

Experimental exposure to toluene in combination with ethanol intake

Psychophysiological functions

by Anders Iregren, MSc,¹ Torbjörn Åkerstedt, PhD,² Birgitta Anshelm Olson, MSc¹
Francesco Gamberale, PhD¹

IREGREN A, ÅKERSTEDT T, ANSHELM OLSON B, GAMBERALE F. Experimental exposure to toluene in combination with ethanol intake: Psychophysiological functions. *Scand J Work Environ Health* 12 (1986) 128—136. Effects of experimental exposure to toluene (3.2 mmol/m³, ie, 300 mg/m³) for 4.5 h and ethanol ingestion (15 mmol/kg) on the results of four performance tests, symptoms, mood, and physiological indices of wakefulness were studied in 12 male volunteers. Toluene exposure produced symptoms like headache and local irritation, as well as a weak depression of heart rate during rest, but did not reduce performance capability. Ethanol ingestion impaired performance on two of the tests and also increased heart rate. Mood was likewise altered by ethanol, but no increase in subjective symptoms due to ethanol ingestion could be demonstrated. Physiological indices of wakefulness were not affected by toluene exposure or by ethanol intake. No interaction effects were found.

Key terms: performance, reaction time, symptoms, threshold limit value.

Acute narcotic effects on central nervous system (CNS) functions from exposure to organic solvents have long been established and during the last few decades, for many agents, systematically studied. Long-term effects of solvent exposure have also been reported from a large number of investigations. Recent reviews have been made by Anshelm Olson (4) and Gamberale (12).

Many of the investigations have been performed on workers exposed to mixtures of solvents, eg, house painters and spray painters (9, 14, 15, 20). On the basis of results from these studies, and the results from investigations of workers exposed to a single solvent, eg, rotogravure printers (17), it has been proposed that at least part of the effects of the solvent mixtures could be due to potentiating interactions.

Since many of the solvents are metabolized through the same enzyme system, interactions are conceivable. For some combinations of agents, ie, methyl ethyl ketone with methyl n-butyl ketone and trichloroethylene with styrene, potentiating effects of the interaction on the peripheral nervous system and the sensory organs have been demonstrated in animal experiments (7, 22, 23).

In human subjects CNS effects of interaction between ethanol and many pharmaceuticals are well known. (See, eg, references 19, 26.) Since consump-

tion of ethanol is common, simultaneous exposure to ethanol and toxic agents at the workplace is possible. Although possible interactions between these agents might have implications both for workplace safety and productivity, only a few investigations on interactions of this type have been performed.

Ferguson & Vernon (11) investigated the effects of exposure to 300 and 1 000 ppm (ie, approximately 1 500 and 5 000 mg/m³) of trichloroethylene in combination with ethanol intake (35 ml/70 kg). They concluded that low blood levels of alcohol markedly augmented the adverse effects of trichloroethylene on performance, and the effects seemed to be additive. Stewart and co-workers (27) studied effects of perchloroethylene (25 and 100 ppm, ie, approximately 175 and 700 mg/m³) and ethanol ingestion (0.75 and 1.5 ml/kg). No effects of perchloroethylene were found, nor were there any interactions.

The effects of ethanol intake (0.35 g/kg) and exposure to 200 ppm (1 000 mg/m³) of trichloroethylene were reported by Windemüller & Ettema (30). They found simultaneous exposure to ethanol and trichloroethylene to have more pronounced performance effects than exposure to either agent separately. Savolainen (25) investigated the effects of ethanol ingestion (0.4 and 0.8 g/kg) and xylene exposure (6.0 and 11.5 mmol/m³, ie, approximately 600 and 1 200 mg/m³) and to a combination of both. At the higher concentration of xylene, performance on psychological tests tended to deteriorate, and a dose-related decrement in performance was observed after the consumption of ethanol. The effects of the combination of xylene and ethanol were additive.

¹ Research Unit of Psychophysiology, National Board of Occupational Safety and Health, S-171 84 Solna, Sweden.

