ORIGINAL ARTICLE

Psychomotor performance and subjective symptoms at low level toluene exposure

M Zupanic, P Demes, A Seeber

Occup Environ Med 2002;**59**:263–268

See end of article for authors' affiliations

Correspondence to:
Dr M Zupanic, Institut für
Medizinische Psychologie
und Medizinische
Soziologie, D-52057
Aachen, Pauwelsstrasse
30, Raum, Ebene 03-D 17,
Germany; zupanic@
arb-phys.uni-dortmund.de

Accepted
17 October 2001

Objectives: Possible effects of long term occupational exposure to toluene below the level of 100 ppm on psychomotor performance and subjective symptoms were investigated in a cross sectional approach.

Methods: From German rotogravure printing plants 278 male workers, mean age 39.8 years, mean duration of employment 14.9 years, were examined. A mean lifetime weighted average exposure (LWAE) of 45.1 ppm toluene in ambient air was found for 154 exposed workers (rotogravure printing area), with a mean current exposure of 24.7 ppm. The corresponding data for a second group of 124 workers with very low exposure (endprocessing area) had LWAE of 9.3 ppm and a current exposure of 3.3 ppm toluene. Psychomotor performance (steadiness, line tracing, aiming, tapping, and peg board) and subjective symptoms were examined.

Results: No significant differences between the two exposure groups were found by analysis of variance (ANOVA). By stepwise linear regression analyses there were weak associations of LWAE with one performance variable and two symptoms scales, but the results were not significant after correction for the α error. Psychomotor performance was mostly affected by age (maximum explained variance up to 13%), and handedness (up to 9%), whereas subjective symptoms are mostly affected by anxiety (up to 38%).

Conclusions: The weak associations between long term exposure to toluene should be used to indicate further longitudinal investigations. The results of this cross sectional study show no obvious dose response relation for psychomotor functions and subjective symptoms among workers exposed to toluene at a current exposure level of 1–88 ppm.

Toluene is widely used as an industrial solvent with well known neurobehavioural effects, but there are few epidemiological cross sectional studies focusing on possible effects at an exposure level below 100 ppm. This degree of exposure takes place in rotogravure printing plants, where workers are occupationally exposed to toluene. Subjective symptoms have been reported in a significant dose-response relation (50 to 100 ppm),¹ and long term exposure (more than 12 years) scored significantly higher on a symptom index than shorter exposure (1–12 years) and no exposure, as in the controls.² Furthermore, it was found that the score in several tests correlated negatively with the sum of neuroaesthetic symptoms complained of by printers, but the variables reflecting exposure showed only a weak association with the performances.³

Neurobehavioural effects were found in association with long term exposure to time weighted average (TWA) toluene exceeding 100 ppm, with impaired performances on tests of visuospatial function, number learning, and word recognition.² In an occupational setting with a mean exposure of 88 ppm toluene impaired performances of the exposed workers compared with their matched controls were found for the grooved peg board, trail making, visual reproduction, Benton visual retention, digit symbol, and digit span tests.⁴ At a mean exposure of below 50 ppm neurobehavioural effects due to long term exposure to toluene were suspected.³ After adjusting the results for verbal intelligence, there was less decrease in the differences found between exposed printers and controls in most of the tests.

Results from short term (6–8 hours) chamber experiments with exposure to toluene under various controlled conditions were obtained by different working groups. Several non-specific complaints, headache, fatigue, eye irritations, and feeling of intoxication increased in a dose dependent way

(0–150 ppm),⁵ or have been reported⁶ or more often reported⁷ by subjects exposed to 100 ppm than by those with lower exposures. At exposures of 100 ppm toluene, a decreased performance in neurobehavioural tests was also described. Performance was affected on manual dexterity,^{5–7} tracking, digit span, pattern recognition, and pattern memory,⁵ colour discrimination, and visual perception,⁶ and, with borderline significance, visual acuity, and multiplication errors.⁷ At exposures below 100 ppm no effect on performance could be verified.

