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Behavioral effects of long-term exposure to a mixture of organic solvents

by HELENA HÄNNINEN, L.Ph., LEENA ESKELINEN, M.A.,
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HÄNNINEN, H., ESKELINEN, L., HUSMAN, K. and NURMINEN, M. Behavioral effects of long-term exposure to a mixture of organic solvents. *Scand. j. work environ. & health* (1976) 240—255. The behavioral effects of long-term exposure to a mixture of organic solvents were investigated in a comparison of the test results of 100 car painters with those of a reference group. The test battery included tests for intelligence, memory, psychomotor performances, and personality. In addition to the comparison of the mean results, two discriminant function analyses were made. In one, only the performance test variables were used, but in the other personality variables were also included. The results indicated impairments in psychological performances, as well as personality changes in the exposed group. Impairments in visual intelligence and verbal memory and a reduction of emotional reactivity were the central features of the adverse effects of solvent exposure, but the behavioral disturbances also involved several other functions, including performance on a verbal intelligence test. The possible role of the differences in the initial intelligence levels were controlled with a separate comparison of the test results of 33 pairs of exposed and nonexposed subjects who were matched for age and for their intelligence level, measured during the military service. The discriminant function analyses were based on the results of these matched subgroups and tested in the rest of the material. According to the results the sensitivity of the psychological test methods was high, but the specificity somewhat low, with regard to solvent exposure. The concentrations of various solvents included in the exposure of car painters were low, the summated exposure corresponding to 32 % of the Finnish threshold limit value. The possible role of a potentiating effect of the solvent in the development of behavioral disturbances is discussed.

Key words: solvents, toluene, behavioral effects, long-term exposure.

Many industrial solvents are known to have neurotoxic effects, and therefore they are also capable of causing behavioral effects.

More is known about the effects of acute solvent exposure on humans than about long-term effects. More is also known about the effects of pure exposures than about the effects of mixed

ones, which, however, are a very common form of occupational hazard.

Toluene, for instance, has been rather intensively studied by behavioral methods with regard to both its acute and long-term effects. Exposure to low concentrations has not been found to cause changes in performances, but exposure to higher concentrations affects reaction times and the speed of perception (13, 26, 27, 37). Moreover, toluene causes changes in subjective experiences and feelings (6, 26).

In experimental studies the behavioral effects of a short exposure to dichloromethane (35), trichloroethylene (30, 31, 37),

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methylchloroform (14), methylene chloride (17, 36), styrene (15), and white spirit (16), among others, have also been investigated. Most of these studies have concerned disturbances in psychomotor and visual functions or disturbances in vigilance.

The documentation of the behavioral effects of long-term exposure to solvents is more scanty. There are some results indicating that exposure to trichloroethylene and other solvents impairs memory and causes neurotic symptoms (7, 8), that exposure to styrene causes disturbances in visuomotor accuracy and psychomotor performance (18, 23), and that some performances of house painters exposed to different mixtures of solvents are impaired (2). In addition widespread disturbances in psychological functions have been found in workers who are exposed to solvents and have been verified as being, or suspected of being, poisoned or who are considerably exposed at work (22).

Although the results of earlier investigations have been somewhat inconsistent, they indicate that solvents affect many psychological functions simultaneously and cause impairment of several performances, as well as subjective changes in the domain of emotions, moods, and feelings. Impairment of visual functions and visual intelligence and changes in the vigilance level seem to be the central features of the psychological effect of solvents. Results concerning disturbances in psychomotor functions or impairments of verbal intelligence are rarer. Memory and learning abilities have not been greatly investigated in recent studies, even though the impairment of memory is known to be very central in the subjective symptomatology of exposed subjects.

This report deals with the psychological changes that occur in car painters exposed to a mixture of organic solvents. Toluene was the most important component of the exposure in question.

MATERIAL AND METHODS

Subjects

The exposed group consisted of 102 car painters from 27 car repair garages. The sample was chosen from all the car paint-

ers in Helsinki (N = 166) by the stratified sampling method so that subjects with various exposure times would be equally represented. The exposure times of the Helsinki car painters and the examined sample are presented in table 1. The subjects' exposure times varied from 1 to 40 years (mean 14.8, SD 8.5); and their age, from 20 to 65 years (mean 35, SD 11).

The nonexposed reference group was chosen from the employees of the Finnish State Railways so that the ages of the subjects were matched within 1 to 2 years. About half of the group consisted of engineers and the other half of locomotive assistants. Noise, vibration, irregular shift work, and mental stress are the most important railroad work factors which might have had a possible effect on the psychological functions tested.

Two of the 102 car painters were excluded from the sample because of brain damage of other etiology, and one locomotive engineer refused to participate in the psychological examination. Thus the final sample consisted of 100 exposed and 101 nonexposed subjects.

Exposure

Solvent concentrations in the air were measured in six randomly selected car repair garages, in which a total of 40 car painters were employed. On the average the car painters used three liters of paint and solvent and spray-painted 5 m² a day.

The paint binders were mainly nitrocellulose, alkyd, acrylic, carbamide, or urethane resins. The solvents and thinners were aromatic hydrocarbons (toluene,

Table 1. The exposure times of the car painters in Helsinki and of the examined sample.

