An investigation of the acute behavioural effects of styrene on factory workers

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ABSTRACT A group of men exposed to styrene in a factory building glass-fibre boats performed a series of behavioural tests at the beginning and end of their shift, and the results were compared with those of a referent group from the same factory. Changes in mood were noted in both groups of workers but were greater in the exposed men; moreover, the change in mood was correlated with blood styrene concentration. In the styrene workers the morning reaction time was slower than that for the referents. During the day the reaction time of the men with low blood styrene concentration ($\leq 5.4 \mu\text{mol/l}$) speeded up and in the afternoon was similar to that of the referents; the reaction time for the men with high blood styrene concentration ($\geq 5.5 \mu\text{mol/l}$) was unchanged. Data taken from a questionnaire indicated that the men exposed were much more likely than was the referent group to report feeling unduly tired. They also reported feeling more tired on Friday night than Monday night, suggesting that the styrene might have a cumulative effect through the week.

In recent years there have been several reports that volatile organic solvents may produce behavioural changes. Gamberale, in his review,¹ listed over a dozen solvents for which he considered there was good evidence for adverse behavioural effects. Styrene with, in Britain, a threshold limit value of 100 parts per million is included in the list, the more convincing evidence coming from subjects exposed to high concentrations. Exposure-chamber studies with styrene, for example, have shown that at relatively high concentrations ($\geq 350 \text{ ppm}$) there is a significant slowing in reaction time²; it may be that other performance tests are also adversely affected, some workers reporting they are,³ others that they are not.²

Studies of workers exposed to styrene in the field have also shown that reaction time may be prolonged,^{4,5} that there may be disturbance in visuomotor accuracy,⁶ and that there may be an increased reporting of so-called pre-narcotic symptoms, including dizziness, nausea, fatigue, and

difficulties in concentration.⁷ The slowing in reaction time has been shown in one study at least⁵ to be related to the duration of exposure, but there is some preliminary evidence⁸ that it may recover when exposure is discontinued.

The present study was set up in April 1979 to determine whether a short series of tests, acceptable to men working in British industry, could detect acute changes in performance of the type reported elsewhere.

Material and methods

SUBJECTS

All the men in the study were employed in a factory building glass-fibre boats. The hulls of the boats are built in moulds by spraying a mixture of resin and glass fibre that is then rolled on the mould by hand. Two men, a sprayer and a roller, work together on each mould. Styrene is used as the solvent for the resin and exposure to the vapour occurs both during spraying and rolling. The pattern of work is such that most spraying and rolling is done during the morning to allow suf-

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ficient time for the resin to cure so that the hull can be released the next day.

Of the 30 men exposed to styrene, 29 volunteered to take part in the study. In fact only 27 were finally included as one left the company and one was absent from work on the day he was due to be tested. A referent group was also tested, 27 volunteers of much the same age as the exposed group being taken from the area of the factory where the boats were fitted out. The mean age of the exposed group was 23, and of the referents 26. Biographical information obtained by questionnaire (see below) suggested that the exposed and referent groups had a similar level of academic attainment, about half of each group having taken some examination, all at a low level, while at school.

TESTING PROCEDURE

Each man in the study completed a set of tests at the beginning (0730) and end (1630) of his shift. The tests were all conducted on a Monday to allow as much styrene as possible to be eliminated over the weekend—the half-life of styrene in the blood being about 16 hours. On the Friday afternoon before testing, the men were given a practice run on all the tests to reduce problems associated with learning. Because testing could only be carried out in small groups and the results are susceptible to time-of-day effects, test sessions were conducted on five consecutive Mondays.

Six tests were used to measure different aspects of performance. The reaction time test was one of unprepared simple reaction time (R T Wilkinson and D Houghton, in preparation) to a visual stimulus presented at intervals randomly from 3 to 12 seconds. The response was to press a button as quickly as possible, the test lasting 10 minutes. This apparatus has been used in several studies—for example, in examining the effects of sleep deprivation.⁹

A vigilance task (after Kappauf and Powe¹⁰) was also given, the subject being required to check a page of printed numbers against numbers read at speed on a tape recording. The test lasted seven minutes during which time ten errors could have been seen. There were six versions of the sheet of printed numbers with the errors distributed at random. Each man was allocated a different sheet in the morning and afternoon.