² National Institute for Psychosocial Factors and Health, and the Karolinska Institute, S-104 01 Stockholm, Sweden.

Reprint requests to: Mr A Iregren, Research Unit of Psychophysiology, National Board of Occupational Safety and Health, S-171 84 Solna, Sweden.

A significant deterioration with alcohol, and a tendency for performance and mood to deteriorate more when alcohol and toluene were administered together, were found by Cherry and co-workers (6), who studied the effects of exposure to 80 ppm (300 mg/m³) of toluene and alcohol intake (0.4 g/kg) separately and in combination.

The present investigation was carried out to study the effects of toluene exposure and ethanol intake, separately and in combination, on psychological test performance, symptoms, mood, and physiological indices of wakefulness.

Subjects and methods

Subjects

Twelve men aged 22–44 years and weighing 64–86 kg volunteered as subjects. They all received a thorough medical examination before the exposure, and they were carefully informed about the experiment. Information was given about the maximal exposure levels to be used, but the subjects were unaware of the actual exposure levels, as well as of the order between the conditions. They were all moderate users of alcohol.

Exposure chamber

The exposure sessions were carried out in a 11.5-m³ chamber (1.8 × 2.8 × 2.28 m). The temperature was kept constant at 24°C, and the airflow to the chamber was 115 m²/h.

Experimental design

The order of the exposure conditions was balanced according to a 4 × 4 Latin square. See table 1. The exposure conditions used were toluene, ethanol, a combination of toluene and ethanol, and a control condition. Thus each subject acted as his own control in a repeated measurement design, according to which the subjects were randomly assigned to the exposure groups. The interval between the exposure sessions was 14 d, and the sessions were always carried out on the same day of the week for any subject. The subjects were exposed individually in the chamber. Under the toluene and control conditions a small amount of ethanol (1 ml) was added to the surface of each drink to give a smell of alcohol. No attempt was made to mask the presence of toluene.

The level of toluene exposure corresponded to the Swedish occupational standard, 3.2 mmol/m³ (300 mg/m³). The amount of ethanol was individually determined and corresponded to 15 mmol/kg of body weight (ie, approximately 150 ml of 40 % ethanol at 70 kg). The ethanol was diluted in orange juice and served with ice; it was consumed in about 15 min. The toluene exposure lasted a total of 4.5 h, and the ethanol

dose was administered after 70 min of exposure. This interval was chosen to produce maximum blood levels of toluene and ethanol at the same time. To achieve good control of the ethanol uptake, the subjects were given a light standardized breakfast before entering the exposure chamber.

The subjects carried out a battery of four performance tests three times within each exposure occasion. The first test session was performed immediately before the onset of exposure, and the other two sessions were carried out after 2 and 3.5 h of exposure. The time for the second testing was chosen to coincide with the maximal concentration of toluene and ethanol in the blood.

On the day before the first exposure occasion, each subject attended a training session, containing extensive information about the experiment and test routines, as well as two repetitions of the performance test sequence.

The heart rate (HR), electroencephalographic (EEG), and electrooculographic (EOG) recordings were made continuously during the exposure. On four occasions during each exposure session these registrations were performed under standardized conditions, to facilitate the interpretation of the EEG data. Communication with the subjects during the experiment took place via telephone.

Performance tests

A microcomputer (ABC800, Luxor AB, Motala, Sweden) was used to administer the automated performance tests. The equipment included a computer with a dual disc drive, a printer, a reaction-time panel with adapter, an external millisecond clock, and a modified numerical keyboard.

After the training session the tests were self-administered, and the subjects were told via the telephone to start a test sequence. The computer then provided the instructions, administered the test items, registered the responses, and stored the results automatically. The experimenter surveyed the testing on the printer, which was placed outside the exposure

Table 1. Order of the four exposure conditions in the subgroups: toluene (3.2 mmol/m³ or 300 mg/m³), ethanol (15 mmol/kg), combination of toluene and ethanol, and control condition.