Exposure time (years)	Car painters in Helsinki	Car painters in the sample
1—5	37	21
6—10	44	21
11—15	45	19
16—20	15	15
21—25	11	11
≥26	14	13
Total	166	100

xylene), aliphatic hydrocarbons (white spirit), alcohols (ethanol, isopropanol, butanol), esters (ethyl acetate, buthyl acetate, ethyl glycol acetate), ketones (acetone, methyl ethyl ketone, methyl isobutyl ketone), and terpenes (pinene). The rest of the paint was composed of pigments and fillers (organic and inorganic dyes, zinc chromates, titanium dioxide, talc), catalysts (phosphoric acid), plasticizers, siccatives, and antiskinning agents.

During spray-painting the paint and the solvent are nebulized by means of compressed air, and the workers are therefore exposed to vapors and particulate aerosols. In the course of the study the 27 car repair garages were visited and, in general, the spray-painting of cars took place in efficiently ventilated chambers. During spraying, which took 1 to 2 h per day, the workers wore a filter mask. The air of the workroom was contaminated by solvent vapors and paint dusts from the priming, grinding, and cleaning of surfaces for painting and occasionally by exhaust gases containing carbon monoxide, nitrogen oxides, and soot. On the average the carbon monoxide concentration was low (0–20 ppm).

The median age of the car repair shops was 15 years, and the ventilation installations were, on the average, about 10 years old.

Table 2. Mean concentrations of organic solvents in the breathing zone of 40 car painters. (Sampling period = 1 h; number of car repair garages = 6; number of samples = 54)

Solvent	Mean concentration (ppm)	Percentage of the TLV ^a	TLV ^a (ppm)
Toluene	30.6	15.3	200
Xylene	5.8	5.8	100
Buthyl acetate	6.8	4.5	150
White spirit	4.9	2.5	200
Methyl isobutyl ketone	1.7	1.7	100
Isopropanol	2.9	0.7	400
Ethyl acetate	2.6	0.7	400
Acetone	3.1	0.3	1,000
Ethanol	2.9	0.3	1,000
Total		31.8	

^a TLV = threshold limit value.

The mean solvent concentrations in the ambient air are presented in table 2. The average of the sum of the percentage was 31.8 % of the Finnish threshold limit value (TLV) for solvent mixtures. The range of separate components was 4 to 212 % of the TLV. The variation, with time, of the 1-h average concentrations during a workday was evaluated by repeated sampling. The average standard deviation of the logarithms of the sum of the percentages was 0.27.

There were no marked differences in work conditions and solvent exposures between the six car repair garages since the work methods, equipment, and paints used were essentially the same. Therefore, the six car repair garages were representative of the 27 car repair garages visited.

For the elimination of acute effects the test battery was always administered at least 16 h after the cessation of the last exposure.

Psychological methods

The psychological examination of the subjects was performed in conjunction with medical examinations performed by a neurologist, a neurophysiologist, a neuroophthalmologist, and an occupational health physician.

The test battery was chosen according to the following principles: (a) the methods should cover a broad range of various psychological functions; (b) especially tasks measuring various aspects of memory and psychomotor functions should be included; (c) the test battery should contain tests used previously in toxicopsychological investigations; (d) the tests should be easy to administer and suitable even for use in routine health examinations of workers exposed to solvents and field investigations. Hence stationary equipment was not used, reaction time measurements being the only exception.

The test battery contained one test for verbal intelligence, three visual tests, four memory or learning tasks, four tests of psychomotor performances, and the Rorschach test for measuring personality changes.

The psychological tests and variables used in the statistical analyses

Similarities (Sim) from the Wechsler Adult Intelligence Scale (WAIS) (33) was used for the measurement of verbal intelligence and abstraction. There was no time limit.

Picture Completion (PC) from the WAIS was used for the measurement of visual intelligence and observation. There was no time limit.

Block Design (BD) from the WAIS measured visual intelligence and abstraction. Each subtask had a time limit.

Figure Identification (FI) (11) measured speed of perception and memory for visual details. The time limit was 5 min, and the number of attempted tasks was used as the variable for the speed of perceptions.

Digit Span (DSp) from the WAIS and the WMS (Wechsler Memory Scale) (32) measured the subjects' memory for digits. As the digits must be recalled both forwards and backwards, the test demands attention and concentration.

Logical Memory (LogM) from the WMS measured verbal memory. The task (recalling a short story) demands the ability to concentrate on spoken verbal material and recall it.

Associate Learning (AssL) from the WMS was used for the measurement of verbal memory and learning. It consists of 10 pairs of words to be learned during three trials. Before each trial, the word pairs are read to the subject, and the subject has to recall the second word when he hears the first one.

The *Benton test for visual reproduction* (Ben repr) was used for the measurement of visual memory (1). In this test the subject must draw one or three simple figures after a 10-s presentation. The test contained 10 subtasks. The test score was the number of correctly drawn figures.

The *Benton test for visual retention* (Ben ret) was used. After seeing a test design containing one or three figures, the subject has to recognize it among four different designs. The test contains 10 subtasks.