Digit-symbol substitution and forward and backward digit-span tests, derived from the Wechsler Adult Intelligence Scale, were also administered, different versions being used for the two test sessions. The digit-span tests were conducted using a prerecorded tape to ensure uniformity of delivery. Motor function was tested by asking the men to tap a pencil as quickly as possible for one minute;

the test was recorded on tape for subsequent analysis.

Finally, the men were asked to complete visual analogue scales¹¹ that reflected their feelings of physical and mental tiredness, general health, and sleepiness.

QUESTIONNAIRE

During the Friday introductory session, each man was given a questionnaire to be completed during the weekend and returned on Monday morning. The questionnaire was designed to provide information on age and level of educational achievement (to compare the two groups), length of exposure to solvents, long-standing neurological disorders, state of present health, and use of drugs and alcohol. In addition the men were asked about selected symptoms during the past 12 months. The list of symptoms was compiled from those previously reported as being related to solvent exposure; certain other symptoms such as abdominal pain, which were thought to be unrelated to solvent exposure, were also included so that any tendency towards over-reporting among the exposed group might be detected.

ASSESSMENT OF EXPOSURE

Personal monitoring—Personal exposure was measured by wearing a gas-diffusion button for four hours in the morning and three hours in the afternoon. Time-weighted average airborne concentrations of styrene were calculated for the morning and the afternoon and for exposure throughout the day of testing.

Biological monitoring—Blood was taken at the end of the day from all men in the study so that blood styrene concentrations could be measured, head-space analysis being used for this purpose. In addition the men in exposed occupations collected all their urine from the time they came to work until they went to bed. A separate container was used to collect each specimen of urine; mandelic-acid concentration was measured in the separate specimens by gas chromatography.

Results

BIOLOGICAL AND ENVIRONMENTAL EXPOSURE MEASUREMENT

The mean of each measure is shown in table 1. The mean blood styrene concentration of the exposed group was more than ten times that of the referents; the range for the exposed was 2.0–20.9 $\mu\text{mol/l}$, and for the referents 0.2–1.2. Information from the diffusion buttons worn by those in exposed occupa-

Table 1 Means and standard deviations of biological and environmental measures

	Mean	Standard deviation	No
Blood styrene ($\mu\text{mol/l}$)			
Subjects	6.9	4.1	27
Controls	0.6	0.3	27
Urinary mandelic acid ($\mu\text{mol}/\text{mmol creatinine}$)			
Average	581	413	26*
Peak	964	808	26*
Personal exposure (TWA, ppm)			
Morning	117	63	27
Afternoon	52	35	27
Average	92	46	27

*One man claimed to have passed no urine during the day. His blood styrene concentration was three times the mean of the exposed group and his performance on the reaction time task, which required sustained attention, was too erratic to be included with the analysis of the whole group.

Table 2 Correlation coefficients for biological and environmental measures

BLOOD	—					
MAV	0.32	—				
MPEAK	0.19	(0.96)	—			
AM	0.46**	0.78***	0.75***	—		
PM	0.18	0.35*	0.29	0.43**	—	
AV	0.44**	0.76***	0.71***	(0.96)	(0.65)	—
	BLOOD	MAV	MPEAK	AM	PM	AV

Coefficients shown in brackets contain values from the same data set.

BLOOD = Blood styrene concentration.

MAV = Mean urinary mandelic-acid concentration.

MPEAK = Peak urinary mandelic-acid concentration.

AM = Morning exposure (TWA).

PM = Afternoon exposure (TWA).

AV = Average exposure (TWA).

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

tions showed that exposure to styrene vapour was twice as great in the morning as in the afternoon; this was to be expected from the nature of the process. The mean time-weighted exposure was just below the current threshold limit value of 100 ppm.

Table 2 shows the correlation between the two biological measures and exposure. Morning exposure correlated significantly with both blood styrene concentration and urinary mandelic-acid excretion. Blood styrene and mandelic acid did not correlate.

Mean changes in visual analogue scores (arc sin transformed) during day. A negative score indicates deterioration.

R = Referent group.

E = Exposed group.

*Zero change for referent group.

