to solvent exposure. Taking into account the potential auditory damage induced by solvent exposure due to the neurotoxic properties of such substances, the present research aimed at studying the possible auditory processing disorder (APD), and possible hearing difficulties in daily life listening situations that solvent-exposed workers may acquire.

Materials and Methods: Fifty workers exposed to a mixture of organic solvents (xylene, toluene, methyl ethyl ketone) and 50 non-exposed workers matched by age, gender and education were assessed. Only subjects with no history of ear infections, high blood pressure, kidney failure, metabolic and neurological diseases, or alcoholism were selected. The subjects had either normal hearing or sensorineural hearing loss, and normal tympanometric results. Hearing-in-noise (HINT), dichotic digit (DD), filtered speech (FS), pitch pattern sequence (PPS), and random gap detection (RGD) tests were carried out in the exposed and non-exposed groups. A self-report inventory of each subject’s performance in daily life listening situations, the Amsterdam Inventory for Auditory Disability and Handicap, was also administered.

Results: Significant threshold differences between exposed and non-exposed workers were found at some of the hearing test frequencies, for both ears. However, exposed workers still presented normal hearing thresholds as a group (equal or better than 20 dB HL). Also, for the HINT, DD, PPS, FS and RGD tests, non-exposed workers obtained better results than exposed workers. Finally, solvent-exposed workers reported significantly more hearing complaints in daily life listening situations than non-exposed workers.

Conclusions: It is concluded that subjects exposed to solvents may acquire an APD and thus the sole use of pure-tone audiometry is insufficient to assess hearing in solvent-exposed populations.

Key words: Auditory processing disorder, Dichotic tests, Filtered speech, Solvent exposure, Speech discrimination in noise

INTRODUCTION

It has been suggested that the effects of at least one type of organic solvent (toluene) on hearing may be dependent on a combination of both the oto- and neuro-toxicity [1]. The ototoxicity induced by solvent exposure has been demonstrated through animal and human studies [2–5]. Many of the human studies indicated solvent-related impairment of the central auditory nervous system in workers exposed to a mixture of solvents [6–11]. In a group of 11 solvent-exposed workers, Odkvist et al. [12] found that six of them presented abnormal results for interrupted speech tests and long latency evoked potentials. An important point to consider is that all of the workers had hearing thresholds and conventional speech discrimination scores as expected for their age and previous noise exposure. Also, all of the subjects were already presenting solvent-related neuropsychological symptoms when the audiological assessment was carried out.

In another study [10] by the same research team, that concerned a group of workers exposed to solvents and jet fuel,
a high percentage of abnormal results was found for discrimination of interrupted speech and long latency evoked potentials. In this study, 16 out of 31 subjects had a confirmed diagnosis of the psychoorganic syndrome and the rest of the subjects presented neuropsychiatric symptoms. Similarly, Laukli & Hansen [7] reported abnormal results for filtered speech and long latency evoked potentials in workers exposed to solvent mixture, and Varney et al. [11] abnormal results for a dichotic listening test in solvent-exposed workers. Moen et al. [8] examined the P300 response of the auditory event-related brain potential in a group of workers exposed to low levels of organic solvents in a paint factory and in a non-exposed control group. The results showed that the latency of the P300 response was prolonged among the exposed workers compared to the control group, when tested before the summer vacation. Also, for the exposed group, the latency of the P300 response was significantly longer before than after the summer vacation. These findings suggest both chronic and acute adverse effects of solvent exposure on the central auditory system.

Similar results were obtained by Steinhauer et al. [13]. The researchers found a prolongation of the P300 latency in painters acutely exposed to solvents, and an enhanced N250 amplitude negativity in painters even during a period of four days free of solvent exposure. The results were statistically significant in comparison to non-exposed control group. Taking into consideration the findings of these two studies, long latency evoked potentials may be useful to identify acute auditory damage induced by solvents and when monitoring solvent-induced auditory damage in solvent-exposed populations. Table 1 summarizes the research on solvent-induced effects on the central auditory system.