Day	Exposure condition			
	Group 1 (N = 3)	Group 2 (N = 3)	Group 3 (N = 3)	Group 4 (N = 3)
1	Control	Toluene	Ethanol	Toluene + ethanol
2	Toluene	Control	Toluene + ethanol	Ethanol
3	Ethanol	Toluene + ethanol	Control	Toluene
4	Toluene + ethanol	Ethanol	Toluene	Control

chamber. The performance tests were administered in the order that follows.

Choice reaction time (CRT). A cross (105×95 mm) having one arm slightly shorter than the others was displayed on the screen. The items were of three levels of difficulty, the arms having been reduced by 5, 10, or 15 mm. The subject's task was to indicate, as rapidly as possible, which arm of the cross had been shortened. A specially designed response panel, a keyboard with only five keys, made it possible for the subject to reply without having to divert his attention from the screen. The five keys comprised one centrally positioned key, which was the resting position, and four keys placed analogously to the arms of the cross. All combinations of direction and the level of difficulty were randomly distributed within each sequence of 12 stimuli. Reaction time was measured for 144 presentations in the test, and the stimuli were presented at fixed intervals of 4 s, for a total test time of about 10 min.

Simple reaction time (SRT). The simple reaction-time task was to press a button as quickly as possible when a light came on. A total of 176 stimuli were administered during 11 min at intervals varying between 2.5 and 5.0 s. The first minute served as practice, after which performance capacity was assessed for 10 min.

Color-word vigilance (CWV). In the color-word vigilance test, constructed especially for this study, one of the Swedish words for "red," "yellow," "white," or "blue" was presented on the screen. These words were chosen because in Swedish they are all three-letter words. The word could be written with text in any one of the colors. The task was to press a button as fast as possible when there was congruency between the meaning of the word and the color of the text. The interval between consecutive stimuli was fixed at 2 s, and the 16 possible combinations of words and colors were randomly distributed within each sequence of 16 stimuli. The total testing time for 256 items was about 8 min.

Memory reproduction (MR). In the test for memory reproduction 17 series of alternating letters and figures were presented on the screen. The number of characters for each series was gradually increased from four to eight. Each series was presented for 4 s, after which the subject was required to repeat it on the keyboard during the ensuing response time of 17 s. Data were analyzed with respect to the number of correctly reproduced elements (maximum 94).

Symptoms and mood

After the two first tests in each testing sequence the subjects rated the extent to which they experienced

specific symptoms, which were nausea, headache, or irritation of the eyes, nose or the respiratory tract, using the following four response categories: no, negligibly, slightly, quite considerably.

The subjects also rated their mood with respect to six different dimensions, ie, with respect to being "bored," "not concentrating," being "stressed," being "sleepy," being "irritated," and being "intoxicated." The rating scales ranged from -10 (less than normally) to +10 (more than normally). For the dimension "intoxicated," the scale ranged from 0 to +10.

Physiological registrations

During the exposure sessions the subjects carried a small four-channel tape recorder (Medilog, Oxford Instruments), which continuously recorded HR, EEG and EOG. A fourth channel registered the time during the experiment, and on it the subject also indicated special events, such as performance tests or periods for standardized physiological registrations.

HR electrodes were placed in standard positions on the chest, and the EEG electrodes were placed in positions Cz and Oz according to the international 10-20 system. The electrodes registering eye movements were placed diagonally across the left eye, to allow for registration of eye movements both horizontally and vertically. Two reference electrodes were applied, one on the left ear and one on the skull bone directly behind the left ear.

These physiological measures were recorded continuously during the experimental sessions, and at four occasions during each exposure session registration was performed during standardized conditions. Two of these occasions consisted of 5 min of focusing on a black dot on the chamber wall, immediately followed by 2 min with the eyes closed. The other two occasions were two 10-min sleep latency tests, in which the subjects were instructed to lie down comfortably, relaxing with the eyes closed (1). One period of each type was performed at the beginning of the exposure, ie, before the subject consumed the ethanol dose, and one period of each type towards the end of exposure after the ingestion of the ethanol.