The *Santa Ana Dexterity Test* (12) measures the subjects' psychomotor speed. It demands both eye hand coordination and coordination between the movements of the wrist and fingers. A separate score was given for the performance of the right (SA right) and left (SA left) hands and for the coordination of two hands (SA coo).

Finger tapping measures motor speed. It was performed with a simple counter. The subject had to tap it with the thumb as fast as possible. A separate score was given for the performances of the right (FT right) and left (FT left) hands (sum of tappings during four 10-s trials).

Reaction times were measured by reaction time measuring equipment constructed at the Institute of Occupational Health, Helsinki. In the task the subject reacts to visual signals by pressing a bar with the right or left hand. The signals are presented randomly with 2-, 4-, or 6-s intervals.

The subjects performed *simple reaction-time* tasks separately with the right (RT right) and left (RT left) hands. The score was the cumulative time for 40 reactions.

In the *choice reaction time* (RT choice) task there are three visual signals, i.e., three separate lights placed on a panel. The subject has to react to the light on the right side with the right hand, to the light on the left side with the left hand, and not to react to the light in the middle. There were 25 signals in incidental order with 2-, 4-, or 6-s intervals. The ordinary task was preceded by an exercise trial. The score was the cumulative time for reactions in the ordinary task.

In addition the *Mira test* (20, 25) was used as a test for psychomotor behavior and psychomotor ability. The task is to draw a simple pattern without optic control, i.e., without seeing the paper and pencil. In the staircase subtask used the subjects have to draw stairs first upwards and then, without looking, continue with downward stairs so that an angle of 90 degrees is formed. The drawing is made separately with the right and left hands. The test demands the learning and mastering of simple motor patterns and the control of hand movements. Two variables were used. One indicated the size of the stairs; and the other, the form level of the performance. The size of the stairs

(Mi size) was measured as the number of stairs in a distance of 8 cm. For the form level (Mi form) 1 to 4 points were given, depending on the qualitative aspects of the performance.

Personality was investigated by the *Rorschach personality test* (21). Using its variables in statistical analyses is known to be a problem because of the relative subjectivity of the scoring and the high intercorrelations between the scores used in clinical practice. Five variables were used that had been developed earlier by one of us (H.H) (20). They are supposed to measure adaptability (Ada), emotionality (Emo), spontaneity (Spon), rational self-control (Rat), and originality of perception (Orig). In addition three variables were included that were based on the content analyses of the answers developed by DeVos (10), namely, hostility (Host), anxiety (Anx), and bodily preoccupation (Bod Pre), and also the number of responses (R), rejections (Rej), and the average latency times (rt) were included as separate variables.

The Mira test and the Rorschach test were scored blindly by two independent psychologists. In cases of divergent scores a third independent psychologist acted as a referee.

In order to control the possible effects of differences in the initial intelligence levels on the results, we used psychological test results recorded during the subjects' military service as the estimation of the initial intelligence levels. All subjects had not been tested during their military service, however, because the tests were not administered regularly until after 1958. It was, however, possible to form 33 pairs matched both for age and for the intelligence level recorded during military service, i.e., at the age of about 20 years. The military test battery consisted of three factor tests measuring different aspects of intelligence. In our study the total score was used. For the car painters this intelligence score represented in principle their performance level before exposure, although some of them had been employed in car painting garages already before their military service. The mean exposure time after the earlier psychological examination for the 33 car painters was 7.4 years (± 4.1 SD). The mean age was 27 years.

Additional data about the subjects were gathered with a questionnaire and a structured interview. One part of the questionnaire concerned the subjective symptoms of the subjects. A detailed report on the validity of subjective symptoms with regard to the effects of solvents will be given elsewhere. In the present study we compared the psychological findings with the following subjective symptom complexes: sleep disturbances, fatigue, disturbances of memory and vigilance, absentmindedness, emotional lability, and neurovegetative lability.

Statistical methods

The statistical analyses of psychological data contained several steps.

First the differences in the mean levels of the test scores between the age-matched exposed group and the reference group were examined. The same mean level comparison was also performed with regard to the smaller subgroup of pairs further matched with respect to initial intelligence level, as indicated by test results recorded during military service.

In the evaluation of the effect of the pairwise matching procedure, correlation coefficients for all the contemplated test variables between the compared groups were calculated.

When matching resulted in a high positive correlation, a *t*-test for paired data was employed; otherwise in the significance testing the two groups were treated as stochastically independent series. In the latter case two different situations were encountered. In one we could assume that the population variances were equal in the groups and therefore applied the ordinary Student's *t*-test for the two sets of observations. In the other the variance homogeneity condition was not obtained, and we applied an approximate *t*-test, according to Welch (34), which modified the degrees of freedom of the *t*-distribution. In both cases a bilateral testing was used.

The normality of the sampling distribution of the psychological test scores was assessed through visual inspection only. Those data which did not display the characteristic features of a normal distribution pattern, i.e., symmetrical unimodal distribution, with few extreme values on

either tail (sigmoid cumulative distribution function) were either discarded or dichotomized and tested by a paired chi-square test for a fourfold table (24).