Thus, the results from the cited cross sectional and experimental studies indicated only weak effects of toluene on psychomotor performances at an exposure below 100 ppm, whereas symptoms due to toluene can often be noticed. It is not clear whether the neurobehavioural effects found depended on the acute exposure to toluene (experimental studies), the current exposure to toluene (cross sectional studies), or the long term exposure (individual working life). The study introduced here is part of the second cross section of an epidemiological long term study in German rotogravure printing plants and discriminates methodically between current and long term exposure. Both exposure values were taken into account when investigating effects on psychomotor performance and subjective symptoms after low level occupational exposure to toluene. The study was supported by the German liability insurance association "Berufsgenossenschaft", controlled by an independent scientific committee,

Abbreviations: LWAE, lifetime weighted average exposure; MLS, motor performance series (Motorische Leistungsreihe); PNF, psychological-neurological questionnaire (Psychologisch-Neurologischer Fragebogen); MANCOVA, multiple analyses of covariance; R^2 , coefficient of determination

Table 1 Exposure data and demographic characteristics of the groups (means, SDs, medians, interquartile ranges)

Variables	Exposed n=154				Controls n=124			
	Mean	SD	Median	Range	Mean	SD	Median	Range
Age (y)	39.3	9.6	39.0	31.0–48.0	40.5	9.5	39.5	32.0–48.0
Education (y)	9.3	1.2	9.0	9.0–10.0	9.1	1.4	9.0	8.0–10.0
Employment (y)	15.3	9.7	11.9	7.5–23.3	14.5	8.6	10.5	7.5–19.8
Long term exposure, LWAE (ppm)	45.1	16.4	41.4	34.2–57.9	9.3	7.6	6.2	5.8–10.6
Current exposure (ppm)	24.7	17.6	20.1	11.1–34.5	3.3	4.8	1.9	1.3–2.9

and checked for the data protection regulations by the regional administration Arnsberg (document 21.8-4-1/97). The study fulfilled the standards for non-therapeutical biomedical research (declaration of Helsinki 1987), so that no further ethical approval was necessary.

METHODS

Subjects

From 14 German rotogravure printing plants, 278 male workers voluntarily participated. This representative sample corresponds to about a fifth of the total workforce. The workers were subdivided into two exposure groups. Printers or print helpers from the rotogravure printing area with moderate exposure to toluene formed the exposed group (n=154). Workers with very low exposure to toluene from the endprocessing area of the same plants were considered to be controls (n=124).

Exposure

Individual exposure to toluene was measured by two variables (both in the standard unit parts per million, ppm), reflecting long term and current exposure. Long term exposure was calculated as lifetime weighted average exposure (LWAE). The calculation was based on individual job exposure matrices, which were assessed during a standardised interview about the manner and duration of occupationally related contact to toluene. These data were combined with representative historical measurements of toluene concentration in the air from five printing plants in the past 3 decades. The product of the different concentrations of toluene for all of the different jobs (cumulative lifetime exposure) was weighted by the exposure time of the person's working life (LWAE). The current exposure to toluene was calculated as the mean of two to four measurements during normal working days with pumped (or active) sampling in the breathing zone of all participants. These measurements were carried out by technicians of the German liability insurance association. Table 1 shows exposure data and demographic characteristics of the two exposure groups.

There were no significant differences between the two groups for age, educational level, and duration of employment. The mean exposures of the exposed group were below the German threshold limit value (TLV) for toluene (50 ppm), but 31% of the participants had values above the TLV for long term exposure and 11% for current exposure. The mean current exposure of the controls was just above the olfactory detection threshold of toluene (2 ppm).⁸ Neither a value for long term exposure nor for current exposure lie above the TLV. The ratio of current exposure to LWAE amounts to 1:1.7 for the exposed and 1:2.9 for the controls. The values of long term and current exposure are significantly correlated ($r=0.418$, $p=0.00$).

Psychomotor performance testing

Manual dexterity functions were examined by five subtests of the computer administered test battery motor performance

series (Motorische Leistungsserie, MLS).⁹ The MLS covers five human performance functions of manual dexterity from Fleishman's 11 factors of psychomotor performance. These factors reflect abilities which are based on physical condition, former experiences, and training. The MLS is mainly used in neuropsychological and pharmacopsychological investigations in patients with Parkinson's disease^{10,11} or depression,¹² to assess psychomotor abilities or impairment. The MLS has also been used in neurotoxicological investigations. No acute effects of trichloroethylene¹³ and a weak effect of manganese on psychomotor performance (peg board) were found.¹⁴ Detailed descriptions of the subtests and normative data (healthy right handed subjects) were published recently.¹⁵ In the present study the five subtests of the MLS steadiness (second smallest hole in the MLS board), line tracing, aiming, tapping, and peg board were used in this sequence to examine dynamic and static elements of psychomotor performance of the upper limbs. Speed (total time) and precision (errors, error time) were measured as variables. Every single task had to be done with the right hand first, then with the left hand, independently of the manual laterality. At the end, the peg board was presented, with demands for two hand coordination.

