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by Moller C, Odkvist L, Larsby B, Tham R, Ledin T, Bergholtz L

Affiliation: Department of Otolaryngology, Faculty of Health Sciences, University Hospital, Linkoping, Sweden.

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Otoneurological findings in workers exposed to styrene

by Claes Möller, MD, Lars Ödkvist, MD, Birgitta Larsby, PhD, Richard Tham, MD, Torbjörn Ledin, MD, Lars Bergholtz, MD[1]

MÖLLER C, ÖDKVIST L, LARSBY B, THAM R, LEDIN T, BERGHOLTZ L. Otoneurological findings in workers exposed to styrene. *Scand J Work Environ Health* 1990;16:189—94. An otoneurological test battery was administered to 18 workers with long-term exposure (6—15 years) to styrene at levels well below the current Swedish limit (110 mg/m³). The results were compared with those of a reference group. Disturbances were found in the central auditory pathways of seven workers. Tests reflecting central processing of impulses from different sensory equilibrium organs were abnormal for 16 workers. The most relevant tests seemed to be static posturography and the rotatory visual suppression test. In the posturography the styrene group had a significantly larger sway area than the reference group. In the visual suppression test, the styrene workers displayed a significantly poorer ability to suppress vestibular nystagmus than the reference group. It was concluded that styrene exposure in industrial environments at moderate or low levels causes central nervous system disturbances which are not always diagnosable with psychometric tests but can be apparent in special otoneurological tests.

Key terms: audiology, electronystagmography, posturography, vestibulomotor-oculomotor reflex, visual suppression.

There are several reports indicating that the central nervous system (CNS) components of the equilibrium and auditory systems are sensitive to exposure to solvents (1—4). It has been suggested that examinations of these systems may be of diagnostic use in studies of workers exposed to solvents in industrial environments. The purpose of this investigation was to test the validity of this hypothesis.

Subjects and methods

A possibility to investigate workers exposed to styrene was offered in connection with the closure of a small plastics boat plant. This group of workers seemed ideal for different reasons. They had all worked for a long time in the same factory with exposure to only one solvent. The exposure level was rather well known. At the time of the investigation the acute effect of the solvent could be neglected, as none of the workers were exposed to solvents any longer.

Definition of the groups

Eighteen men, aged 28—61 (mean 40) years were studied. All had been employed in the same plastics boat plant with exposure to styrene for 6—15 (mean 10.8) years. Measurement of airborne styrene in the work areas had been performed annually. High exposure consisted of styrene concentrations of 50—100 mg/m³, and low exposure was levels below 25 mg/m³ (current Swedish occupational exposure limit 110 mg/m³). Peak exposures above 300 mg/m³ had been exceptional. For further details of the exposure see reference 5.

Along with the otoneurological examination, a neuropsychiatric investigation was performed (5). With the aid of a questionnaire it was found that several of the workers had neurasthenic symptoms such as abnormal fatigue, headache, and memory losses. A psychometric examination displayed borderline results in three cases, but eventually none of them were diagnosed as having a psychoorganic syndrome.

All of the subjects used alcohol, but none of the use was considered abusive (<37 cc/week). Thirteen of the subjects smoked. None had a history of metabolic, neurological, or psychiatric diseases.

The reference group (A) used for the evaluation of the results of the smooth-pursuit eye movement test, the saccade test, and the visual suppression test (see the section on the otoneurological test battery) comprised 18 industrial workers free of exposure to styrene or other solvents. They were selected to cover the same age range and the same smoking and alcohol habits as the exposed workers [age 30—54 (mean 39) years]. Eleven referents smoked, and all 18 used alcohol moderately (< 37 cc/week).

The other reference group (B) was used for assessing the results of the static posturography. This group has been presented in a previous paper (6). It comprised 52 men aged 35—64 (mean 48) years, who worked in the construction industry and were unexposed to industrial solvents.

[1] Department of Otolaryngology, Faculty of Health Sciences, University Hospital, Linköping, Sweden.