Electroencephalographic data

The EEG recording was subjected to spectral analysis (fast Fourier transformation) in 15-s intervals. The result was integrated across the delta (0.5-3.9 Hz), theta (4-7.9 Hz), and alpha (8-11.9 Hz) bands. The obtained spectral power density was then averaged across the 5 min with open eyes and across the 2 min with closed eyes. For the sleep latency test the spectral analysis only served as an aid in detecting sleep onset and was combined with the traditional sleep-stage scoring procedure (24).

Statistical analysis

The exposure effects on the performance tests and physiological measures were evaluated with the analysis of variance (ANOVA). The ANOVA model was adapted to a 4 × 4 Latin square design with repeated measurements between and within the exposure occasions (29). Since the first performance measurement each day was performed before the onset of exposure as a base-line measurement, the analysis of data from the tests was based on differences between the two subsequent measures and the base-line value.

Two additional analyses of variance were performed to evaluate any possible effects of repeating the performance tests. Data from the conditions in which no performance effects of exposure were found were used to analyze the differences due to repetition within an exposure occasion, and data from the base-line measurements were used to evaluate the differences due to repetition over exposure occasions.

Results from the questionnaire evaluating mood differences and symptoms were analyzed with the Friedman two-way analysis of variance by ranks (10).

The results from the performance tests are presented graphically as Z diagrams. The standardized mean scores (ie, Z-values) have been calculated according to the formula $Z = \pm (\bar{X}_e - \bar{X}_b) / S_b$, where $\bar{X}_e$ is the mean value of the performance variable for a measurement during exposure, $\bar{X}_b$ is the mean value of the base-line measurement on the same day, and S_b is the standard deviation of the performance variable calculated on all values from the base-line measurements.

The Z-values have then been adjusted so as to make the data from the control condition to appear as zero in the diagrams, and a negative value always represents a poorer performance.

Results

Choice reaction time

The results from the choice reaction-time test, which are presented in figure 1 and table 2, revealed no significant effects of exposure, nor were there any interactions.

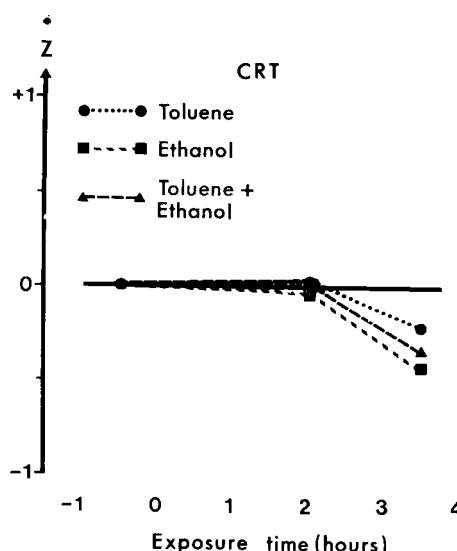


Figure 1. Differences between the base-line and subsequent measurements of choice reaction time (CRT) during the various exposure conditions in relation to the control condition. The differences are expressed as standardized mean scores (ie, Z-values). See the Methods section for the calculation of the Z-values.

Table 2. Test performance over the different exposure conditions and on the three measurement occasions (1 = base line, 2 = after 2 h of exposure, and 3 = after 3.5 h of exposure)

Test/variable	Exposure condition											
	Control			Toluene			Ethanol			Toluene + ethanol		
	1	2	3	1	2	3	1	2	3	1	2	3
Choice reaction time												
Mean	697	714	713	690	711	733	725	750	795	699	719	757
SD	104	102	102	92	106	112	129	121	145	114	118	149
Simple reaction time: level												
Mean	269	274	278	277	275	276	274	312	319	272	298	312
SD	45	44	52	61	48	46	63	66	65	61	59	64
Simple reaction time: variation												
Mean	69	71	75	70	72	73	69	88	98	62	77	97
SD	35	31	29	34	28	25	39	44	35	36	29	32
Color-word vigilance												
Mean	530	517	518	520	516	510	531	551	537	533	546	539
SD	26	26	27	33	35	35	31	39	37	41	34	36
Memory reproduction												
Mean	85	87	87	85	86	85	85	85	87	83	85	86
SD	4.8	4.0	3.8	5.1	4.2	5.1	5.5	5.8	5.2	7.7	4.9	5.6