Symptoms questionnaire

Subjective symptoms were measured with the psychological-neurological questionnaire (Psychologisch-Neurologischer Fragebogen, PNF). This questionnaire was developed for screening purposes in neurobehavioural examinations¹⁶ and was recently newly validated.¹⁷ It includes 42 questions about the frequency of symptoms within the past 3 months. The scores are added up in six scales and as sum of complaints. The scales are psycho and neurovegetative lability, neurological symptoms, lack of activation and motivation, excitability, lack of concentration and memory difficulties, and special symptoms that appear especially in subjects exposed to neurotoxicants (alcohol intolerance, and unpleasant taste and smell).

Statistical analyses

To compare the two exposure groups multiple analyses of covariance (MANCOVA) were carried out. The factors exposure (exposed or controls) and handedness (right or left handed) were taken into account at the analyses of the (logarithmically transformed) psychomotor performance data. As covariates the well known confounders of performance and symptoms in neuropsychological examinations were chosen.¹⁸ The covariates were age, education, self reported diseases or medical treatment, the alcohol consumption variable carbohydrate-deficient transferrin,¹⁹ and consecutive working days before examination. The working days before examination were included as a parameter of workload, which is independent of exposure to toluene. Self reported data about a medical diagnosis of liver disease, diabetes mellitus, neurological disease, or a medical treatment (sedative medication or β adrenergic inhibitors) from 45 subjects were taken into account. The MANCOVA of the (z transformed) subjective symptoms

Table 2 Psychomotor performances (MLS variables) of the groups (means, SDs, medians, interquartile ranges)

Variables hand	Exposed (n=154)				Controls (n=124)			
	Mean	SD	Median	Range	Mean	SD	Median	Range
Steadiness:								
Number of errors:								
Right	9.0	9.6	6.0	2.0–13.0	9.1	10.1	5.5	2.0–13.0
Left	11.0	12.9	8.0	3.0–14.2	11.4	11.9	7.0	3.0–17.7
Error time:								
Right	0.8	2.2	0.4	0.1–0.9	0.7	1.0	0.3	0.1–0.8
Left	0.8	1.0	0.5	0.1–1.1	0.8	1.0	0.4	0.1–1.4
Line tracing:								
Number of errors:								
Right	21.2	9.0	20.0	16.0–25.0	20.6	7.5	19.5	16.0–26.7
Left	25.0	11.1	23.0	18.0–30.0	24.2	10.3	23.5	18.2–28.7
Error time:								
Right	1.9	1.0	1.7	1.3–2.4	1.8	1.0	1.7	1.1–2.3
Left	2.4	1.3	2.2	1.6–3.0	2.3	1.2	2.1	1.4–3.0
Total time:								
Right	22.5	9.2	21.2	16.4–26.8	22.7	9.7	21.2	15.9–28.0
Left	22.4	10.0	21.4	16.3–26.2	22.3	9.0	19.7	16.3–28.0
Aiming:								
Number of errors:								
Right	0.4	0.6	0.0	0.0–1.0	0.3	0.8	0.0	0.0–1.0
Left	1.1	1.5	1.0	0.0–2.0	1.3	2.1	0.0	0.0–2.0
Error time:								
Right	1.5	2.7	0.0	0.0–2.0	1.3	4.1	0.0	0.0–1.0
Left	5.1	9.8	1.5	0.0–7.0	6.3	12.3	0.5	0.0–8.0
Total time:								
Right	8.8	1.7	8.6	7.5–10.0	8.7	1.8	8.6	7.5–9.8
Left	9.1	1.8	8.8	7.9–10.2	9.0	1.9	8.8	7.6–9.9
Tapping:								
Number of hits:								
Right	207.4	22.6	206.0	192.5–222.0	206.2	22.5	204.5	191.0–214.7
Left	185.5	24.5	184.0	169.0–202.5	183.0	26.4	181.0	163.2–198.0
Peg board:								
Total time:								
Right	67.1	8.8	66.9	60.7–72.2	67.8	10.4	67.6	60.3–73.6
Left	67.2	8.7	66.6	60.4–72.3	67.9	10.2	67.9	60.4–73.2