The linear combination of variables differentiating best between the exposed and nonexposed subjects was searched for by multiple discriminant analysis according to the technique reported by Cooley and Lohnes (9). The analysis was based on the results of the matched subgroups, which were formed from subject pairs individually matched with regard to both intelligence and age.

The solvability of the eigenvector v , which maximizes the mean difference between the populations, was assured in the within-groups or W-metrics by the condition $v'Wv = 1$. Since the discriminant function was not only used for the separation of the two groups, but also for the measurement of the distance between them, the eigenvectors were normed by letting the length of the vector v equal unity or

$$\|v\| = \sqrt{v_1^2 + v_2^2 + v_3^2} = 1.$$

So that the relative contributions of the test variables to the discriminant function could be found, these normalized vectors

were scaled by multiplying them with the square roots of the corresponding diagonal elements of matrix W . The numerical values of the discriminant function were obtained from the standardized variables, i.e., the variables were expressed in a standard measure (zero mean, unit variance), whence also the expected value and the variance of the total sample discriminant function score equal zero and unity, respectively. In the test for the applicability of the discriminant function, discriminant score values were calculated for all subjects and used for the assignment of the subjects to the groups to which they most probably belonged according to their test results.

RESULTS

Differences in performances

Table 3 presents the mean performances and their standard deviations for both groups (with the group sizes $N = 100$ and 101), as well as the probabilities for such differences occurring by chance.

Table 4 presents the data obtained in the comparison of the pairs matched for initial intelligence and age ($N = 33/33$).

Table 3. Performance tests: means, standard deviations and significances between the group means (age-matched groups).

Test	Means and standard deviations		Significances of differences (t-test)
	Exposed ($N = 100$)	Nonexposed ($N = 101$)	
Sim	19.4 $\pm$ 3.1	2.9 $\pm$ 2.1	***
PC	14.9 $\pm$ 2.9	16.2 $\pm$ 2.3	***
BD	34.6 $\pm$ 7.0	39.6 $\pm$ 5.6	***
FI	32.0 $\pm$ 9.0	36.7 $\pm$ 9.8	***
DSP	10.6 $\pm$ 1.6	11.5 $\pm$ 1.8	***
LogM	11.7 $\pm$ 3.7	13.9 $\pm$ 3.1	***
AssL	15.3 $\pm$ 3.6	17.1 $\pm$ 2.6	***
Ben repr	21.1 $\pm$ 3.1	22.6 $\pm$ 2.3	***
Ben ret	8.2 $\pm$ 1.5	8.7 $\pm$ 1.3	*
SA right	44.7 $\pm$ 5.7	47.5 $\pm$ 5.8	**
SA left	42.3 $\pm$ 5.4	43.6 $\pm$ 5.1	
SA coo	29.0 $\pm$ 5.4	31.5 $\pm$ 5.7	**
FT right	202.5 $\pm$ 29.2	209.6 $\pm$ 23.8	
FT left	186.7 $\pm$ 28.5	196.4 $\pm$ 22.4	*
RT right	12.4 $\pm$ 2.9	11.9 $\pm$ 1.4	
RT left	12.1 $\pm$ 3.0	11.7 $\pm$ 1.4	
RT choice	9.1 $\pm$ 1.8	9.1 $\pm$ 1.2	
Mi size	18.8 $\pm$ 3.8	20.3 $\pm$ 4.6	** ^a
Mi form	2.2 $\pm$ 1.0	2.0 $\pm$ 0.8	*

^a Paired t-test.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Table 4. Performance tests: means, standard deviations and significances between the group means (groups matched for age and initial intelligence).

Test	Means and standard deviations		Significances of differences (t-test)
	Exposed (N = 33)	Nonexposed (N = 33)	
Sim	19.2 ± 2.8	20.7 ± 2.2	*
PC	15.3 ± 2.9	16.4 ± 1.8	
BD	36.1 ± 6.7	40.8 ± 5.6	*** ^a
FI	35.9 ± 10.8	40.6 ± 10.5	
DSp	10.8 ± 1.6	11.8 ± 1.7	*
LogM	12.6 ± 3.5	14.2 ± 3.2	*
AssL	15.4 ± 3.3	17.1 ± 2.8	* ^a
Ben repr	21.8 ± 2.7	22.9 ± 2.2	
Ben ret	8.3 ± 1.5	8.9 ± 1.1	
SA right	47.4 ± 4.6	49.1 ± 6.3	
SA left	44.4 ± 4.6	45.4 ± 4.8	
SA coo	30.8 ± 5.3	33.2 ± 5.5	
FT right	207.3 ± 23.7	216.4 ± 19.5	
FT left	192.2 ± 22.0	202.9 ± 19.8	*
RT right	11.5 ± 1.6	11.6 ± 1.4	
RT left	11.5 ± 1.6	11.4 ± 1.6	
RT choice	8.6 ± 1.0	8.6 ± 1.3	
Mi size	19.6 ± 4.1	21.5 ± 4.8	
Mi form	1.9 ± 1.0	1.9 ± 0.8	

^a Paired t-test.

* $p < 0.05$; ** $p < 0.01$.

Table 5. Personality variables: means, standard deviations and significances between the group means (age-matched groups).

