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by [Gamberale F](#), [Annwall G](#), [Hultengren M](#)

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Exposure to methylene chloride

II. Psychological functions

by FRANCESCO GAMBERALE, psychologist, GÖREL ANNWALL, B. A., and MAY HULTENGREN, engineer¹

GAMBERALE, F., ANNWALL, G. and HULTENGREN, M. Exposure to methylene chloride: II. Psychological functions. *Skand. j. work environ. & health* 1 (1975) 95—103. The effect of the solvent methylene chloride on psychological functions such as reaction time, short-term memory, and numerical ability was studied in 14 healthy male subjects. Each subject was tested repeatedly during exposure to 870, 1,740, 2,600, and 3,470 mg/m³ of methylene chloride in inspiratory air and during control conditions. Samples of subject alveolar air were taken every third minute during the experiments. No statistically significant impairment in the performance of examined functions could be observed during exposure to methylene chloride as compared to control conditions. In exposure to the highest concentration a greater irregularity of response was obtained for subject reaction time than under control conditions.

Key words: experimental psychology, methylene chloride, psychophysiological functions.

The presence of methylene chloride in air becomes apparent at concentrations exceeding 1,000 mg/m³. A sweet, chloroform-like smell can then be detected before the senses are dulled. The smell of methylene chloride is penetrating at concentrations around 3,500 mg/m³.

According to Lehmann and Schmidt-Kehl (11) no subjective symptoms are produced by exposure to concentrations under 8,000 mg/m³ for 30 min. Symptoms appeared with increasing rapidity as the concentration rose above this level, and dizziness, fatigue, and grogginess appeared after only a few minutes of exposure to 23,800 mg/m³. Stewart et al. (18) reported that subjects exposed to 3,500 mg/m³ began to complain of a slight headache after about 60 min of exposure. However, the headaches disappeared quickly when exposure was terminated. Subjective

symptoms similar to those found by these authors have been reported by many authors in conjunction with protracted exposure to methylene chloride (3, 10, 21).

We were able to find only two references dealing with the possible effect of methylene chloride on man's psychophysiological function. DiVincenzo et al. (4) found that the ability of subjects to perform simultaneous arithmetic operations and a coordination test was not affected by 4 h of exposure to 350 mg/m³ and 700 mg/m³ of methylene chloride. Schlipköter et al. (16) found that a 4-h exposure to 2,800 mg/m³ of methylene chloride produced a rise in the threshold for flicker fusion and impaired performance in a vigilance test.

The metabolism of methylene chloride results in an increase in carboxyhemoglobin (COHb) (1). Stewart et al. (18) maintained that exposure to methylene chloride in concentrations close to the threshold limit value may elevate the COHb concentration to more than 5 %. The detrimental effect of carbon monoxide on the human nervous system is a known fact. However, the question of the COHb levels at which the central nervous system is

¹ Work Psychology and Technology Divisions, Department of Occupational Medicine, National Board of Occupational Safety and Health, Stockholm, Sweden.

Reprint requests to: Tjlf laborator Francesco Gamberale, Kungl. Arbetarskyddsstyrelsen, Arbetsmedicinska avdelningen, Arbetspsykologiska enheten, Fack, 100 26 Stockholm 34, Sweden.

first affected has been the subject of contention (2, 13, 14, 15, 19, 20).

The objective of the present investigation was to study the extent to which man's cognitive and psychomotor reactions are affected by exposure to methylene chloride. The study was performed, where applicable, according to the same patterns as in previous studies (5, 6, 7, 8).

SUBJECTS

Fourteen healthy men from 20 to 30 years of age were used as subjects. They were all students or employees at the Department of Occupational Medicine.

METHOD

Experimental design

The subjects were divided at random into two equally large groups. Those in one group were studied individually first under experimental conditions with exposure to methylene chloride and then, 7 days later, under control conditions with exposure to ordinary atmospheric air. The subjects in the other group were studied under identical conditions, but in the reverse order. The two different conditions for individual subjects were started and concluded at the same times of day.

During experimental conditions subjects were exposed for four continuous 30-min periods to 870, 1,740, 2,600, and 3,470 mg/m³ of methylene chloride in inspiratory air. The increase in concentration after each 30 min period took place without any break in exposure. The mixture was supplied via a breathing valve with very slight resistance. The taste and smell of the gas was disguised by introducing a cannister containing menthol crystals into the tube leading to the mouthpiece. The concentration of methylene chloride in alveolar air was measured every third minute with gas chromatography.