included the factor exposure (exposed or controls) and the covariates already mentioned. The second factor of the analyses was the personality trait anxiety,²⁰ a moderator of symptoms. The sample has been dichotomised at the median of the raw value into groups with low or high anxiety.

To examine dose-response relations stepwise analyses of linear regression were computed. The individual values of exposure (long term or current) were taken into account as independent variables, besides the covariates already mentioned. Probability of $p < 0.05$ was used for inclusion in the stepwise analyses.

RESULTS

Covariates

As there were no significant differences between exposed and control groups in the covariates used in the analyses, a detailed presentation is not given (table 1 for age and education). Of the subjects 91% were right hand. They were examined after a mean (SD, range) 2.4 (1.2, 0–5) consecutive working days. The mean (SD, range) value of the alcohol consumption variable was 16.3 (10.3, 6.4–97) U/l, the mean (SD, range) anxiety was computed as 35.1 (7.6, 21–66).

Psychomotor performance

From the five MLS subtests, 20 variables were available about the domain of precision and speed of psychomotor performance. Descriptive statistics for performance data of the two groups are given in table 2.

Generally, average psychomotor performance of the workers was found to be in the normal range (ranked percentage 40–60), compared with the norms of the test battery MLS. This applied to both hands and the difference between right and left hand performance. The results for the right hand, the dominant hand for most of the subjects, were better than those for the left hand.

Mean performances of the two exposure groups were comparable. Results from the MANCOVA are given in table 3. With different subdivisions into subtests of the MLS, variables were regrouped by aspects of performance on precision (including errors, and error times) and speed (total time or number of hits).

MANCOVA showed no significant differences between the exposure groups, although most variables (13 of 16) depended on handedness. This was obvious for both precision and speed. There were no effects of interaction between the factors exposure group and handedness. The analyses showed some significant results of the covariates. With a higher age, a self reported disease or medical treatment, more years at school, and more consecutive working days before examination there were more errors or prolonged processing times on several variables. The covariate for alcohol consumption positively affected performance on tapping.

Analyses of linear regression were carried out with the dependent variables mentioned in table 3. Out of 32 analyses there was one weak effect of the long term exposure on one dependent variable (line tracing, error time, right hand) with explained variance of 2.8%. The result was not significant after correction for the α error according to Bonferroni.²¹ There was

Table 3 MANCOVA of psychomotor performances

	Factors		Covariates					
Variables	Exposure	Hand	Age	School	Day	Alcohol	Disease	Estimated mean (95% CI)
Precision: number of errors, error time:								
Steadiness:								
Number of errors:								
Right	0.3	7.0**	5.7*	2.1	0.2	0.1	5.4*	1.90 (1.67 to 2.12)
Left	0.0	2.1	0.4	1.3	2.1	0.1	6.1*	1.69 (1.45 to 1.93)
Error time:								
Right	0.2	4.3*	5.0*	1.6	0.1	0.1	3.6	3.53 (3.19 to 3.88)
Left	0.0	3.9*	0.1	1.1	3.3	0.0	8.3**	3.19 (2.85 to 3.53)
Line tracing:								
Number of errors:								
Right	0.2	9.6**	0.0	4.5*	0.0	2.6	3.2	3.07 (2.98 to 3.16)
Left	0.0	6.3**	0.6	7.6**	0.0	1.6	2.2	3.03 (2.94 to 3.12)
Error time:								
Right	2.9	5.7*	0.1	0.2	0.2	0.4	5.7*	5.20 (5.09 to 5.32)
Left	0.0	12.0***	0.9	4.9*	0.0	0.4	5.9*	5.16 (5.05 to 5.27)
MANCOVA: Precision	1.3	9.0***	1.3	2.0*	0.7	1.7		
Speed: total time, number of hits:								
Line tracing:								
Total time:								
Right	0.5	1.6	2.0	4.3*	1.4	0.2	0.5	7.68 (7.60 to 7.77)
Left	0.0	0.2	2.3	5.7*	0.2	0.0	0.4	7.64 (7.55 to 7.73)
Aiming:								
Total time:								
Right	1.3	16.0***	24.9***	2.3	3.4	1.2	0.6	6.82 (6.78 to 6.86)
Left	2.3	16.8***	20.4***	3.7	3.4	0.9	1.8	6.73 (6.69 to 6.76)
Tapping:								
Number of hits:								
Right	1.0	6.6**	4.0*	1.1	0.9	8.0**	2.3	5.30 (5.28 to 5.32)
Left	0.0	30.0***	1.2	2.2	1.7	2.7	0.3	5.27 (5.24 to 5.29)
Peg board:								
Total time:								
Right	0.7	5.4*	25.8***	0.8	6.6**	0.9	8.1**	8.78 (8.75 to 8.81)
Left	0.6	6.9**	26.2***	0.8	6.6**	0.9	8.0**	8.78 (8.76 to 8.81)
MANCOVA: Speed	0.9	22.7***	4.9***	1.6	1.3	1.9	1.5	
MANCOVA: All	1.0	14.1***	3.3***	1.5	1.0	1.8*	1.2	

