

Effects of Occupational Exposure to Toluene: A Neuropsychological Study on Workers in Singapore

K W Boey,**PhD*, S C Foo,***MSc, PhD*, J Jeyaratnam,****MD, PhD*

Abstract

The neuropsychological functionings of workers (n = 29) occupationally exposed to low level of toluene (mean blood toluene level 1.25 ug/ml, standard deviation [SD] 0.37 ug/ml) were assessed by a test battery based on the recommendation of US National Institute of Occupational Safety and Health. The data revealed that the exposed workers performed poorer than a control group (mean blood toluene level 0.16 ug/ml, SD 0.06 ug/ml) in short-term memory, sustained attention and concentration, visual scanning, perceptual-motor speed, and finger dexterity. Results of the study confirmed that exposure to toluene may result in different degree of impairments of brain functions.

Ann Acad Med Singapore 1997; 26:184-7

Key words: Brain function, Neurotoxic effects, Solvent

Introduction

In the past, toluene poisoning was associated with clinical evidence of optic and peripheral neuropathy. Computerised tomographic scans of toluene abusers have shown widened sulci, enlargement of the subarachnoid cisterns and dilated ventricles.¹ Increasingly, it is being recognised that impairment of brain functions may exist among people exposed to toluene in the absence of overt evidence of clinical toluene poisoning. Such subclinical evidence of toluene poisoning has been reported in many case studies.² Nevertheless, not many large-scale group studies were conducted in relation to toluene exposure in the workplace. Furthermore, research in this area came mainly from Western industrialised countries,³ though local studies have also been reported.^{4,5} This study was conducted in Singapore to assess the neuropsychological functioning of workers occupationally exposed to toluene.

Materials and Method

Subjects

The sample of this study consisted of 29 workers (mean age 25.6 years, standard deviation [SD] 5.7 years) who were occupationally exposed to toluene for an average of 4.9 years (range 1 to 13 years, SD 3.5 years). A matched control group of non-exposed workers (mean

age 25.1 years, SD 6.3 years) was also recruited for purpose of comparison. Both groups were drawn from an electronic factory in Singapore. These subjects were approximately matched in age and ethnicity, but there was a slight difference in years of education between the two groups. The mean value of years of education of the exposed workers was 6.0 years (SD 2.8 years), whereas for the control group, it was 8.2 years (SD 2.4 years). This difference would be taken into consideration when comparing workers' performance on the neuropsychological tests.

The blood samples were taken at the end of the work shift. Specifically, at the last 20 minutes of the work shift, subjects went to a toluene-free room and blood samples were taken at about 5 minutes after the subjects left the workplace. The exposed workers had a mean value of blood toluene level of 1.25 ug/ml (SD 0.37 ug/ml) whereas the control workers had a mean value of 0.16 ug/ml (SD 0.06 ug/ml). Personal exposure in terms of time-weighted average (TWA) was also monitored using passive absorption monitors. The 8-hour TWA levels in environmental air were 90.9 ppm for the exposed group and 12.2 ppm for the control group. The environmental exposure indices for toluene as recommended by American Conference of Government Industrial Hygienists (ACGIH) is 50 ppm, and at the 8-hour

* Senior Lecturer

Department of Social Work and Social Administration
University of Hong Kong

** Associate Professor

*** Senior Fellow

Department of Community, Occupational and Family Medicine
National University of Singapore

Address for Reprints: Dr Boey Kam Weng, Department of Social Work and Social Administration, University of Hong Kong, Pokfulam Road, Hong Kong.

threshold limit value (TLV)-TWA of 100 ppm of toluene in air, the biological exposure index of toluene in venous blood should be less than 1 mg/l at end of a shift.

Measures

Neurobehavioural tests were conducted on Wednesdays or Thursdays between 9.00 a.m. and 11.00 a.m. for both the exposed and controls at the Department of Community, Occupational and Family Medicine, National University of Singapore. The measurements adopted in the present study were based on the recommendation of the National Institute of Occupational Safety and Health.⁶ These measures comprised tests covering a broad range of neuropsychological functioning. In deciding on the tests to be used, special emphasis was given to short-term memory, sustained attention, concentration, and fine motor function which were generally regarded as sensitive indicators of impairment of brain functions. A total of 8 tests which yielded 14 test scores were included in the present test battery. These tests are briefly described below. Detailed description of the tests can be found elsewhere.^{7,8}

Logical memory (LM): This test was adapted from the Wechsler Memory Scale (WMS) to provide a measure of verbal short-term memory. It consisted of two short stories with 22 and 24 memory units respectively. The subject was asked to give his immediate free recall of each story after it had been read to him. The score of this test was the average number of memory units recalled for the two stories.