Reprint requests to: Dr C Möller, Department of Otolaryngology, University Hospital, S-58 185 Linköping, Sweden.

Otoneurological test battery

There are several quantitative noninvasive methods for examining the auditory and equilibrium systems. These tests reflect functions of different parts of the systems and are good indicators of the locations of lesions. Lesions of the peripheral sensory auditory organ, the cochlea, can be detected with pure-tone audiometry. The central pathways of the auditory system can be investigated by different discrimination tests (eg, tests for maximum speech discrimination, tests for the discrimination of interrupted speech, and auditory evoked responses).

The balance function is maintained by integration of sensory signals from the proprioceptive, visual, and vestibular systems transformed into motor command signals. Information of this integration can be assessed by posturography. The visual and vestibular systems are intimately connected within the vestibuloocular reflex (VOR) and the oculomotor system, the purpose of which is to maintain a steady retinal image of the environment during head movements. Visual and vestibular impulses are integrated in the brainstem, giving rise to eye-position command signals to the eye muscle nuclei. Different parts of these systems can be examined by registration of eye movements in electrooculography during different types of stimulation. Vestibular stimulation may be obtained by caloric irrigation of the ears, which affects the semicircular canals of the labyrinths. Visual stimulation can be obtained by having the subject look at a moving target with his or her head fixed (as in the smooth-pursuit eye movement test). Finally the integration process can be investigated by analyses of the saccades, ie, the quick movements of the eyes (ie, in the computerized saccade test) and by giving conflicting visual and vestibular stimuli (eg, with the visual suppression test).

Previous reliable normal reference values do not exist for several of the tests used for the examination of the vestibulooculomotor and oculomotor systems. It was thus considered necessary to use a reference group of industrial workers, unexposed to solvents in these cases, and otherwise normal reference values were used as specified.

The first test was standard pure-tone audiometry.

Then came the tests for maximum speech discrimination of 50 monosyllabic words. A score of 90 % or less was considered pathological. The normal reference group comprised 513 subjects between the ages of 20 and 74 years (7).

Third came the discrimination of interrupted speech with three interruption rates (4, 7 and 10/s). The subject was considered abnormal if the discrimination score was below 90 % for at least one of the rates. The normal reference group comprised 105 subjects aged 17—60 (mean 32) years (8).

Cortical response audiometry using a frequency glide stimulus with quantification of the response latency was fifth. The result was considered abnormal if the value exceeded 167 ms for the 50-Hz glides and/or 140 ms for the 200-Hz glides. The normal reference group comprised 44 subjects aged 15—73 (mean 54) years (9).

Static posturography was used with the body sway calculated during upright stance by means of a force plate on which the displacement of the central pressure between the feet and ground was registered and the total sway areas were calculated with the subject's eyes open and closed (6). The results were considered abnormal if the sway area exceeded the mean (±2 SD) of reference group B.

A caloric test was performed by irrigation of the ear canals with warm (44°C) and cold (30°C) water for 40 s with calculation of the generated nystagmus. The results were considered pathological when the caloric asymmetry between the ears exceeded 20 %.

A computerized smooth-pursuit eye movement test was performed with the use of a laser dot on the wall in front of the subjects, moving with either a sinusoidal frequency sweep (0.2—2.0 Hz, maximum velocities 20°/s and 40°/s), or a pseudorandomized pattern (0.2—2.0 Hz, maximum velocity 40°/s). Gain was calculated as the ratio between eye velocity and target velocity as a function of frequency. Phase was estimated as the temporal relationship (expressed in degrees) between the eye velocity and the target velocity (10). The test results, concerning gain or phase, were regarded as pathological if the values at four or more of the frequencies tested exceeded the mean (±2 SD) of the corresponding measurement of reference group A.

A computerized saccade test was performed with voluntary fast eye movements (saccades), calculated from assessments of latency in milliseconds and maximum velocity in degrees per second (11). The test results were regarded as pathological if the values exceeded the mean (±2 SD) of the corresponding measurement of reference group A.