VISUAL ANALOGUE SCORES

Table 3 shows the morning visual analogue scores (arc sin transformed) for each of the four scales; there was no difference between the groups. For the purposes of this and subsequent analyses, the exposed group has been split into those with low ($\leq 5.4 \mu\text{mol/l}$) and high ($\geq 5.5 \mu\text{mol/l}$) blood styrene concentrations. Changes in scores during the day are shown diagrammatically (fig) and in more detail in table 4. There is a clear trend, from referent to high blood styrene group, for scores to worsen through the day. The changes in visual analogue scores differ for the three groups on scores of physical and mental tiredness and general health, but only the change in "health" score is significant when comparing all exposed with the men in the referent group. Although the extent of deterioration shows a weak trend between the referent group and the low blood styrene group on all four scores, it is the high

Table 3 Morning analogue score. (Standard deviations in parentheses)

	Sleepiness	Physical tiredness	Mental tiredness	General health	No
Referent group	3.6 (1.5)	3.0 (1.4)	3.5 (1.3)	1.9 (1.3)	27
Exposed group					
Low blood styrene concentration	3.9 (1.2)	3.7 (0.9)	3.6 (1.0)	2.7 (1.3)	13
High blood styrene concentration	3.5 (2.2)	2.5 (1.7)	2.7 (1.5)	1.7 (1.0)	14
All exposed	3.7 (1.8)	3.1 (1.4)	3.1 (1.3)	2.2 (1.3)	27
Test of difference between referent and all exposed	F = 0.0	F = 0.1	F = 0.8	F = 0.7	54
	NS	NS	NS	NS	
Test of difference between 3 groups (referent, low, high)	F = 0.2	F = 2.2	F = 2.4	F = 2.6	54
	NS	NS	NS	NS	

Table 4 *Change in analogue score during shift (negative score reflects deterioration). (Standard deviations in parentheses)*

	<i>Sleepiness</i>	<i>Physical tiredness</i>	<i>Mental tiredness</i>	<i>General health</i>	<i>No</i>
Referent group	0.7 (2.4)	-0.3 (1.8)	0.0 (1.8)	0.3 (1.0)	27
Exposed group					
Low blood styrene concentration	0.3 (2.0)	-0.4 (1.4)	-0.1 (1.2)	0.1 (1.1)	13
High blood styrene concentration	-0.6 (3.1)	-2.3 (2.6)	-1.6 (2.2)	-0.8 (1.2)	14
All exposed	-0.2 (2.6)	-1.4 (2.3)	-0.9 (1.9)	-0.4 (1.2)	27
Test of difference between referent and all exposed	F = 1.5 NS	F = 3.6 NS	F = 2.5 NS	F = 4.7 p < 0.05	54
Test of difference between 3 groups (referent, low, high)	F = 1.2 NS	F = 5.1 p < 0.01	F = 3.6 p < 0.05	F = 5.1 p < 0.01	54

blood styrene group that shows the greater deterioration.

Among the exposed group, blood styrene concentrations were correlated with changes in physical and mental tiredness and general health scores but not with changes in the sleepiness scores. The values of the correlation coefficients were 0.47, 0.34, and 0.32; the corresponding p values were < 0.01, < 0.05, and < 0.05. Changes in visual analogue scores were not related to urinary mandelic-acid concentrations but changes in physical and mental tiredness did correlate with morning exposure ($r = 0.36$ and 0.33 ; $p < 0.05$).

As would be expected, changes in analogue scores during the day were intercorrelated. A change in physical tiredness, for example, was highly correlated with changes in sleepiness ($r = 0.81$) but less so ($r = 0.43$) with a change in the score on "general health." Because of these correlations, an attempt was made to see whether the differences between the change scores apparent in table 4 were compatible with a single underlying deterioration in mood or feeling or whether each scale contributed to a discrimination between the three exposure groups; the referent group, the low blood styrene group, and high blood styrene group. A step-wise discriminant analysis was carried out using the four change scores to attempt to discriminate the three groups. It was found that with three groups to be discriminated, only a change in one scale, that of general health, contributed to a discrimination between the groups. Using this it was possible only to discriminate between the high blood styrene group and the other two groups with lower exposure. There was no significant difference between the referent group and those with lower blood styrene concentrations.