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$, F values.

no effect of current exposure to toluene on psychomotor performance. Altogether, not more than 20% of the performance variance was explained, mostly by age (explained variance up to 13.4%) and handedness (up to 9.0%). Amounts of performance variances explained by the other covariates reached at maximum 4.0% from education, 1.8% from consecutive working days before examination, 2.6% from the alcohol consumption variable, and 4.3% from self reported diseases or medical treatment.

Subjective symptoms

From the questionnaire PNF, seven dependent variables were available, with six symptoms scales and the sum of symptoms. Descriptive statistics for data on subjective symptoms of the two groups are given in table 4.

Compared with the test norms, the mean data on symptoms of the workers were within the normal ranges

(ranked percentage 40–60) for every symptoms scale. The greatest number of symptoms were in the scale psychovegetative and neurovegetative lability. This depended on the non-specific nature of the symptoms in this scale (headache, fatigue, dizziness) and not on specific complaints of workers exposed to toluene. Mean symptoms of the two exposure groups were comparable. Results from MANCOVA are given in table 5.

The analyses with the six symptoms scales showed no significant differences between the two exposure groups, whereas all subjective symptoms very strongly depend on anxiety. Subjects with higher anxiety tended to report more symptoms than subjects with low anxiety. There were no effects of interaction between the factors exposure group and anxiety. Only two of the covariates showed a significant effect on different symptom scales. With a higher age and educational level more symptoms were mentioned.

Table 4 Subjective symptoms (PNF scales) of the groups (means, SDs, medians, interquartile ranges)

Variables	Exposed (n=154)				Controls (n=124)			
	Mean	SD	Median	Range	Mean	SD	Median	Range
Psychovegetative and neurovegetative lability	7.4	4.3	7.0	4.0–10.0	7.2	4.3	7.0	4.2–9.7
Neurological symptoms	2.1	2.4	1.5	0.0–3.0	1.8	2.4	1.0	1.0–3.0
Lack of activation and motivation	4.8	2.6	4.5	3.0–6.2	4.5	2.6	5.0	2.0–6.0
Excitability	2.3	1.9	2.0	1.0–4.0	2.5	1.9	2.0	1.0–4.0
Concentration or memory difficulties	3.2	2.4	3.0	1.0–5.0	3.4	2.4	3.0	1.0–5.0
Special symptoms	3.6	3.0	3.0	1.0–5.0	3.4	3.0	3.0	1.0–5.0
Sum of symptoms	23.5	13.0	23.0	13.0–32.0	22.9	13.0	22.0	15.0–30.0