A visual suppression test of the VOR was performed with a broad-frequency band rotatory test with the subjects seated in a rotatory chair mounted on a strong hydraulic motor. Chair movement patterns were sinusoidal frequency sweep (0.25—3.25 Hz) and pseudorandomized oscillation (0.75—4.50 Hz) with a maximum velocity of 65°/s. The subjects were instructed to fixate on a dot on a frame moving with the chair, in order to suppress the VOR. Gain (eye velocity/head velocity) and phase (temporal relationship expressed in degrees between eye and head velocity) were calculated (12). The results were considered to be pathological when the gain and phase exceeded the mean (±2 SD) at four or more frequencies when compared with the results of reference group A. Each subject underwent a thorough clinical otoneurological assessment including gait, tendon reflexes, gross motor function, and cranial nerves.

For the statistical analysis Student's paired t-test, Wilcoxon's rank sum test, or two-factor repeated analyses of variance (ANOVA) were performed.

Results

The results of the individual workers exposed to styrene are summarized in table 1.

Auditory system

The pure-tone audiometry and speech discrimination scores did not indicate hearing losses due to causes other than age and/or exposure to noise. Seven workers displayed abnormal results in distorted speech and/or the cortical response audiometry tests (table l).

Equilibrium system

The caloric test was normal for all the workers, and therefore normal peripheral vestibular function (labyrinth) was indicated.

The static posturography test revealed a significantly higher sway area for the styrene group with the eyes open ($P<0.01$) and the eyes closed ($P<0.01$) than for reference group B (Wilcoxon's test). At the individual level 10 of the 18 styrene workers showed pathology in the tests with their eyes open and/or closed (table l).

Group means were also determined in the saccade, smooth-pursuit eye movement, and visual suppression tests with comparison between the styrene workers and reference group A. In the saccade test the latency time was significantly higher in the styrene group ($P<0.01$, Students unpaired t-test). There were no differences in the maximum velocity of the saccades between the two groups (table 2). With the borderline values described in the Methods section, seven of the styrene workers had a prolonged latency time (table l). The mean smooth pursuit gain and phase of the two groups are illustrated in figure 1. A phase lag during predictable stimulation (sinusoidal frequency sweep) and a depression of gain during unpredictable (pseudorandomized) stimulation was seen in the styrene group in the comparison with reference group A ($P<0.01$, ANOVA). With the borderline values described in the Methods section, seven of the styrene workers had a pathological phase shift in this test (table 1).

In both the sinusoidal (figure 2 a) and pseudorandomized (figure 2 b) tests, the VOR suppression tests showed a highly significant impaired ability to suppress the VOR among the styrene-exposed workers when they were compared with reference group A, the result being a higher gain ($P<0.001$ and 0.001; ANOVA). The phase (figure 2 b) showed a significant difference with more pronounced phase leads in reference group A under both test conditions ($P<0.001$ and 0.001, ANOVA). Thirteen of the 18 styrene workers had a pathological gain, and four of them had a pathological phase shift, in the visual suppression test (table 1).

The clinical otoneurological assessments of gait, tendon reflexes, gross motor function, and cranial nerves were all within the normal limits.

Table 1. Individual results of the 18 styrene workers. The requirements for a pathological result are given in the Methods section. (– = normal, + = abnormal)

Worker	Age (years)	Distorted speech	Cortical response adiometry	Saccade test		Smooth pursuit		Visual suppression		Posturography	
				Maximum velocity	Latency	Gain	Phase	Gain	Phase	Eyes open	Eyes closed
1	28	–	–	–	+	–	+	+	+	+	+
2	31	–	+	–	–	–	–	+	+	–	–
3	31	–	–	–	+	–	–	–	–	–	–
4	32	–	–	–	–	–	+	+	–	+	+
5	33	–	–	–	–	–	+	–	–	+	–
6	34	+	+	–	+	–	+	+	–	+	+
7	35	–	–	–	–	–	–	+	–	–	–
8	35	–	–	–	+	–	–	+	+	–	–
9	36	–	–	–	–	–	–	–	–	–	–
10	38	–	–	–	–	–	–	+	–	–	–
11	38	–	–	–	+	–	–	+	–	–	+
12	39	–	–	–	–	–	+	–	–	+	–
13	41	+	–	–	–	–	–	+	–	+	+
14	42	–	+	–	–	–	–	+	–	+	+
15	45	–	–	–	–	–	–	+	+	–	–
16	55	–	+	–	+	–	+	+	–	+	–
17	56	–	+	–	–	–	–	–	–	–	–
18	61	+	+	–	+	–	+	+	–	+	–