Simple reaction time

Simple reaction time was evaluated with respect to mean performance level, as well as with respect to variation in performance. Both the level and variation in performance changed significantly between the exposure conditions ($F_{3,24} = 5.63$, $p < 0.01$, and $F_{3,24} = 3.31$, $p < 0.05$, respectively).

As can be seen from figures 2 and 3 and table 2, these effects were solely due to ethanol ingestion, since

there was no effect of toluene exposure per se. The increase in the reaction-time level was about 10 %, while the increase in variation was close to 30 %. There were no indications of interaction effects.

Color-word vigilance test

As can be seen from figure 4 and table 2, the performance on the color-word vigilance test was signifi-

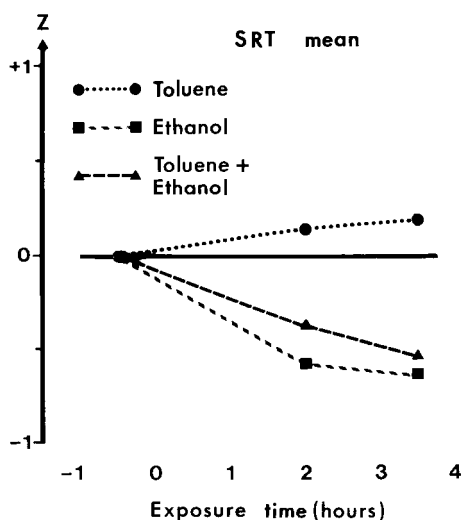


Figure 2. Mean performance level on the simple reaction-time (SRT) test. Differences between the base-line and subsequent measurements during the various exposure conditions in relation to the control condition. The differences are expressed as standardized mean scores (ie, Z-values). See the Methods section for the calculation of the Z-values.

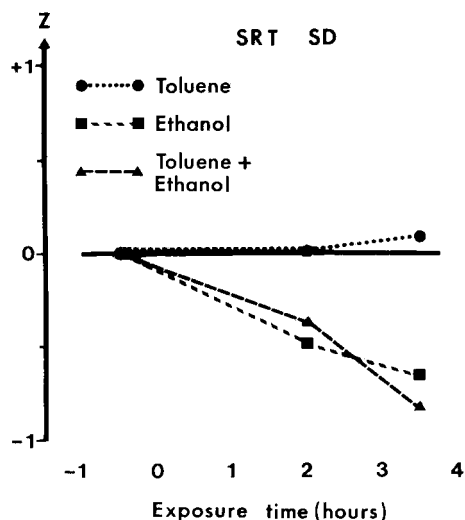


Figure 3. Variation of performance on the simple reaction-time (SRT) test. Differences between the base-line and subsequent measurements for the various exposure conditions in relation to the control condition. The differences are expressed as standardized mean scores (ie, Z-values). See the Methods section for the calculation of the Z-values.

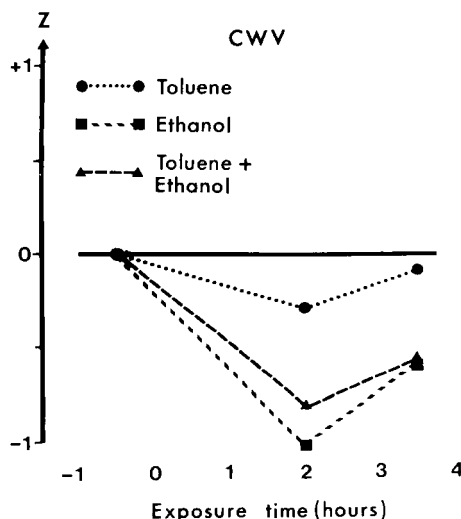


Figure 4. Differences between the base-line and subsequent measurements of reaction times on the color-word vigilance (CWV) test for the various exposure conditions in relation to the control condition. The differences are expressed as standardized mean scores (ie, Z-values). See the Methods section for the calculation of the Z-values.