The study was performed with the subject sitting in a comfortable chair at a desk. Four performance tests were carried out in the final 20 min of each exposure period and always in the same order. At given points in each performance test, subject heart rate was recorded with telemetric equipment (Medenik Hon-

eywell). The air did not contain any methylene chloride during control conditions. In other respects, all operations and measurements were made with the same equipment, in the same manner, and in the same chronological order as in experimental conditions. Thus alveolar air samples were also taken every third minute.

Information on each subject's perception of conditions was collected in the following manner. Immediately after the termination of exposure subjects were asked to assess their condition with respect to the following six variables: calm/hurried, active/passive, relaxed/tense, well-disposed/ill-disposed, unaffected/affected, and alert/tired. Assessments were facilitated with the aid of a 7-point evaluation scale on which extreme values were defined by opposites. After concluded exposure on the second day, all subjects were asked if they had been able to notice any difference between the two experiments in respect to the inspiratory air. The objective of this interview was to determine the extent to which the menthol disguise had been effective.

Performance tests

The following tests were performed in the following sequence during each period of exposure to both methylene chloride and pure air:

Numerical ability: RT Addition (RT = reaction time). The test was performed with the aid of a stimulus/response panel with which the lighting of stimulus lamps and subject responses were electronically recorded. Subjects were instructed to respond to the lamps by touching switches connected to the stimuli. The switches were numbered from 0 to 9 and located in the immediate vicinity of the stimuli, which were also numbered. The test was conducted by administering a series of three stimuli lasting 0.4 s at 0.1-s intervals on a panel. Subjects were instructed to add the numbers represented by the stimuli and to report the answer with the aid of the numbered switches. The sequence for the first 4 and the last 16 series varied at random between the different exposure periods. Performance was measured as the mean value of reaction times for the last 16 series.

Simple reaction time: Test 1. Equipment was the same as in the preceding test. However, this test only utilized one of the stimulus/response units. Subjects were instructed to respond to stimuli by pressing the switch as quickly as possible. The test consisted of a total of 96 stimuli distributed among 6 comparable series, each comprising 16 consecutive stimuli. Each series took about 1 min to perform, and the time elapsing between stimuli varied from 1.7–5.2 s. Performance was measured as the mean value of reaction times for all stimuli. The mean reaction time value for every 1-min time-block was also calculated for an analysis of the change in performance over time according to a method developed by Lisper and Kjellberg (12).

Short-term memory. The equipment was the same as in the preceding tests. The test was conducted so that a series of stimuli, which lasted 1 s, was administered at 1-s intervals on the panel. Subjects were instructed to touch the switches in the same sequence as the presentation as soon as a signal indicating the end of a series was given. Ten different series, in which the number of stimuli increased from 4 to 10, were administered to each subject. Response data were analyzed according to two criteria: 1. the number of correctly reproduced stimuli as a percentage of the total number of stimuli and 2. the number of correctly reproduced series as a percentage of the number of series.

Simple reaction time: Test 2. A manually controlled stimulus/response panel was used. Stimulation was visual, and responses were supplied by touching a switch. Reaction time was recorded with the aid of an electronic counter. Stimuli were administered at 10-s intervals, and an acoustic warning signal was supplied 3 s before the administration of each stimulus. A total of 30 stimuli were supplied in each trial. Performance was measured as the mean value of reaction times for the last 20 stimuli administered.

Thus two tests of simple reaction time were used in the present study. One of the tests, designated as Simple Reaction Time Test 1, was especially designed for the study of changes in performance during the 6-min duration of the test. Changes in performance over time have proved to be a useful and sensitive indicator of

fatigue or lack of sleep (12). The second test, termed Simple Reaction Time Test 2, proved to be the most sensitive of all tests used in our previous studies of solvents and was therefore also included in the present study.

The other two tests, RT Additions and Short-Term Memory, were used in the study of exposure to white spirit (5). However, the tests were modified somewhat prior to the present study so as to tailor them to the equipment used.

RESULTS

Concentration in alveolar air during exposure

The concentration of methylene chloride in alveolar samples taken during experimental conditions is shown in fig. 1. The dots in the figure are the mean values of the 14 subjects. Standard deviations varied from 14.8 to 19.9 % of the respective mean values. The figure shows that the increase in alveolar air concentration was greatest at the beginning of each exposure period when no performance measurements were made. The concentration of methylene chloride in alveolar air was found to correlate closely with the concentration in arterial blood (1). Thus it was possible to obtain a good approximation of the concentration of methylene chloride in arterial blood on the basis of alveolar air measurements during the four periods of exposure.