Considering the neurotoxicity due to solvent exposure, auditory processing (AP) may be impaired in exposed workers. This may adversely affect the workers’ performance in everyday listening situations. AP tests, such as the random gap detection test [17], have been suggested for inclusion into a comprehensive audiological test battery to be used for assessment of solvent-induced hearing loss [18]. Nevertheless, little work has been done to explore the possible AP disorders or the impact on speech discrimination in noise abilities as a result of solvent exposure. Fuente et al. [6], in their study on a group of 10 solvent-exposed workers who were administered a set of AP tests, found significant differences between solvent-exposed and non-exposed workers. The authors suggested that the central auditory processing disorder may be related to solvent exposure. If so, solvent-exposed workers may acquire difficulties in localizing sounds and discriminating speech, especially in the presence of background noise. The aim of the present study was to investigate the possible AP disorders and hearing difficulties in daily life listening situations in a group of workers exposed to solvents.

**METHOD**

**Subject selection**

**Study group**

Participants were recruited from workers at a paint-making factory in Chile. Workers’ personal data such as age and health history as well as airborne solvent concentration and noise level at the different workposts were analyzed. Subjects between 18 and 55 years of age, with a minimum of two years of solvent exposure, were considered for pre-selection. The solvents involved and their mean air concentrations were as follows: toluene: 25.72 mg/m$^3$, xylene: 36.82 mg/m$^3$, and methyl ethyl ketone 17.45 mg/m$^3$. All of these concentrations were below the threshold limit value (TLV) for 8-h work shift in Chile i.e. 300 mg/m$^3$ for toluene, 347 mg/m$^3$ for xylene, and 472 mg/m$^3$ for methyl ethyl ketone. Considering these TLVs, the hygienic effect of solvent exposure was 0.221. Data on noise levels were obtained for the same workposts where solvent concentrations were measured. Only the subjects exposed to noise levels below 85 dBA were considered for participation in the study. Informed consent was obtained from workers prior to commencement of auditory assessment. A questionnaire was administered among the workers who agreed to participate (63 subjects, interviewed) to exclude the persons with confounders for solvent-induced auditory damage. The exclusion criteria included history of ear disease, treatment with ototoxic drugs, arterial
### Table 1. Summary of research on solvent-induced effects on the central auditory system

<table>
<thead>
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<th>Solvent</th>
<th>Procedure</th>
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<tr>
<td>Toluene</td>
<td>A.B.R.</td>
<td>Statistically significant abnormal ABR response among toluene-exposed subjects compared to same age unexposed controls</td>
<td>Abbate et al. [14]</td>
</tr>
<tr>
<td>Toluene</td>
<td>P300</td>
<td>Prolonged latencies and lower amplitudes in the P300 response in toluene-exposed workers compared to controls</td>
<td>Vrca et al. [15]</td>
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<tr>
<td>Carbon disulphide</td>
<td>A.B.R.</td>
<td>Involvement of the auditory ascending tract in the brainstem</td>
<td>Hirata et al. [16]</td>
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<tr>
<td>Industrial solvents</td>
<td>Pure-tone audiometry, speech recognition threshold, maximum speech discrimination score, discrimination of interrupted speech, stapedial reflex thresholds, phase audiometry, A.B.R., and late latency auditory evoked potentials.</td>
<td>The most consistent abnormalities were seen in interrupted speech discrimination and late latency evoked potentials</td>
<td>Odkvist et al. [10]</td>
</tr>
<tr>
<td>Industrial solvents</td>
<td>Pure-tone audiometry, speech recognition threshold, distorted speech discrimination, and late latency auditory evoked potentials.</td>
<td>Scores in distorted speech test and cortical response audiometry latencies significantly lower in the solvent-exposed group than in the control group</td>
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<tr>
<td>Mixture of organic solvents</td>
<td>Dichotic listening test</td>
<td>Among solvent-exposed workers, dichotic listening was frequently impaired in relation to the norms of the test and in comparison to the results for the control group</td>
<td>Varney et al. [11]</td>
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<tr>
<td>Solvent mixture</td>
<td>Long latency evoked potentials, filtered speech</td>
<td>Abnormal results for filtered speech and long latency evoked potentials</td>
<td>Laukli &amp; Hansen [7]</td>
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<tr>
<td>Mixture of aliphatic and/or aromatic solvents</td>
<td>Pure-tone audiometry, spondee discrimination thresholds, speech discrimination, speech discrimination of interrupted speech, stapedial reflex decay, phase audiometry, A.B.R., late latency auditory evoked potentials.</td>
<td>Decreased discrimination scores in interrupted speech</td>
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<td>Solvent mixture</td>
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<td>Prolonged P300 latency among exposed workers compared to non-exposed workers before summer vacation</td>
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<td></td>
<td></td>
<td>Among exposed workers, P300 latency was significantly longer before than after summer vacation</td>
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hypertension, diabetes, head injury, metabolic disease, kidney dysfunction, alcohol abuse, recreational exposure to noise, head injury, and acoustic trauma. Six subjects were excluded because they presented with one or more of these factors. Next, to select the participants, otoscopy, bilateral air and bone conduction pure-tone audiometry (250–8000 Hz) and immittance audiometry were carried out. For inclusion in the study group, the subjects could not have visible pathologic alterations of the ear canal, and had to present audiometric patterns indicating either normal hearing or sensorineural hearing loss, and Jerger type A results in tympanometry [19]. Four subjects were excluded due to the presence of obstructive cerumen in the ear canal. The remaining 53 subjects were referred for pure-tone audiometry and immittance audiometry. Three subjects were excluded due to the absence of type A tympanograms. Finally, 50 male subjects, mean age 36 years (SD = 6.8), with a mean duration of solvent exposure of 13.2 years (SD = 7.7) were selected as the study group.