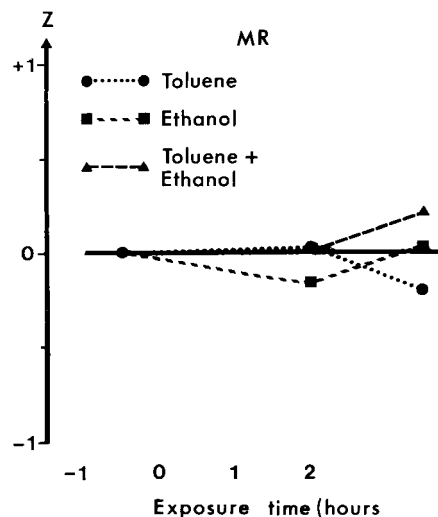


Figure 5. Differences between the base-line and subsequent measurements on the memory reproduction (MR) test for the various exposure conditions in relation to the control condition. The differences are expressed as standardized mean scores (ie, Z-values). See the Methods section for the calculation of the Z-values.

cantly affected by ethanol intake ($F_{3,24}=6.18$, $p<0.01$). After ethanol intake the reaction time on this test increased about 5 %. There were no effects from toluene exposure, nor any effects of interaction.

Memory reproduction

No significant effects could be demonstrated on the memory reproduction test. The results from this test are presented in figure 5 and table 2.

Effects of motivation and learning

According to the additional analyses of variance there were no significant effects of repetition on the simple reaction-time test. A 5 % decrease in reaction time on the choice reaction-time test with repeated measurements over the exposure occasions was found in the analysis of the base-line measurements ($F_{3,33}=4.22$, $p<0.05$). The analyses of effects of repeating the color-word vigilance test revealed a 3 % increase in reaction time over the base-line measurements ($F_{3,33}=3.46$, $p<0.05$) and a 2 % decrease in reaction time within the exposure occasions ($F_{2,20}=5.01$, $p<0.05$).

Heart rate

The HR data, which are presented in figure 6 and table 3, were analyzed separately for each of the different performance tests and for the sleep latency test. Significant effects of exposure on HR were found during all of these tests. For the performance tests ethanol intake was found to increase HR by 2 to 6 beats/min (p -values in the range $0.05 < p < 0.01$). During the sleep latency tests the effect of exposure was also significant ($F_{3,21}=3.43$, $p<0.05$).

There was also a significant decrease in HR over the exposure days. This decrease, which varied between 1 and 2.5 beats/min, was present during all of the tests, and the p -values were between 0.01 and 0.001.

Electroencephalographic data

No significant effects of exposure could be demonstrated with the data from the spectral analysis of the EEG registrations. See table 4.

Sleep latencies

The sleep latencies, where the mean values varied between 4.3 and 6.2 min for the different exposure conditions, were not significantly affected by either exposure or repetition of the measurements.

Symptoms

As shown in figure 7, significantly more subjects reported symptoms during toluene exposure alone and toluene exposure in combination with alcohol intake, as compared to the control condition. This increased symptom rate held for the single symptom "headache" separately (chi square 10.05, $p<0.05$) and for the summation of symptoms (chi square 9.70, $p<0.05$). These differences were due to toluene exposure, while the increase in reported symptoms during ethanol exposure was small.