Digit span (DS): This test provided a measure of immediate auditory memory, sustained attention, and freedom from distractibility. It had two sections (digit forward and digit backward). In digit forward, the examiner read aloud number sequences that were from three to nine digits and the subject's task was to repeat the sequences exactly as he heard them. The digit backward number sequences ran from two to eight digits, and on hearing them read, the subject's task was to say them in an exactly reversed order. The total score for this test was the total number of digits in the longest correctly repeated sequence for the two sections.

Visual reproduction (VR): This was a nonverbal short-term memory test of the WMS. It consisted of 3 cards with printed designs. Each card was exposed for 10 seconds, after which the subject had to draw what he remembered of the design. The score of this test was the total number of details correctly recalled.

Benton visual retention test (BVRT): The BVRT consisted of 10 cards, 2 presenting 1 figure and 8 presenting 3 horizontally arranged figures. Each card was exposed for 10 seconds. The subject was requested to recall the figures by drawing them on paper. The number of figures correctly drawn and the number of errors made

in all drawings served as indicators of nonverbal short-term memory.

Trail making test (TMT): The TMT was selected to measure concentration, visual conceptual scanning, and visual motor tracking. It consisted of two parts, each with 25 circles distributed over a sheet of paper. In part A, the circles contained numbers 1 to 25. The subject was asked to draw a line connecting the circles in numerical sequence as quickly as possible. Part B differed from Part A in that the circles contained numbers 1 to 13 and letters A to L. In connecting the circles, the subject was required to alternate between numbers and letters as he proceeded in ascending sequence. The test was scored as the numbers of seconds needed to finish each part.

Symbol digit modality test (SDMT): This test was administered in 2 formats (written and oral). In the written administration which measured attention and perceptual motor speed, the subject was asked to substitute numbers for 9 different symbols in the space just below the symbols. In the oral administration which assessed attention and concentration, the subject just read out the numbers instead of writing them down in the space. The score for each administration was the number of correct responses made within 90 seconds.

Grooved pegboard test (GPT): This test was selected to provide a measure of finger dexterity and fine motor speed. It consisted of 25 holes with randomly positioned slots. The subject was required to insert the pegs which had a key along one side and must be rotated to match the hole before they could be inserted. The time (in seconds) required to place all 25 pegs in holes for dominant and non-dominant hand were recorded.

Finger tapping test (FTT): The FTT was included to serve as an indicator of fine motor speed. It consisted of a tapping key with a device for recording the number of taps. The subject, with his hand held in a constant position, was required to use his index finger to tap as fast as he possibly could within 10 seconds. The subject was given 5 consecutive trials first with his dominant hand followed by another 5 trials using his non-dominant hand. The score for each hand was the average number of taps for each of the five trials.

Results

The means and standard deviations of the scores of the neuropsychological tests for the exposed and control groups are presented in Table I. As can be seen, the differences on all the measures between the two groups were in the expected direction. Performance of the exposed workers was consistently poorer than that of the unexposed controls. To examine if the differences were statistically significant, analysis of covariance with years of education as covariate was performed. The F-values thus computed are shown in Table I.

TABLE I: MEANS AND STANDARD DEVIATIONS OF NEUROPSYCHOLOGICAL TEST SCORES BETWEEN EXPOSED AND CONTROL GROUPS

Tests†	Exposed group (n = 29)		Control group (n = 29)		F-value
	Mean	SD	Mean	SD	
DS					
- Forward	6.3	1.6	6.8	1.6	3.28
- Backward	4.6	1.2	5.4	1.4	4.72"
- Total	10.8	2.7	11.8	2.9	4.02"
VR	7.1	2.9	8.3	2.8	7.06**
BVRT					
- Correct	6.4	2.1	7.1	2.0	3.32
- Error	5.6	3.8	4.3	3.4	2.29
TMT					
- Part A	44.2	23.7	33.8	11.3	8.64*
- Part B	133.1	85.9	104.3	60.9	4.76"
SDMT					
- Written	40.4	12.6	45.9	11.7	5.41*
- Oral	45.6	12.8	50.7	11.1	4.97"
GPT					
- Dominant	61.2	9.3	57.0	6.9	13.85***
- Non-dominant	68.5	11.6	64.9	9.7	8.12**
FTT					
- Dominant	44.4	8.6	45.1	8.7	0.38
-Non-dominant	41.3	7.5	42.0	7.2	0.30

† Logical memory test was dropped from the analysis as more than half of the subjects did not take the test because of language problems.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

DS: Digit span; VR: Visual reproduction; BVRT: Benton visual retention test; SDMT: Symbol digit modality test; FTT: Finger tapping test; TMT: Trail making test; GPT: Grooved pegboard test; SD: standard deviation

Results of the analysis confirmed that the differences between the two groups of workers were significant on 9 of the 14 test scores after the effect of education had been statistically controlled. Compared with the control group, the exposed group was significantly poorer in verbal and nonverbal short-term memory as measured by DS and VR tests respectively. On the TMT, the exposed group took significantly longer time to complete Part A and Part B, which suggested a deterioration of visual scanning, concentration, and visual motor tracking. Significant findings on the SDMT indicated that workers exposed to toluene were affected in their perceptual motor speed, sustained attention, and concentration. Results of the GPT also found the exposed workers to perform significantly poorer in finger dexterity and fine motor speed.