The relation between the concentration of methylene chloride in alveolar air and the concentration in arterial blood for one of the subjects in the physiological experiments is described in fig. 2. The maximal COHb concentration attainable was estimated at 5 % on the basis of the measurements of COHb performed during the physiological experiments (1).

Subjective perception of conditions

The interview results following the experiments were unequivocal. None of the subjects had been able to distinguish between exposure and nonexposure to methylene chloride. Thus disguising methylene chloride in the inspiratory air with menthol had been completely successful.

Fig. 1. Change in the concentration of methylene chloride in alveolar air during four exposure periods. The dots in the figure refer to the mean values of 14 subjects.

Fig. 2. Relationship between the concentration of methylene chloride in alveolar air and arterial blood. Data from one subject. (Product moment correlation: $r = 0.977$)

Fig. 3. The subjects' subjective evaluation of their own condition after exposure to methylene chloride and after control conditions. The point of intersection in the diagram refers to the mean values of 14 subjects for the respective variable.

Fig. 3 shows the results of the subjects' perception of their own condition after the experimental and control conditions, respectively. Subjects' assessment of their condition after exposure to methylene chloride differed systematically from the assessment made following control conditions. A statistical test of the differences between the two conditions was performed using the Wilcoxon matched-pairs signed-rank test (17). There were no statistically significant differences ($p > 0.05$) for any individual variable. However, a high level of significance ($z = 2.83$; $p < 0.005$) was obtained for the difference between conditions for the sum of the six variables. The results suggest that exposure to methylene chloride exerted a subjectively favorable change in the subjects' experience of condition.

Heart rate during exposure

As shown in fig. 4 heart rate, with few exceptions, was lower during exposure to methylene chloride than under control conditions. However, the differences between conditions were slight and not statistically significant when tested using an analysis of variance.

In other respects the subjects' heart rates varied in the same manner as in our previous studies on solvents (5, 6, 7, 8). Thus a systematic reduction in heart rate was found in repeated testing when the same performance test was used along with a variation in heart rate as a function of the nature of the performance tests. This reduction is the most readily apparent in fig. 4, in which heart rate on the different measurement occasions displayed the same mutual relationship between the different performance tests.

Performance changes during exposure

Table 1 and figs. 5, 6, 7, and 8 describe results for the groups' performances during experimental and control conditions, respectively. Figs. 5, 6, 7, and 8 show that in all four tests the change in performance values during exposure to the different methylene chloride concentrations did not differ systematically from the changes noted under control conditions. A statistical test of the significance of mean value differences between experimental and control conditions calculated for intrapair mean differences resulted in low, non-significant t -values ($p > 0.10$).

Fig. 4. Heart rate in different performance tests during exposure to methylene chloride (solid symbols) and under control conditions (open symbols). The entries in the figure are the mean values of 14 subjects.

Table 1. Mean values (M) and standard deviations (SD) for the performance tests of 14 subjects during exposure to varying concentrations of methylene chloride and under control conditions.

Performance test	Experimental conditions							
	Exposure 1		Exposure 2		Exposure 3		Exposure 4	
	870 ± 50 mg/m ³ M SD		1,740 ± 50 mg/m ³ M SD		2,600 ± 50 mg/m ³ M SD		3,470 ± 50 mg/m ³ M SD	
RT Additions (s)	1.38	0.34	1.34	0.35	1.36	0.34	1.36	0.44
Simple Reaction Time Test 1 (ms)	252	35.3	268	45.4	271	33.8	272	38.2
Short-Term Memory (criterion 1) ^a	88.2	6.78	89.0	7.02	89.0	6.30	90.2	5.49
(criterion 2)	40.7	19.4	48.6	18.3	45.7	18.7	47.1	20.9
Simple Reaction Time Test 2 (ms)	224	35.1	217	29.8	222	31.6	218	27.8
Performance test	Control conditions							
	Exposure 1		Exposure 2		Exposure 3		Exposure 4	
	Air M SD		Air M SD		Air M SD		Air M SD	
RT Additions (s)	1.36	0.49	1.31	0.47	1.32	0.57	1.30	0.52
Simple Reaction Time Test 1 (ms)	251	34.2	271	39.5	276	43.4	266	36.8
Short-Term Memory (criterion 1) ^a	87.4	7.93	89.1	7.24	91.5	4.89	89.1	5.77
(criterion 2)	47.1	17.3	47.1	18.2	49.3	15.4	47.1	14.9
Simple Reaction Time Test 2 (msec)	221	33.7	222	26.2	230	41.2	218	31.4

^a Criterion 1: the number of correctly reproduced stimuli as a percentage of the total number of stimuli; criterion 2: the number of correctly reproduced series as a percentage of the total number of series.