Variable	Means and standard deviations		Significances of differences (t-test)
	Exposed (N = 100)	Nonexposed (N = 101)	
R	13.6 ± 6.4	13.8 ± 4.5	
Rej	0.7 ± 1.1	0.4 ± 1.0	** ^b
rt	16.4 ± 8.5	16.5 ± 8.1	
Ada	11.6 ± 3.1	12.1 ± 3.1	
Emo	8.8 ± 3.3	10.4 ± 3.2	***
Spon	11.8 ± 2.4	11.9 ± 2.6	
Rat	8.6 ± 2.8	7.3 ± 2.8	*** ^a
Orig	1.6 ± 1.7	1.5 ± 1.2	
Host	1.6 ± 1.6	2.4 ± 1.7	***
Anx	3.9 ± 2.0	3.8 ± 2.2	
Bod Pre	0.4 ± 0.8	0.8 ± 1.1	* ^b

^a Paired t-test.

^b Paired χ^2 -test for dichotomized scores.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Fig. 1 illustrates the group differences by presenting the mean performances of the exposed groups (N = 100 and N = 33) in standardized scores; the corresponding reference groups are used as a standard in adjustment.

Table 3 shows significant differences in almost all intellectual performances and

memory tasks. The differences in the psychomotor performances were less marked. However, dexterity in the Santa Ana test and the size of drawings in the Mira test differed significantly between the groups.

For most intelligence and memory variables the comparison between the matched

Fig. 1. Mean performances of the exposed subjects ($N = 100$ and $N = 33$) in standardized scores. (The corresponding reference groups are used as the standards.)

pairs ($N = 33/33$) (table 4 and fig. 1) yielded almost the same absolute differences in test scores, although the statistical significances of the differences were lower due to the smaller size of the compared groups. Except for finger tapping and size of drawing the differences in the psychomotor tasks were slight.

Differences in personality

Table 5 presents the mean results and standard deviations of the Rorschach variables and the statistical significances of the differences between the group mean values ($N = 100/101$). Table 6 presents the corresponding results obtained in the comparison of the matched pairs ($N = 33/33$). Fig. 2 illustrates the differences by presenting the results of the exposed groups, expressed again with reference to the means and standard deviations of the corresponding reference groups.

There were no differences between the groups with respect to the number of answers, or latency times, but there were significant differences in emotionality, rational self-control, and hostility, the exposed being less prone to emotional reactions and expressions of hostility and more

Table 6. Personality variables: means, standard deviations and significances between the group means (groups matched for age and initial intelligence).

Variable	Means and standard deviations		Significances of differences (t-test)
	Exposed ($N = 33$)	Nonexposed ($N = 33$)	
R	12.2 ± 3.7	12.8 ± 4.2	* ^a
Rej	0.8 ± 1.2	0.5 ± 1.3	
rt	15.7 ± 7.4	19.1 ± 10.0	
Ada	10.6 ± 2.8	11.6 ± 2.5	*
Emo	8.3 ± 2.9	9.2 ± 2.5	
Spon	11.3 ± 2.2	11.5 ± 2.9	
Rat	8.8 ± 2.4	7.1 ± 2.8	
Orig	1.1 ± 1.3	1.5 ± 1.0	
Host	1.3 ± 1.6	2.1 ± 1.7	
Anx	3.5 ± 1.6	3.2 ± 2.1	NS ^a
Bod Pre	0.4 ± 0.8	0.8 ± 1.2	

^a Paired χ^2 -test for dichotomized scores.

prone to control their thinking and behavior. The exposed also rejected cards more often.

Differences in the subjective symptoms

Table 7 presents the means and standard deviations of the subjective symptom com-

plexes, as revealed by the questionnaire. The number of questions included in the variables is also indicated in the table. For each question, the subject had to choose one of the following alternative answers: "never," "sometimes," or "often." Each answer was scored with 1, 2 or 3, respectively, and the scores were added together.

The difference between the exposed and nonexposed was the most marked in the amount of disturbances in memory and vigilance and in the amount of absent-mindedness. With respect to sleep disturbances or neurovegetative lability, there were no differences between the two groups.

Discriminant function analyses

Two discrimination analyses were performed, based on the data obtained from the groups matched for intelligence ($N = 33/33$). In the first analysis 11 performance variables were used, namely, the tests for intellectual and visual functions (Sim, PC, BD, FI), the memory tests (DSp, LogM, AssL, Ben repr), and three psychomotor variables (SA, sum of right and left, RT, sum of right and left, and Mi size).

As the first step the analysis chooses the best differentiating combination of variables by multivariate tests for the equality of mean vectors and for the additional information provided by individual vectors (28). The obtained combination consisted of one visual intelligence test (BD) and two memory tests (AssL and DSp). For the other tests the probability of their

Fig. 2. Mean results of the exposed subjects ($N = 100$ and $N = 33$) on the Rorschach personality test in standardized scores. (The corresponding reference groups are used as the standards.)

Table 7. Subjective symptom complexes: means, standard deviations and significances between the group means.