Table 2. Results of the posturography and saccade tests of the styrene-exposed and reference group.

Group	Posturography, sway area				Saccade test			
	Eyes open (mm^2)		Eyes closed (mm^2)		Maximum velocity (°/s)		Latency (ms)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Styrene-exposed	117	83	127	108	362	37	289	52
Reference	71	38	77	48	361	41	249	31

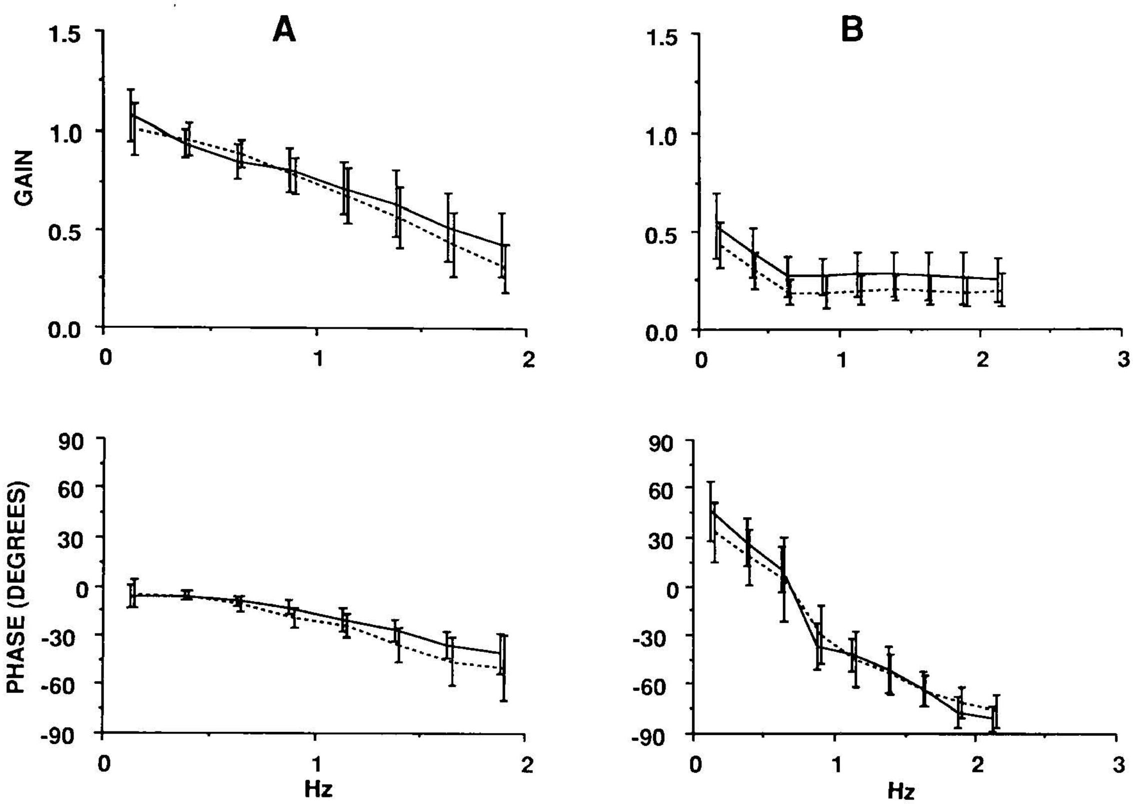

Figure 1. Mean values of gain and phase obtained by the broad-frequency smooth-pursuit test as a function of frequency for the styrene (broken line) and the reference (solid line) group. The vertical line represents one standard deviation. [A = sinusoidal frequency sweep stimulation (maximum velocity 20°/s), B = pseudorandomized stimulation (maximum velocity 40°/s]