Control group
The control group was selected among workers non-exposed to chemicals or to noise above 85 dBA. The controls were recruited from different workplaces with no solvent exposure that were located in the same geographical area as the paint-making factory. They were matched by gender, age (plus/minus 3 years) and education. The educational level was categorized as: secondary education incomplete, secondary education completed, and university studies. The exclusion criteria were the same as for the study group (see above). A total of 72 subjects answered the questionnaire. Nine persons were excluded due to a history of ear disease and one due to arterial hypertension. Also, otoscopy, pure-tone and immittance audiometry were conducted for further selection. The controls had to have no obstructive cerumen in both ear canals, and either normal audiometric patterns or sensorineural hearing loss, and bilateral type A tympanometric results [19]. Seven persons were excluded due to the presence of obstructive cerumen and five due to tympanometric results other than type A. All the persons selected as the control group were men, with the mean age of 35.4 years (SD = 4.6).

Procedure
Subject selection and evaluation procedures were conducted in a double-walled, sound-treated booth. For pure-tone audiometry, an Interacoustics AC33 clinical audiometer was used with TDH-39P headphones, and immittance audiometry was conducted with a Madsen AZ7 middle-ear analyzer. The AP assessment employed a compact disc player (LG 7311N) connected to the audiometer. A 1000 Hz calibration tone recorded in each compact disc was used to determine output intensity. This procedure was carried out each time a compact disc was played. To assess speech discrimination, the Hearing-in-Noise Test (HINT) [20] with Latin American Spanish sentence module was used.

The following instruments were applied both in the study and control group examinations:

Random gap detection (RGD) to assess temporal resolution. At 50 dB HL, stimuli comprising two tones that differed in their onset time were presented binaurally. Subjects were asked to state whether they could hear one or two tones at each presentation. Thresholds for gap detection for each frequency tested (500, 1000, 2000, and 4000 Hz) and for click stimuli were calculated.

Pitch pattern sequence (PPS) to assess temporal ordering. A set of 50 sequences of three-tone bursts differing in their pitch (1430 Hz and 880 Hz) were presented monaurally to each ear at 50 dB SL. Subjects were asked to verbalize the pitch (“low” or “high”) of each stimulus in the sequence. The percentage of correct answers was calculated for each ear.

Dichotic digit test (DD) to assess dichotic stimulation. Twenty sets of two pairs of digits were presented dichotically at 50 dB SL. Subjects were asked to repeat each set of four numbers. The repetition task involved free recall. Total percentage score was obtained by counting the correctly repeated numbers.

Filtered Speech (FS) to assess speech discrimination for degraded verbal material. Twenty-five low-pass filtered monosyllabic words were presented monaurally to each ear.
RESULTS

Descriptive statistics
Figures 1 and 2 show distribution of hearing thresholds for each ear in both the groups. Score distributions for both groups are shown in Figure 3 for HINT subtests, Figure 4 for DD, Figure 5 for FS and PPS, and Figure 6 for RGD.