Table 5 MANCOVA of subjective symptoms

Variables	Factors		Covariates					Estimated mean (95% CI)
	Exposure	Anxiety	Age	School	Day	Alcohol	Disease	
Psycho and neurovegetative lability	0.5	46.0***	0.3	2.3	0.1	0.7	2.6	7.27 (6.82 to 7.72)
Neurological symptoms	0.1	28.5***	7.9**	0.0	0.0	0.5	3.4	1.98 (1.74 to 2.22)
Lack of activation and motivation	0.2	107.3***	0.2	15.8***	1.0	1.4	0.0	4.63 (4.36 to 4.90)
Excitability	0.3	47.5***	0.0	2.6	0.3	0.1	0.0	2.41 (2.19 to 2.63)
Concentration and memory difficulties	0.5	40.4***	4.9*	9.1**	0.0	2.9	0.5	3.30 (3.04 to 3.56)
Special symptoms	0.5	22.3***	0.2	0.1	0.6	1.8	0.2	3.55 (3.22 to 3.88)
MANCOVA: all	1.2	20.0***	3.2**	3.4**	0.3	0.7	0.9	

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$, F values.

Analyses of linear regression were carried out with the dependent variables mentioned in table 5. Out of 14 analyses, long term exposure explained symptoms variance on neurological symptoms (4.7%) and psychovegetative and neurovegetative lability (1.5%). These results were also not significant after correction for the α -error. There was no effect of current exposure to toluene on subjective symptoms. Most variance of symptoms was explained by anxiety (up to 38.0%). The covariates education (up to 3.9%) and age (up to 1.6%) explained a small share of the variance.

DISCUSSION

The results of this study must be discussed in the light of the conditions of examination, the sample of workers studied, and the exposure to toluene. The subjects of the sample were healthy, working, and aware of the groups in which they were studied. They were told that the aim of the study was to examine possible long term health risks (medical and psychological) after lowering the German TLV in 1994 from 100 ppm to 50 ppm toluene. This knowledge did not give rise to any remarkable group differences in the results—for example, increments of performances or decrements in symptoms of the exposed. Furthermore, mean psychomotor performances and subjective symptoms of the workers from the German rotogravure printing plants were found to be within the normal range (ranked percentage 40–60), compared with tests norms.

The mean values for the long term and current exposures to toluene were below the German TLV of 50 ppm, the highest values were below 90 ppm. Therefore, the exposures were lower, but comparable with that (50 ppm to 100 ppm toluene) mentioned in the cited literature.^{1–4} Those results that showed effects of toluene on subjective symptoms and associations with psychomotor performances cannot be confirmed by the present study. In this study, no group differences between the exposed and control groups were found with analysis of variance (ANOVA).

To consider the whole range of individual exposure data, stepwise analyses of regression were computed. Representing the results as coefficient of determination (R^2) showed how much of the variance in the dependent variable (performances or symptoms) is explained by the independent variables (long term or current exposure) in the regression model. Neither long term nor current exposure to toluene resulted in a significant effect on the dependent variables. The methodically assessed discrimination between long term and current exposure is judged to be a strength of this study. Nevertheless, the discrimination did not answer the question whether possible neurobehavioural effects depended on the long term or the current exposure to toluene, because none had a significant effect on psychomotor performance or subjective symptoms.

Thus, the results of this study are not really unexpected and they concur with the existing literature. Until now, there has

been no evidence for adverse effects on psychomotor performance and subjective symptoms from exposure to toluene below 50 ppm.^{5–7} There is only one study that indicated weak effects (neuraesthetic complaints) from toluene below 50 ppm in the workplace.³ This result cannot be confirmed by the present study, as the effects of long term exposure on one performance and two symptoms variables were not significant after correction for the α error. The results of this cross sectional study show no clear dose-response relation for psychomotor functions and subjective symptoms among workers exposed to toluene at a current exposure of 1 to 88 ppm. The observed weak effects of long term exposure to toluene should be used to indicate the need for further investigations in a longitudinal approach.