Discussion

Reference values and reference groups

The audiological tests performed in this study are used in routine clinical practice with well-established limits for normal values. Regarding posturography a previous normal reference material existed, comprising industrial workers without solvent exposure (6). The data from the posturography reference group and the styrene workers of our study were obtained with the same equipment and by the same investigator. Regarding the tests reflecting the vestibulooculomotor and optooculomotor systems, no previous suitable reference data existed. It was thus necessary to develop a reference group with which these tests could be evaluated. This group was selected to be comparable to the styrene group with respect to age and tobacco and alcohol habits. Thus it is unlikely that the discrepancies between the results of the styrene group and the reference group were related to causes other than solvent exposure. The relationship between the exposure level and the otoneurological findings was not assessable due to the small number of styrene-exposed workers.

Usefulness of otoneurological testing in evaluating the toxicity of solvents in the central nervous system

The neuropsychiatric symptoms of the styrene workers were mild. Although many of the workers displayed subjective symptoms in a questionnaire, only three of them displayed pathology in psychometric tests (5). Nevertheless, the neurophysiological tests revealed significant disturbances in some parts of the central equilibrium and auditory systems. The ability to integrate information from different sensory organs participating in the maintenance of equilibrium seemed to be particularly reduced in the styrene-exposed workers. The results are in agreement with those of a similar study on patients with the psychoorganic syndrome, caused by exposure to solvents (1), and with a posturography study of healthy volunteers with acute exposure to xylene and alcohol (13).

It is thus evident that otoneurological tests are valuable in the evaluation of patients with early CNS damage caused by solvents. Controversies about the risks for such lesions during long-term exposure to solvents