Variable	Number of items	Means and standard deviations		Significances of differences
		Exposed ($N = 100$)	Nonexposed ($N = 101$)	
Sleep disturbances	3	5.2 ± 1.5	5.1 ± 1.3	
Fatigue	2	4.1 ± 1.2	3.6 ± 1.0	**
Memory and vigilance	5	9.6 ± 2.4	8.4 ± 1.8	***
Absentmindedness	2	3.3 ± 1.1	2.6 ± 0.7	***
Emotional lability	9	15.5 ± 3.9	14.4 ± 3.3	*
Neurovegetative lability	7	10.2 ± 2.2	9.9 ± 2.2	

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

adding new information about the group differences to that obtained by these three tests was less than 25 %.

Thus in the solution of the discriminant function only the three variables mentioned were needed. Table 8 presents the results of the analysis and the correlations of the discriminant function with the separate variables. The performance on the Block Design test gets the highest weight in the discrimination between the exposed and nonexposed and also correlates best with the discriminant function.

The second analysis included three variables of the Rorschach test (Emo, Rat and Host) in addition to the 11 previously mentioned performance variables. Variables BD, AssL and DSp were again included in the best discriminating combination of the variables. In addition the combination included two Rorschach variables (Rat and Hos). Table 9 presents the result of the second analysis and the correlations of the discriminant function with the separate variables.

Validation of the discriminant functions

The individual probabilities for belonging either to the exposed or to the nonexposed group were calculated for each subject, and the subjects were classified into the groups to which they most probably belonged.

Table 10 presents the percentiles of correct classifications separately for the material used in the discriminant analyses (N = 33/33) and the rest of the material. The percentage of correct classifications in the material not used in the analyses expresses the validity of the discriminant function in determining whether a new subject is affected by solvent exposure. The percentage of correctly classified exposed subjects expresses the sensitivity; and the percentage of correctly classified nonexposed subjects, the specificity of the discriminant functions (38).

For both discriminant functions the sensitivity was slightly better than the specificity. The personality variables included in the second analysis slightly increased the correct classifications in the material on which the discrimination was based, but it did not improve the validity with regard to new cases.

Table 8. Results of the first multiple discriminant analysis.^a

Eigenvalue 0.34 Wilks' lambda 0.75		F (3, 62) = 7.044 p < 0.001
Variable	Scaled eigenvector in W-metrics ^b	Correlation with the discriminant function
BD	0.67	0.75
DSp	0.50	0.60
AssL	0.55	0.54
Means and standard deviations of the discriminant function		
Exposed group		-0.57 ± 0.93
Nonexposed group		0.57 ± 1.07

^a See the section on statistical methods.

^b Note: $\sqrt{0.67^2 + 0.50^2 + 0.55^2} = 1$.

Table 9. Results of the second multiple discriminant analysis.^a

Eigenvalue 0.49 Wilks' lambda 0.67		F (5, 60) = 5.883 p < 0.001
Variable	Scaled eigenvector in W-metrics	Correlation with the discriminant function
BD	0.54	0.66
DSp	0.37	0.52
AssL	0.50	0.47
Rat	-0.38	-0.47
Host	0.44	0.44
Means and standard deviations of the discriminant function		
Exposed group		-0.69 ± 1.0
Nonexposed group		0.69 ± 1.0

^a See the section on statistical methods.

Table 10. Percentages of correct classifications.

Group size	First discrimi- nant analysis		Second discrimi- nant analysis	
	Exposed	Non- exposed	Exposed	Non- exposed
33	73	76	76	82
69	75	62	73	62
100	74	66	74	68

Fig. 3. Percentage distribution of the Bayes' probabilities of belonging to the exposed group according to the first discriminant analysis.

Fig. 4. Percentage distribution of the Bayes' probabilities of belonging to the exposed group according to the second discriminant analysis.

The distributions of the Bayes' probabilities of belonging to the exposed group according to the discriminant analyses are presented in fig. 3. Fig. 4 presents the corresponding distribution of probabilities according to the second analysis.

A comparison of figs. 3 and 4 shows that, although the personality variables included in the second analysis did not improve its validity in terms of correct classifications, the discriminant function yielded by the second analysis nevertheless gave a sharper differentiation between the two groups. When the probabilities of the subjects belonging to their proper group were calculated according to the first discriminant function, the modes of a posteriori probability distribution were about 70 % in both the exposed and nonexposed group. When the probabilities were calculated according to the second function, the mode of corresponding probabilities was about 80 % in the exposed group and about 90 % in the nonexposed one.

When the subjects with probabilities between 50 and 75 were considered borderline cases and when only a probability of belonging to the exposed group of higher than 75 % was assumed to indicate a behavioral disturbance peculiar to solvent exposure, the prevalences of exposed and nonexposed subjects with behavioral disturbances were 35 and 12 %, respectively, according to the first discriminant function, and 44 and 11 %, respectively, ac-

cording to the second discriminant function with the personality variables included.

When, correspondingly, a probability of belonging to the nonexposed group of higher than 75 % was assumed to be a valid indicator of undisturbed psychological functioning, the prevalence of undisturbed subjects was, according to the first discriminant function, 6 % in the exposed group and 25 % in the nonexposed one, the corresponding percentages according to the second discriminant function being 11 and 40.