In order to examine the accuracy of the neuropsychological tests in differentiating the exposed versus non-exposed workers, a discriminant function analysis was performed. When all the 9 significant scores of the 5 tests were entered concurrently into the

TABLE II: CORRELATIONS BETWEEN NEUROPSYCHOLOGICAL TEST SCORES AND THE DISCRIMINANT FUNCTION

	Coefficient
Visual reproduction	-0.54
Digit span	
Backward	-0.42
Total	-0.42
Trail making test	
Part A	0.55
Part B	0.43
Symbol digit modality test	
Written	-0.56
Oral	-0.50
Grooved pegboard test	
Dominant	0.58
Non-dominant	0.36

analysis, the percentages of exposed and non-exposed workers correctly classified by the derived function were 83% and 79% respectively (average 81%). Table II shows the correlation of the 9 discriminating test scores with the discriminant function.

Discussion

In general, this study presents evidence that exposure to toluene (TWA 90.9 ppm) would result in impairments of certain neuropsychological functioning, particularly in the area of short-term memory, attention and concentration, visual scanning, perceptual motor speed, and finger dexterity. As years of education may also affect neuropsychological performance, analysis controlling the effect of this factor was performed. Results of the analysis confirmed that the impairments of the exposed workers remained significant. Such impairments were successfully detected by several neuropsychological tests used in the present study. Discrimination function analysis confirmed that the tests were able to differentiate significantly the exposed from the non-exposed workers. Further analysis was also performed by dropping the scores on SDMT-oral and DS-total in view of the problems encountered when highly correlated variables were included in a linear model of multivariate analysis.² The analysis indicated that the discriminative power of the neuropsychological tests remained essentially unchanged. It may be worth mentioning that subjects in this study were also assessed on neurophysiological measures of conduction velocities and somato-sensory evoked potentials. However, no significant differences were found in these neurophysiological parameters between the toluene exposed workers and their controls. Results of the present analysis, therefore, suggested strongly that neuropsychological tests were more sensitive than biological measures in the detection of early deterioration in brain functions induced by exposure of low levels of

toluene.

To conclude, the validity of neuropsychological tests in detecting neurotoxic effect of exposure to low level of toluene was established. However, it needs to be recorded that due to the small sample size of the present study, it was not possible to demonstrate a statistically significant dose-response relation between blood toluene values and neuropsychological performance. Further, it must be recognised that the present study compared the average neuropsychological performance between exposed and non-exposed workers. As such, the data cannot be used to decide on diagnostic cut-off values for use on an individual basis.

REFERENCES

1. Cavanaugh J B. Some clinical and neuropathological correlations in four solvent intoxications. In: Cheery N, Waldron H A, editors. *The Neuropsychological Effects of Solvent Exposure*. Havant, Hampshire: Colt Foundation, 1983:7-22.
2. King M. Long term neuropsychological effects of solvent abuse. In: Cherry N, Waldron H A, editors. *The Neuropsychological Effects of Solvent Exposure*. Havant, Hampshire: Colt Foundation, 1983:75-84.
3. Andersen I, Tarkowski S. *Organic Solvent and the Central Nervous System*. Copenhagen: World Health Organization, 1985.
4. Foo SC, Ngim C H, Salle I, Jeyaratnam J, Boey K W. Neurobehavioral effects in occupational chemical exposure. *Environ Res* 1993; 60:267-73.
5. Chia SE, Ong C N, Phoon W H, Tan K T, Jeyaratnam J. Neurobehavioural effects on workers in a video tape manufacturing factory in Singapore. *Neurotoxicology* 1993; 14:51-6.
6. National Institute for Occupational Safety and Health. *Behavioural and Neurological Evaluation*. Cincinnati, Ohio: US Department of Health, Education and Welfare, 1977.
7. Hanninen H, Lindstrom K. *Behavioural Test Battery for Toxicological Studies*. Helsinki: Institute of Occupational Health, 1979.
8. Lezak M D. *Neuropsychological Assessment*. New York: Oxford Univ Press, 1983.
9. McGee D, Reed D, Yano K. The results of logistic analysis when the variables are highly correlated: An empirical example using diet and CHD incidence. *J Chron Dis* 1984; 37:713-9.