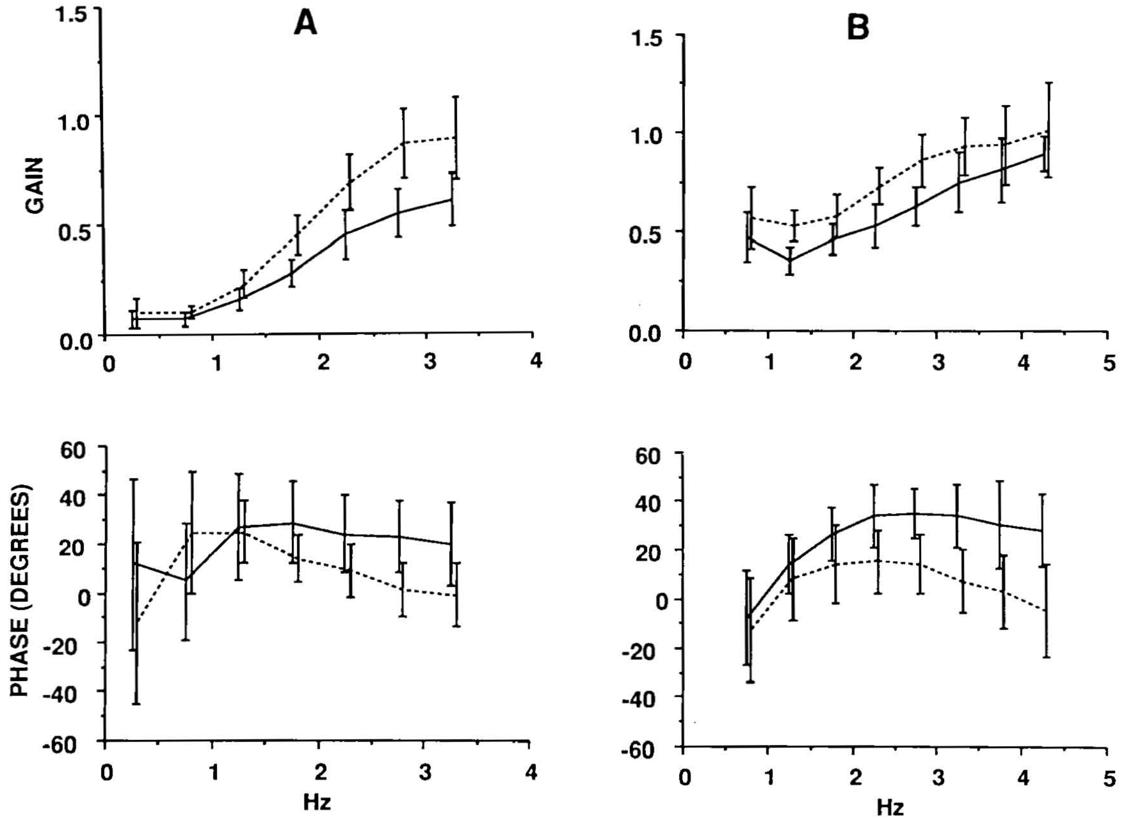

Figure 2. Mean values of the gain and phase obtained with the visual suppression test as a function of frequency for the styrene (broken line) and the reference (solid line) groups, during fixation on a small dot moving with the chair. [A = sinusoidal frequency sweep stimulation (0.25—3.25 Hz), B = pseudorandomized stimulation (0.75—4.25 Hz)]

(14) may reflect the lack of good experimental and clinical tests. The otoneurological test battery described in the present study could improve the understanding of this problem.

Location of the damage

Previous reports have demonstrated cochlear loss in animals after long-term exposure to toluene (15). The tests primarily reflecting the cochlear function were however normal in the styrene-exposed workers. Some mild high-frequency hearing loss, explained by age and conceivable noise exposure, was noted. These findings are in agreement with those of an earlier study on solvent-exposed workers with psychoorganic syndrome tested under the same conditions (1) and the findings of a study of workers exposed to solvents and jet fuel (2). In tests probably reflecting more central auditory pathways, ie, the test for distorted speech and the cortical response audiometry, some workers in the present study demonstrated abnormal results. This finding could indicate styrene-related damage to the auditory system, presumably at cortical-subcortical levels.

No signs of labyrinthine or peripheral vestibular lesions were found among the styrene workers, but tests reflecting central vestibulooculomotor and optooculomotor mechanisms, ie, the saccade test, the smooth-pursuit test, and the visual suppression test, were abnormal. The saccadic system is thought to be originated and controlled by the brainstem-cerebellum, and saccadic abnormalities have previously been found in patients with cerebellar lesions (16). The smooth pursuit pathways are complex, engaging several systems within the CNS such as the optic accessory tract, the cerebral hemispheres, the brainstem, and the cerebellar flocculus (16). The reduction of gain during unpredictable pseudorandomized stimulation in the styrene group demonstrates that the overall ability to perform smooth-pursuit eye movement was reduced. The increase in phase lag, found during sinusoidal stimulation, indicates disturbances of central motor programs for anticipating stimulus patterns. This finding is in accordance with findings in patients with brainstem-cerebellar disorders (17).

The VOR provides compensatory eye movements during head rotation and therefore stabilizes visual fixation of a steady target. However, if the target is moving with the head, the VOR has to be suppressed in order for a stable image to be produced on the retina. The cerebellum is probably of crucial importance in systems providing inhibitory signals to the VOR (18). The significantly decreased ability to suppress this reflex among the styrene-exposed workers both with a predictable (sinusoidal) and an unpredictable (pseudorandomized) stimulus thus indicates a disturbance of cerebellar function. The decreased phase lead in the exposed workers reflects an impaired ability to anticipate the stimulus movement as in the smooth-pursuit test. The results are in agreement with findings of decreased VOR suppression ability in solvent-exposed workers with a confirmed diagnosis of psychoorganic syndrome (1).

Thus many of the present results suggest lesions in the brainstem-cerebellum and perhaps even at cortical levels. This suggestion is supported by reports on different cerebellar and behavioral symptoms among abusive solvent sniffing subjects (19, 20).

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