The analysis was then repeated, with the referent and low-exposure groups combined. Here it was found that three of the analogue change scores contributed to distinguishing between the 14 men in the high blood styrene group and the rest of the men in the study (table 5). A highly significant discrimination was achieved ($p < 0.001$), indicating that men with high and low blood styrene show an

appreciably different pattern of change in score on the visual analogue scales of physical tiredness, sleepiness, and general health.

Table 5 *Summary of discriminant analysis using changes in analogue score to discriminate 14 men in high blood styrene group from other 40 men in study*

<i>Variables used to discriminate the groups</i>	<i>F value (to remove variable from an analysis including the other three variables)</i>	<i>Significance</i>
Changes during the day in:		
Sleepiness	5.5	p < 0.05
Physical tiredness	7.0	p < 0.05
Mental tiredness	0.5	NS
General health	4.9	p < 0.05

QUESTIONNAIRE DATA

Although questions were asked on 16 symptoms or diseases, the only significant difference to emerge from the answers given related to tiredness. Each man in the study was asked whether, during the past 12 months, he considered himself to have felt unduly tired. Of the exposed workers, 52% said that they had, but only 19% of the referent group ($p < 0.05$). The exposed workers also reported feeling more tired on Friday night than on Monday night; this was recorded by 67% of exposed men compared with 33% of the referents. There may be some evidence here for a cumulative effect of exposure to styrene over the week.

PERFORMANCE TESTS

Pencil and paper tests

The scores obtained in the morning pencil and paper tests and the changes observed in the end of shift tests are shown in tables 6 and 7. The three groups were not distinguished by their morning scores in any test; when change in score during the day was examined only the backward digit-span test showed a result that might be thought significant, the high blood styrene group performing least well.

Table 6 Morning performance tests: mean scores. (Standard deviations in parentheses)

	Digit/symbol substitution (No correct)	Span forwards (longest series correct)	Span backwards (longest series correct)	Vigilance (total correct)	No	Reaction time (ms)	No
Referent group	60.2 (9.5)	6.3 (1.3)	4.9 (1.3)	7.4 (2.3)	27	230 (27)	26
Exposed group							
Low blood styrene concentration	52.7 (7.2)	6.2 (1.0)	4.2 (1.3)	6.8 (2.6)	13	251 (40)	13
Exposed group							
High blood styrene concentration	58.7 (10.1)	6.0 (1.1)	4.9 (1.2)	6.5 (1.8)	14	253 (27)	13
All exposed	55.8 (9.2)	6.1 (1.1)	4.6 (1.2)	6.6 (2.2)	27	252 (34)	26
Test of difference between referents and all exposed	F = 3.0 NS	F = 0.2 NS	F = 1.3 NS	F = 1.5 NS	54	F = 7.0 p < 0.05	52
Test of difference between 3 groups (referent, low, high)	F = 3.0 NS	F = 0.2 NS	F = 0.5 NS	F = 0.8 NS	54	F = 3.4 p < 0.05	52

Table 7 Change in mean performance test scores during shift: (negative score reflects deterioration). (Standard deviations in parentheses)

	Digit/symbol substitution	Span forwards	Span backwards	Vigilance	No	Reaction time (ms)	No
Referent group	-3.1 (5.5)	0.3 (1.1)	0.2 (1.0)	-0.3 (1.7)	27	-5.5 (22.8)	26
Exposed group							
Low blood styrene concentration	-1.5 (6.1)	-0.08 (1.2)	0.8 (1.2)	-0.2 (1.6)	13	+16.8 (28.2)	13
Exposed group							
High blood styrene concentration	-5.0 (5.7)	0.5 (1.5)	-0.3 (1.3)	-0.4 (1.4)	14	+1.1 (22.4)	13
All exposed	-3.3 (6.0)	0.2 (1.4)	0.3 (1.3)	-0.3 (1.5)	27	+8.9 (26.2)	26
Test of difference between referent and all exposed	F = 0.0 NS	F = 0.0 NS	F = 0.0 NS	F = 0.0 NS	54	F = 4.5 p < 0.05	52
Test of difference between 3 groups (referent, low, high)	F = 1.3 NS	F = 0.7 NS	F = 3.4 p < 0.05	F = 0.1 NS	54	F = 3.7 p < 0.05	52

Reaction time

The mean morning reaction time of the exposed group was greater than that of the referent group (table 6). Although this tendency for the exposed group to do worse than the referent group was present in other performance tests carried out in the morning (tables 6 and 7), it was only in reaction time that the difference was sufficiently pronounced to require more detailed discussion (see below).