DISCUSSION

Comparison of the exposed and nonexposed subjects

We compared behavioral features of a group of car painters with those of a nonexposed group in order to determine the possible psychological effects caused by the mixed solvent exposure of car painters. The study concerned subclinical effects of low levels of exposure, the average level of the total exposure being only 32 % of the Finnish TLV with little variability between the car painting garages. The possibility of higher exposures in the past could not be ruled out however.

As the intelligence performances differ-

ed considerably between the two examined groups, the question arose of whether these, and maybe also other differences between the groups, were due to differences in the initial intelligence levels of the two groups and not to the effects of solvents.

The use of reference groups in behavioral studies is always a problem, mainly because of the possibility of unequal motivation among the experimental and reference groups in the test situation and unequal initial levels. Due to the different selection of employees for different occupations, and even for different plants, the latter problem is hard to avoid in behavioral studies in industrial epidemiology. If the effects are limited to a few psychological functions only and the other functions are left intact, the problem can be solved with the study of the differences in behavioral profiles. When the effects cover a broad range of functions, the possibility of differences in initial levels becomes crucial.

In our investigation we decided to use employees from the Finnish State Railways as reference subjects because they were willing to accept the psychological examination as a part of their health examination, and they were also motivated to cooperate in the test situation. The other advantages of this group as a reference group were its suitable age distribution and its homogeneity with regard to health status and work conditions. Moreover, the reference subjects lived in the same geographical area as the car painters.

The role of possible differences in the initial intelligence levels before the commencement of exposure was controlled by psychological test results recorded during the military service of the subjects. In a comparison of 33 pairs matched both for intelligence at the age of about 20 years (during military service) and for age, the same group differences were found as between the entire samples. This result confirmed that the group difference could not be explained by initial differences between the exposed and nonexposed subjects.

The validity of our results concerning the group differences is also dependent on the adequacy of the statistical tests used. There are three assumptions underlying the t-test for the equality of the mean val-

ues, namely, normality of the sampling distributions, homogeneity of variances, and independence of errors in the test scores. Although no exact testing for non-normality was done, in significance tests the stipulation of normality may be regarded as practically complied with for large samples if they pass a symmetry test. The two sets of data had an equal and large number of observations (i.e., more than 30) on all the psychological test variables. As a consequence, only in a few instances did the rejection of the variance homogeneity assumption on the basis of an F-test lead to a differing significance level in the t-test for mean levels from what an ordinary t-test would have yielded. Given these conditions, there is both theoretical (4, 5) and empirical (e.g., 3 and references therein) evidence to support the notion that the t-test is a robust test; i.e., it is only inconsequentially affected by a violation of the underlying assumptions.

The paired sample t-test was used when matching was not regarded as irrelevant, i.e., when it made the responses of the numbers of pairs correlate positively. In such a situation the differences of pairwise responses are independent, and the t-test of the differences is often more powerful than the ordinary t-test.

The differences between the psychological performances of the exposed and nonexposed subjects could be confirmed by the t-test when whole samples were considered, but the statistical significances of the t-test were rather low when the groups matched for initial intelligence were considered, not because of smaller differences but because of smaller group sizes. The difference was further confirmed by a multiple discriminant analysis yielding the maximum separation between the two sets of data; both the Wilks' lambda and the t-test for the difference of the mean scores of the discriminant function reached a level of high statistical significance. The choice of variables sufficient for significant separation of the groups was an additional advantage of the use of the multiple discriminant analysis.

Moreover, we could test the generalizability of the result and the practical applicability, i.e., the sensitivity and specificity, of the discriminant scores by using the discriminant scores of the subjects not included in the analysis to classify them

into either the exposed or to the non-exposed group. The number of subjects classified into the exposed group was significantly higher among the exposed subjects than among the nonexposed ones. The fact that about 25 % of the exposed subjects had a higher probability of belonging to the nonexposed group was in accordance with our expectations, since it was reasonable to assume that only some part of the car painter group would display effects of solvent exposure. The number of nonexposed subjects classified into the exposed group was a more serious disadvantage; it indicated that the central nervous system dysfunction measured by the tests is not very specific for solvent exposure and that the psychological methods have a high sensitivity to mild behavioral disturbances of different origins. However, when only the subjects with a probability of higher than 75 % were regarded as subjects with central nervous system dysfunction, the percentage of such subjects was reduced to 11 in the nonexposed group, against 44 in the exposed group. The percentages probably correspond better to the true prevalences of central nervous system dysfunctions in both groups.

The checking of possible etiologic factors causing behavioral disturbances in the reference group remained outside the scope of this investigation. The earlier-mentioned work loads of the reference subjects, as well as central nervous system dysfunctions due, for instance, to a heavy use of alcohol or some neurological disease, may be possible causes for the disturbances.

Nature of the psychological changes

According to our results, visual intelligence, as measured by the Block Design test, and the memory functions, measured by the verbal memory test, were the most affected by solvent exposure. The sensitivity of visual performances with respect to long-term exposure to solvents has been proven even in earlier studies (2, 22, 23), but in these studies Block Design was not the most sensitive visual test. The performance on Block Design contains both an intellectual and a pure visual component. In addition, the test demands

concentration. From our results the most affected component cannot be determined. Possibly an impairment of all of them accounts for the sensitivity of this test to the exposure of car painters.