Differences between groups
Pure-tone audiometry: The mean pure-tone thresholds (250–8000 Hz) for both groups were better than 20 dB HL. Between-group differences in hearing thresholds were compared using Mann-Whitney test. Significant differences were noted for hearing thresholds at 1 kHz, 2 kHz, 3 kHz, and 6 kHz for the right ear (p < 0.05), and at 1 kHz, 2 kHz and 3 kHz for the left ear (p < 0.01). Figures 1 and 2 summarize the findings for the right and left ear, respectively.

HINT test: Mann-Whitney test was used for each condition measured. Statistically significant differences at 50 dB SL. Subjects were asked to repeat each word. The percentage of correct answers was calculated for each ear. Hearing-in-Noise Test (HINT) to assess speech discrimination in quiet and in noise. To calculate the speech reception threshold (SRT), a set of sentences was presented binaurally (HINT SRT) in quiet. Subjects were asked to repeat each sentence heard. Then, to assess speech discrimination in noise, the signal-to-noise ratios (SNRs) for speech discrimination were calculated for different noise conditions. HINT uses three noise conditions: noise and sentences delivered from the same location (in front of the subject), that is, no spatial separation between the noise and the sentences — HINT 1; noise delivered to the right ear (90° azimuth) and sentences delivered to the left ear (270° azimuth) — HINT 2; noise delivered to the left ear (270° azimuth); and sentences delivered to the right ear (90° azimuth) — HINT 3. Finally, a composite score was calculated by combining the results of HINT 1, 2, and 3 — HINT composite.

Amsterdam Inventory for Auditory Disability and Handicap (AIADH) to assess the subjects’ self perception of their own listening performance in daily activities. The questionnaire, developed by Kramer et al. [21], was adapted into Spanish by Fuente et al. [22]. The inventory consists of 30 questions regarding listening activities such as sound discrimination, sound localization, speech discrimination in quiet and noise, and sound detection. A copy of the questionnaire and a pen were given to each individual subject. The completed questionnaire was immediately reviewed for possible blank questions and the subject returning the questionnaire was asked to answer them.

Data analysis
Mann-Whitney test was used to explore differences between groups for each outcome: pure-tone thresholds for the right ear, pure-tone thresholds for the left ear, DD right and left ears scores combined, FS right and left ears scores combined, PPS right and left ears scores combined, scores for RGD, and scores for the AIADA. Also, Wilcoxon signed rank test was applied for differences in DD scores between right and left ears for each group of subjects.

*Significant differences between groups. Mann-Whitney U test (p < 0.05).
between the control and study groups were found for HINT SRT, HINT 1, HINT 2, HINT 3 and HINT composite (Z = -4.16, p < 0.01; Z = -1.98, p < 0.05; Z = -3.43, p < 0.01; Z = -2.05 p < 0.05; Z = -3.53, p < 0.01, respectively). The controls showed better results (dB and SNRs) than solvent-exposed workers.

DD, FS, and PPS tests: When Mann-Whitney test was used, statistically significant between-group differences in test scores (right and left ear scores combined) were found for DD (Z = -2.15, p < 0.05), FS (Z = -4.60, p < 0.01), and PPS (Z = -3.50, p < 0.01). The group of solvent-exposed workers had lower scores than the non-exposed workers. Also, for the DD in solvent-exposed group, significant differences were found between right and left ear scores. Right ear scores were significantly better than left ear scores (Wilcoxon signed rank test: Z = -3.31, p < 0.01).

RGD test at 1000 Hz, 2000 Hz, and 4000 Hz: Statistically significant between-group differences (Mann-Whitney test) in the gap detection thresholds were noted (Z = -3.16, p < 0.01; Z = -2.80, p < 0.01; Z = -4.52, p < 0.01, respectively). The control group obtained lower (better) gap detection thresholds than the group of workers exposed to solvents.

Fig. 2. Hearing thresholds for the left ear in the study group (n = 50) and control group (n = 50). Thresholds are in dB HL. Boxes represent scores for 50% of cases. The line crossing the box represents the median value. The whiskers protruding from the box go out to the lowest and highest score values. Outliers (circles) represent values between 1.5 box-lengths and 3 box-lengths from the edge of the box. Extremes (asterisks) represent values of more than 3 box-lengths from the edge of the box.