The afternoon reaction time showed a rather different pattern. The referent group with a mean score of 236 ms (SD = 36) had slowed down slightly from 230 ms in the morning; in contrast, the exposed group had, on average, speeded up, their mean afternoon score of 243 ms (SD = 29) being rather faster than that (252 ms) recorded in the morning. The size of the change in reaction time among the exposed group was, however, in line with

the expectations generated by table 4; the high blood styrene group had speeded up very little, recording an afternoon reaction time of 252 ms (SD = 27), but the reaction time for those with low blood styrene concentrations was now almost identical with that of the referent group (234 ms, SD = 29).

Tapping test

There were only slight differences in the tapping scores between the exposed and the non-exposed workers both at the start and the end of the shift; nor were substantial differences observed during the day.

Discussion

Although the concentrations of styrene were not

sufficient to produce any convincing changes in most of the objective tests of performance, they were associated with subjective changes in physical and mental tiredness and in the feeling of general well-being during the day. The visual analogue scores showed that workers with high blood styrene concentrations ($\geq 5.5 \mu\text{mol/l}$) reported more physical and mental tiredness at the end of the day; they also thought that their general health had deteriorated. This group also had consistently slow reaction times, both in the morning and the afternoon. The exposed workers also reported symptoms of tiredness more frequently than the referent group.

The interpretation of these positive results, however, is difficult. Prior knowledge of the general purpose of the study might well have affected the verbal response of the exposed group. Such knowledge might lead men to report more symptoms or a greater deterioration in mood during the day. Were this the complete explanation, however, it might be expected that an excess of other symptoms, such as headache, would also be found. This was not the case. More convincing, however, is that knowledge of the purpose of the investigation could not explain the correlation between changes in visual analogue scores and blood styrene concentrations among the exposed groups. These men would not have known the concentration of solvent in their blood.

The correlation between physical tiredness and blood styrene concentration, however, raises a further problem as it has been shown by Åstrand *et al*¹² that blood styrene concentrations increase with physical work even when the level of styrene in the atmosphere is constant. Thus it may be that the men who work hardest through the day, and who presumably feel the most tired, tend to have high blood styrene concentrations—that is, the blood styrene concentration may result from working hard, and it is the hard work, not the styrene, that causes the man to feel tired. The correlation between morning exposure and mood change, however, suggests that exposure to styrene may contribute directly to feelings of tiredness.

The reaction-time test was expected to be the most sensitive of the behavioural measures used in the study. A slowing after brief exposure has been the most consistent finding from experimental studies in Scandinavia, and the form of the test used in the present study has been found to be sensitive to lack of sleep.⁹ No slowing of reaction time associated with styrene was, however, found in the workers tested. Although the solvent workers had slow morning reaction times (after a weekend without exposure), they speeded up during the day. Such an improvement in reaction time after exposure in the field has been reported elsewhere⁴ but is contrary to expecta-

tion if styrene has a narcotic effect and does not conform with the results of exposure chamber studies. It may be that in the field other factors must be taken into account. Alcohol did not seem to be the explanation as the two groups reported, on average, that they had had the same amount to drink the previous evening.

The study of a second group of workers in the field would allow further investigation of the slow morning reaction time. Possibly differences between groups, although statistically significant, arose by chance, and replication in a further study would give more credibility to the results reported here. It is of interest to note, however, that within the present study the group with the low blood styrene concentration speeded up much more through the day than the high blood styrene group, their end-of-shift reaction time being identical with that of the referent group. This might suggest that styrene may be inhibiting only at high concentration, this being in line with the results of the visual analogue scores.

Although some of the results of this study are consistent with the hypothesis that styrene affects mood and behaviour, it is none the less inescapable that several measures gave negative results. Possibly the short testing procedure used here was not sufficiently sensitive (see Wilkinson¹³) to pick up, in a sample of this size, the effects reported elsewhere. Equally, it may be that although at concentrations of styrene below the current British threshold limit value changes in mood are found, acute effects on performance are minimal.

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