As expected from the findings of Lisper and Kjellberg (12), there was, under both conditions, a natural decrease in the subjects' reaction time over the 1-min time-blocks (fig. 6). However, no differences between conditions could be found in the rate of decrement. The decrement of the subjects' reaction time over the 1-min time-blocks was most pronounced in exposure periods 1 and 2 and less pronounced in the following two exposure periods. This latter result was probably due to some sort of training effect, which counteracted the decrement in performance over time.

The standard deviation for the 96 and 20 stimuli, respectively, in the two simple reaction time tests was calculated for each subject. The objective of these calculations

was to obtain individual measures of the regularity of response on the two tests. Since the standard deviations can vary with the level of performance, they were also calculated as the percentage of each respective mean value.

Both variation measures tended to increase with increasing exposure to methylene chloride as compared to control conditions. However, a statistical test of significance disclosed that the differences between conditions were only significant for Simple Reaction Time Test 1 in exposure period 4 ($t = 2.44$ and 2.55 , respectively; $p < 0.05$). Thus exposure to the highest concentration of methylene chloride affected subject reactions in at least one of the reaction time tests. However,

Fig. 5. Change in mean performance values in the RT-Addition test with a varying degree of exposure to methylene chloride (solid symbols) and under control conditions (open symbols).

this effect was manifested in greater unevenness in subject performance without any change in average reaction time.

DISCUSSION

The objective of the present investigation was to study psychological functions in man during exposure to the solvent methylene chloride. A similar experimental design was employed as in our previous studies of the solvents toluene (6), methylchloroform (7), styrene (8), and white spirit (5). These studies examined performance changes and subjective reactions during exposure to concentrations close to the threshold limit value for each substance. In the present investigation subjects were exposed for a total of 2 h to concentrations of methylene chloride corresponding to 50, 100, 150 and 200 % of the threshold limit value (500 ppm, i.e., 1,740 mg/m³). Subject performance was studied with respect to reaction time, short-term memory, and numerical ability.

Fig. 6. Change in mean performance values in Simple Reaction Time Test 1 with a varying degree of exposure to methylene chloride (solid symbols) and under control conditions (open symbols).

Fig. 7. Change in mean performance values in the Short-Term Memory test with a varying degree of exposure to methylene chloride (solid symbols) and under control conditions (open symbols).

Fig. 8. Change in mean performance values in Simple Reaction Time Test 2 with a varying degree of exposure to methylene chloride (solid symbols) and under control conditions (open symbols).

Reaction time was studied using two different tests. One of the tests was identical to the one which proved to be especially sensitive to exposure effects in previous studies of solvents. The second test was especially adapted to the study of performance changes over time.

As in our previous studies on solvents the measures adopted to disguise exposure proved to be effective. No subjective symptoms were reported by subjects during interviews after the experiment.

According to the questionnaire, however, subject assessment of their condition after exposure differed systematically from assessments made after control conditions. The results suggest that exposure to the solvent had a certain perceptually positive effect on the subjects' experiences.

No statistically significant impairment in the performance of studied functions could be observed during the 2 h of exposure to methylene chloride as compared to control conditions. However, exposure to the highest concentration, i.e., 1,000 ppm or 3,480 mg/m³, produced certain indications pointing to a commencing detrimental effect of the solvent. Thus performance on one of the tests of reaction time, despite

unchanged average performance, was found to be significantly more irregular during exposure than under control conditions. A similar change in psychomotor behavior was observed by Gamberale and Svensson (9) in anesthetic nurses exposed to low concentrations of anesthetic gases.

An analysis of the results as a whole suggests that brief exposure to the solvent methylene chloride at concentrations at or immediately above the present Swedish threshold limit value has no detrimental effect on man's psychomotor and cognitive functions.

In the present study, during exposure subjects attained a COHb level approaching 5 %. Thus the results also suggest that a COHb level of this magnitude does not have a detrimental effect on the studied functions.

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