Authors' affiliations

M Zupanec, P Demes, A Seeber, Institute of Occupational Physiology, University of Dortmund, Ardeystrasse 67, 44139 Dortmund, Germany

REFERENCES

- 1 Ukai H, Watanabe T, Nakatsuka H, et al. Dose-dependent increase in subjective symptoms among toluene-exposed workers. *Environ Res* 1993;**60**:274–89.
- 2 Eller N, Nøttestrøm B, Laursen P. Risk of chronic effects on the central nervous system at low toluene exposure. *Occup Med (Lond)* 1999;**49**:389–95.
- 3 Ørbæk P, Nise G. Neurasthenic complaints and psychometric function of toluene-exposed rotogravure printers. *Am J Ind Med* 1989;**16**:67–77.
- 4 Foo SC, Jeyaratnam J, Koh D. Chronic neurobehavioral effects of toluene. *Br J Ind Med* 1990;**47**:480–4.
- 5 Echeverria D, Fine L, Langolf G, et al. Acute neurobehavioral effects of toluene. *Br J Ind Med* 1989;**46**:483–95.
- 6 Bælum J, Anderson I, Lundqvist GR, et al. Response of solvent-exposed printers and unexposed controls to 6 hour toluene exposure. *Scand J Work Environ Health* 1985;**11**:271–80.
- 7 Andersen I, Lundqvist GR, Møllhave L, et al. Human response to controlled levels of toluene in 6 hour exposures. *Scand J Work Environ Health* 1983;**9**:405–18.
- 8 Ruth JH. Odor thresholds and irritation levels of several chemical substances: a review. *American Industrial Hygiene Association* 1986;**47**:142–51.
- 9 Schoppe KJ. Das MLS-Gerät. Ein neuer Testapparat zur Messung feinmotorischer Leistungen. *Diagnostica* 1974;**20**:43–46.
- 10 Przuntek H, Welzel D, Schwarzmann D, et al. Primary combination therapy of early Parkinson's disease. A long term comparison between the combined regimen bromocriptine/levodopa and levodopa monotherapy: first interim report. *Eur Neurol* 1992;**32**:36–45.
- 11 Ringendahl H. Normierung der Motorischen Leistungsserie (MLS) für die Messung feinmotorischer Störungen beim Morbus Parkinson. *Nervenarzt* 1998;**69**:507–15.
- 12 Classen W. Psychometric findings in treatment using the selective MAO-A inhibitors moclobemide and maprotiline. *Psychiatr Prax* 1989;**16**:41–3.
- 13 Konietzko H, Elster A, Bencsáth A, et al. Psychomotorische Reaktionen unter definierter Trichloräthylenbelastung. *Arch Toxicol* 1975;**33**:129–39.
- 14 Dietz MC. Untersuchungen zu Maßnahmen der arbeitsmedizinischen Prävention bei Arbeitnehmern mit langjähriger Manganexposition. Poster, 39. Jahrestagung der Deutschen Gesellschaft für Arbeitsmedizin und Umweltmedizin eV, Wiesbaden: DGAUM, 1999.
- 15 Kraus PH, Przuntek H, Kegelmann A, et al. Motor performance: normative data, age dependence and handedness. *J Neural Transm* 2000;**107**:73–85.
- 16 Seeber A, Schneider H, Zeller HJ. Ein psychologisch-neurologischer Fragebogen (PNF) als Screeningmethode zur Beschwerdenerfassung bei

- neurotoxisch Exponierten. *Probleme und Ergebnisse der Psychologie* 1978;**65**:23–43.
- 17 **Kiesswetter E**, Sietmann B, Seeber A. Standardization of a questionnaire for neurotoxic symptoms. *Environ Res* 1997;**73**:73–80.
 - 18 **Lezak MD**. *Neuropsychological assessment*, 3rd ed. Oxford: Oxford University Press, 1995.
 - 19 **Cotton F**, Adler M, Dumon J, *et al*. A simple method for carbohydrate-deficient transferrin measurements in patients with alcohol abuse and hepatogastrointestinal diseases. *Ann Clin Biochem* 1998;**35**:268–73.
 - 20 **Laux L**, Glanzmann P, Schaffner P, *et al*. *Das Stait-Trait-Angstinventar. Theoretische Grundlagen und Handanweisung*. Weinheim: Belz Testgesellschaft, 1981.
 - 21 **Gamble JF**. Low-level hydrocarbon solvent exposure and neurobehavioral effects. *Occup Med* 2000;**50**:81–102.

Have your say

eLetters

If you wish to comment on any article published in *Occupational and Environmental Medicine* you can send an eLetter using the eLetters link at the beginning of each article. Your response will be posted on *Occupational and Environmental Medicine* online within a few days of receipt (subject to editorial screening).

www.occenvmed.com