**Significant differences between groups. Mann-Whitney U test (p < 0.01).

Fig. 3. Boxplots of the scores for the study group (n = 50) and control group (n = 50) in HINT subtests. Scores are in dB signal-to-noise ratio. HINT 1: noise and sentences delivered at 0° azimuth; HINT 2: noise delivered to the right ear (90° azimuth) and sentences delivered to the left ear (270° azimuth); HINT 3: noise delivered to the left ear (270° azimuth) and sentences delivered to the right ear (90° azimuth); HINT composite: calculated by combining scores for the three HINT conditions. The boxes represent scores for 50% of cases. The line crossing the box represents the median value. The whiskers protruding from the box go out to the lowest and highest score values. Outliers (circles) represent values between 1.5 box-lengths and 3 box-lengths from the edge of the box.

Z = -2.80, p < 0.01; Z = -4.52, p < 0.01, respectively). The control group obtained lower (better) gap detection thresholds than the group of workers exposed to solvents.

AIADH: Significant differences between groups were found for questions number two (Z = -2.22, p < 0.05), seven (Z = -1.98, p < 0.05), eight (Z = -2.38, p < 0.05), nine (Z = -2.03, p < 0.05), nineteen (Z = -2.09, p < 0.05), twenty (Z = -2.22, p < 0.05), twenty-one (Z = -2.05, p < 0.05), twenty-six (Z = -3.04, p < 0.01), and for the total score on all questionnaire items (Z = -2.11, p < 0.05).
Exposed workers had lower scores than non-exposed workers. This translates as more hearing difficulties reported by the workers for a given listening activity.

DISCUSSION AND CONCLUSION

Both the solvent-exposed and non-exposed subjects as a group presented mean normal hearing thresholds. However, significant between-group differences were observed for some of the hearing thresholds. Solvent-exposed workers had worse hearing thresholds than non-exposed subjects. This finding is consistent with other studies reporting on adverse effect of solvents on the hearing threshold [4,5]. Also, the SRT (HINT SRT) for both groups showed significant differences. Non-exposed workers obtained a better SRT than the solvent-exposed group. However, it is expected that the solvent-exposed group who had higher hearing thresholds than non-exposed workers, should also have an elevated SRT. Significant differences between groups were also observed for the other HINT subtests (speech discrimination in noise). Solvent-exposed workers consistently obtained higher SNRs than the non-exposed controls for HINT 1, HINT 2, and HINT 3. This finding suggests that the study group may have difficulties in understanding speech in the presence of background noise. This group also had a poorer performance than non-exposed workers on the FS, PPS, DD and RGD tests. Moreover, solvent-exposed subjects showed significant differences between right and left ear scores for DD. This would indicate a right ear advantage. A slight right ear advantage for dichotic digits has been observed in healthy persons.
The results of the present research are consistent with previous studies reporting central auditory dysfunction in workers exposed to solvents \cite{7,10,11}. Two of these studies have used an audiological test battery including electrophysiological measurements and only one behavioural AP test: either filtered speech or discrimination of interrupted speech \cite{7,10}. The third study employed a dichotic listening task in audiological assessment \cite{11}. The results of this test were affected in workers exposed to solvents, as were those of the dichotic digit test in the present study. The present research included different behavioural AP tests as recommended by the American Speech-Language-Hearing Association (ASHA) \cite{25}. Thus, the AP assessment conducted in this study has been a comprehensive one and different aspects of AP have been investigated.

Considering the results of the present research and the evidence from the studies discussed in the Introduction, the sole use of pure-tone audiometry may be insufficient to assess hearing in solvent-exposed populations. This technique is valuable only for assessing basic sound detection capacity among solvent-exposed subjects. The use of AP and speech discrimination tests such as HINT is a broader approach to elucidate the auditory damage induced by solvent exposure. Taking into account the possible AP disorder and listening difficulties that solvent-exposed workers may acquire, AP assessment in conjunction with self-reports on hearing performance should be considered as a part of the audiological test battery when assessing this population. Further research is needed to better characterize the solvent-induced damage to the central auditory pathways and to determine the optimal audiological test battery for use with this group of patients.

**REFERENCES**