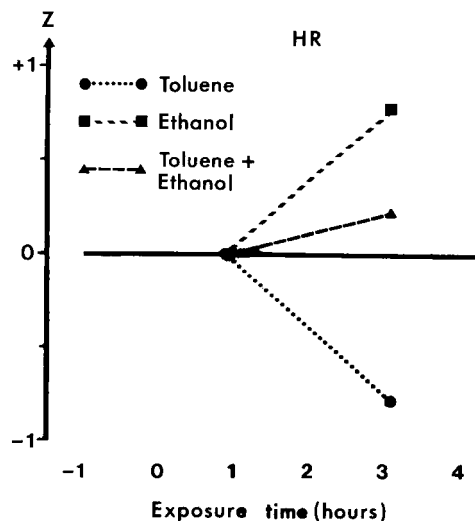


Figure 6. Heart rate (HR) during the sleep latency tests. Differences between the initial and the following measurement for the various exposure conditions in relation to the control condition. The differences are expressed as standardized mean scores (ie, Z-values). See the Methods section for the calculation of the Z-values.

Table 3. Heart rate (beats/min) over the different tests, exposure conditions and measurement occasions (1 = base line, 2 = after 2 h of exposure, and 3 = after 3.5 h of exposure)

Test/variable	Exposure condition											
	Control			Toluene			Ethanol			Toluene + ethanol		
	1	2	3	1	2	3	1	2	3	1	2	3
Choice reaction time	67	60	63	67	60	63	64	61	68	65	63	68
Simple reaction time	66	65	62	67	66	63	63	66	65	69	68	64
Color-word vigilance	66	67	61	67	65	60	63	67	65	65	71	67
Memory reproduction	68	70	64	68	67	63	67	72	66	67	73	69
Sleep latency	50	54	.	55	54	.	52	61	.	50	56	.

Table 4. Results from the fast Fourier transformations of the electroencephalographic registrations. The data are expressed in arbitrary units, and the number of subjects, the means, and the standard deviations for the theta and alpha bands are presented separately for the different exposure conditions, for registrations with the subjects' eyes open and closed, and for the measurement occasions (1 = base line and 2 = after 3 h of exposure)

Variable	Exposure condition											
	Control				Toluene				Ethanol			
	Open		Closed		Open		Closed		Open		Closed	
	1	2	1	2	1	2	1	2	1	2	1	2
Theta												
Number	9	10	10	10	10	10	9	9	8	8	8	8
Mean	8	10	14	13	11	9	11	12	6	9	10	13
SD	10	11	15	12	15	11	8	10	5	5	6	7
Alpha												
Number	8	10	10	10	10	10	9	9	7	8	8	8
Mean	8	9	25	20	14	12	28	30	12	13	29	26
SD	9	10	22	15	19	20	19	25	14	14	29	28

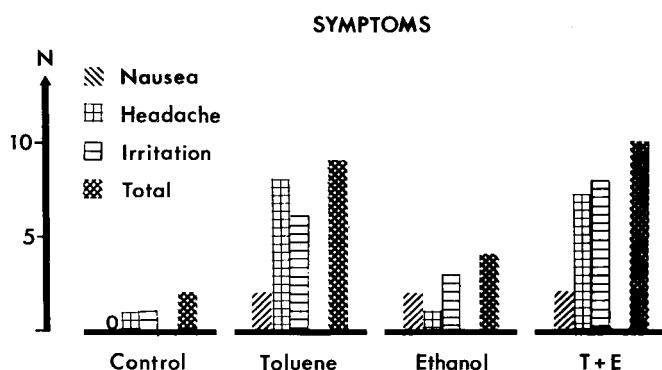


Figure 7. Number of subjects reporting an increase in symptoms during the different exposure conditions. (T + E = toluene + ethanol).

Mood

The analysis of the mood ratings showed no differences with respect to feeling "bored," "not concentrating," feeling "stressed," feeling "sleepy," or feeling "irritated." There was a highly significant difference with respect to feeling "intoxicated" (chi square 24.32, $p < 0.001$) in conjunction with ethanol ingestion.

Blood alcohol levels

The maximum blood levels of ethanol varied between 12 and 25 mmol/ml with a mean value of 16, which corresponds to approximately 0.09 ‰. (See reference 28 for detailed information on the blood alcohol and blood toluene levels.)

Discussion

The present investigation was designed to study the acute effects on performance, physiological measures of wakefulness, symptoms, and mood during exposure to a toluene concentration corresponding to the Swedish occupational standard and after ingestion of ethanol, as well as possible interaction effects of these exposures.