Memory disturbances among workers exposed to solvents have also been demonstrated earlier (8), but most recent investigations have either omitted the examination of memory functions or failed to show any effect on memory, except on visual memory. According to our results verbal memory was more affected than visual memory. Performance on the verbal memory tests used in this study depends on the ability to concentrate on spoken verbal material and the ability to keep it in mind. It is possible that the poor performance of the car painters was partly due to distractability and not only to poor memory.

The impairment discovered in the performances of the car painters was not restricted to the four previously mentioned tests. On the contrary, solvent exposure seemed to affect a broad range of mental functions. The impaired functions included verbal intelligence, which in some earlier studies (2, 19) has been considered resistant to diffuse central nervous system disturbances. As the verbal intelligence was measured by Similarities only, we could not determine whether the inferior result of the exposed subjects was dependent on the impairment of verbal reasoning, abstraction, or communication. In this test the subject had to answer spoken questions, and maybe this property of the test accounts for the car painters' failure on it. It is possible that a paper and pencil test for verbal intelligence could have given a different result concerning the verbal intelligence level of the exposed subjects.

The psychomotor performances of the exposed subjects indicated moderate clumsiness of hand movements. However, in a comparison with the effects of carbon disulfide on psychomotor performances measured by the same test methods (19), the retardation of psychomotor speed was very slight.

There were no significant differences in the mean reaction times between the exposed and nonexposed subjects. Toluene, among other solvents, has been shown in earlier studies to increase reaction times

both in acute and long-term exposures when concentrations exceed 200 ppm (13, 26, 27, 37). According to our results reaction time is not a sensitive measure of effects due to low-level solvent exposure, even after long-term exposure.

The psychological syndrome of the exposed subjects also included emotional changes. As the measurement and interpretation of behavioral features belonging to the domain of moods and emotions is very problematic, this area of behavior is very often disregarded in behavioral toxicology. It is however important with regard to chemical interventions of the central nervous system, as well as with regard to the subjective well-being and social abilities of the exposed persons. For studying the effects of solvents on personality, we used the Rorschach personality test, even though we knew the difficulties inherent in the interpretation of the results.

There are two alternative interpretations to the personality changes indicated by our results. They can be due to toxic effects on the brain centers regulating the emotional aspects of behavior, or they can be due to the subjects' emotional or maybe compensatory reaction to a situation created by impairments in mental functions. For the present we are inclined to interpret the reduction of emotional reactivity and the reduction of aggressions (Hostility) as immediate toxic effects. The increased rational control of thinking and behavior can even reflect increased psychological tension induced by a toxic effect on the central nervous system, but it can also be understood as a compensatory feature.

The subjective symptoms that were increased in the exposed group corresponded to the psychological picture of toxic effects as described in the preceding text. According to both, impairment of memory and concentration and a relative inability to keep rapport with the environment seemed to be central features of the effects of solvent exposure.

However, although the differences between the average test performances of the exposed and nonexposed subjects were statistically significant, the impairments discovered in the exposed group can be considered rather slight. There were more poor performances among the ex-

posed subjects than among the nonexposed ones, but the individual test results were in general within the limits of normal variation. This result does not mean that the behavioral changes found in this study are harmless. The practical significance of mild or moderate memory impairment or a mild decline of intellectual capacities and psychomotor skills, as well as a slight change in emotional reactivity, is difficult to evaluate, but nevertheless they imply reduced resources to cope with the various demands of everyday life.

Some final remarks

There is some toxicological evidence to support the conclusion that the effect of combined solvent exposure can be more hazardous than the summated effects of the components (29). However, very little is known about the interaction of solvents. In addition very little is known about the action mechanisms and sites in the central nervous system.

As the available data concerning central nervous system effects of the separate solvents present in the exposure of car painters is scanty, we cannot know which of the components is the most responsible for the effects indicated by our results. Since impairments appeared in an extensive area of psychological functions, a combined effect can be supposed. Moreover, the fact that there were measurable effects seems to indicate a potentiating effect of solvents when they are together. The mean concentrations of separate solvents were between 0.3 and 15.3 % of the corresponding TLVs, and it must be considered rather improbable that these levels would cause measurable adverse effects when occurring alone, or even if their interaction caused a simple summated effect.

The potentiated effect need not necessarily be potentiality in a toxicological sense. The impairments in car painters' performances can alternatively be a result of minor disturbances in several functions, caused by separate components of the exposure. It can be hypothesized that each one of these disturbances could be compensated for in the test situation, as well as in everyday life, when occurring alone, but that their combination does not

leave many possibilities for compensation and thus causes a potentiated effect on the behavioral level.

Safe TLV values for mixed exposures can only be based on thorough toxicological research on the interactions of the separate agents. This research should also include research on the interaction of the effects on the behavioral level. Currently the TLVs for mixed exposures are based on insufficient data. Therefore, periodical health examinations of persons working in mixed exposures and epidemiologic research with such workers must be considered highly important.

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