Exposure to toluene for 4.5 h at 3.2 mmol/m³ (300 mg/m³) was not found to affect the performance on any of the tests used. This finding is in accordance with the results of previous investigations (3, 5, 6). In studies in which performance effects of toluene have been demonstrated, the toluene exposures have been markedly higher than in the present experiment (13, 16).

The moderate ethanol dose given did result in gross performance changes on two of the tests, ie, simple reaction time and color-word vigilance. For the simple reaction-time test both the level and variability of performance increased markedly. These findings are also in accordance with results from previous investigations, as, for example, in the study by Cherry and co-workers (6), in which still lower blood alcohol levels led to performance deterioration.

HR proved to be sensitive to exposure, both to toluene and to ethanol. Interestingly, toluene seems to have a small narcotic effect even at the present low exposure level, as demonstrated by the depression of HR during the sleep latency test. However, this depression must be weak, as it disappeared when the mental load on the subjects increased during the performance testing.

Ethanol intake had an opposite effect on HR, increasing it by 2 to 6 beats/min during the testing following the ingestion of the ethanol dose. This increase in HR is also in accordance with the results of earlier investigations (eg, reference 21).

Previous studies have indicated a slowing of alpha dominant frequency and/or an increase in alpha amplitude during the first hour after alcohol ingestion (8, 18). The significance of these changes is, however, not known. The present use of EEG parameters aimed at measuring effects on alertness, and the second measurement was positioned 2 h after ingestion. A reduction of alertness during the test session would have been seen as an increase in power density in the theta band with the subjects' eyes open and closed or as an increase in the alpha band with their eyes open and/or a decrease with their eyes closed (2). None of these changes occurred. Similarly, sleep latency was not affected. These, together with the lack of increase in sleepiness ratings, clearly indicate that the ingestion of alcohol (or exposure to toluene) did not affect alertness, at least not when measured 2 h after ingestion.

The symptoms and mood ratings proved to be affected by exposure. Under conditions with toluene exposure there were increases in reported headache and a tendency to experience more local irritation. Ethanol intake did not have any impact on these measures. On the other hand, ethanol greatly affected rated intoxication, but toluene did not. The other mood ratings were not affected. According to these data it should be more effective to use symptom ratings in the study of solvent effects, while ratings of mood seem to be more useful for studies of ethanol effects.

Two of the performance tests appeared to be sensitive to repetition of the measurement, ie, the tests of choice reaction time and color-word vigilance. Thus performance on the choice reaction-time test improved over the exposure occasions. This improvement was probably due to training effects, since it tended to be larger for the more difficult items. With this test, there was also a tendency towards poorer performance with repeated measurements during the day, which was possibly caused by increasing mental fatigue or decreasing motivation. For the color-word vigilance test, on the other hand, performance improved slightly during the exposure sessions. This improvement might have been due to increasing arousal during the day. But, then again, performance declined over the exposure sessions. This decline could hardly be caused by increasing mental fatigue, but rather by diminishing motivation on the part of the subjects.

Although there were no effects of toluene on performance or EEG measures at the present exposure level, toluene produced irritation and headache in the majority of the subjects. There was also an indication of narcotic effects of toluene even at this low exposure level, since HR during rest was somewhat lower during the toluene exposure than during the control condi-

tion or after ethanol intake. Ethanol ingestion, on the other hand, was associated with a clear deterioration of performance on two of the tests used. It did not have any effect on symptoms, but clear effects on mood ratings were found.

There were no indications of any combined effects of toluene exposure and intake of ethanol. This result is consistent with previous findings (6).

To conclude, while a moderate dose of ethanol produced markedly lowered performance levels, as well as mood changes, 4.5 h of toluene exposure at levels corresponding to the Swedish exposure limit (3.2 mmol/m³ or 300 mg/m³) produced only slight symptoms of discomfort and local irritation among some of the exposed subjects. These results are also in accordance with those of previous studies (3, 5, 6).

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