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Neurobehavioral Effects of Occupational Exposure to Organic Solvents Among Pharmaceutical Laboratory Workers in Iran

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Abstract

Background: *Workers exposed to organic solvents are at risk of developing chronic central nervous system disorders. The aim of this cross-sectional study was to investigate the neurobehavioral effects of occupational exposure to organic solvents among pharmaceutical laboratory workers.*
Methods: *The study groups consisted of 78 laboratory workers as the exposed group and 98 office workers as unexposed controls. The subjects were studied with the World Health Organization neurobehavioral core test battery (WHO-NCTB) by running Simple Reaction Time (SRT), Benton Visual Retention Test (BVRT) and Purdue Pegboard tests.*
Results: *The SRT and BVRT test scores were poorer among the laboratory workers. However, no significant differences were found between the two groups for the Purdue Pegboard Test.*
Conclusions: *The results of this study suggest that occupational exposure to organic solvents could induce a neurobehavioral deficiency in pharmaceutical laboratory workers. Therefore, objective neurobehavioral tests should be used for assessing the relation between exposure and effect and also as a guide for establishing standards in the control of workplace exposure.*

Keywords: Occupationalexposure, Solvents, Laboratory personnel.
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Introduction

Organic solvents are widely used in pharmaceutical laboratories, and exposure to organic solvents is common in occupational settings.[1,2]The main exposure route of these volatile solvents (which include petroleum, ether, methanol, chloroform, ethyl acetate, and acetone) is usually through inhalation or skin contact.[3,4]Although most pharmaceutical laboratories use these solvents, long-term exposure to them has significant side effects on the health of the human body. These include neurobehavioral effects, which have been variously described as painter's syndrome, chronic solvent syndrome, toxic encephalopathy, CNS effects, dementia, and organo-psycho syndrome.[5]

Many studies have shown the neurotoxic effects of organic solvents. In 1986, for the first time, a study on car-workers showed evidence of the effects of organic solvents on the workers' nervous systems.[6]Similarly, a study on paint industry workers demonstrated an increased risk of neuropsychological symptoms such as headaches and dizziness, memory deficiency, conceptual problems, and mood/sleep disorders in its solvent-exposed group.[7]In Iran, one recent study has reported subtle neurobehavioral changes among workers in the rubber industry.[8]

Many laboratory workers use volatile organic solvents without knowing their side effects on health. There is little information regarding the relation between toxicity and the pathologic features of organic solvents and the neurobehavioral alterations induced by those solvents.[9]

The purpose of the present study was to investigate neurobehavioral changes at a pharmaceutical laboratory through a comparison of workers with solvent exposure and those without. This study was performed for the first time among Iranian pharmaceutical laboratory workers in order to detect subclinical symptoms of chronic central nervous system (CNS) toxicity due to solvent exposure.

Materials and Methods

In this cross-sectional study, 78 workers with solvent exposure were selected from a pharmaceutical laboratory at the Tehran University of Medical Sciences (TUMS), Faculty of Pharmacy. Subjects per day at this laboratory, where each had worked and been exposed to solvents for approximately two years. They were excluded if they had a smoking habit, diabetes mellitus, a history of drug consumption, alcohol consumption within 24 hours of testing, substance abuse, inadequate sleep before testing, or a history of neurologic disease, a head trauma, epilepsy, or a psychiatric disorder. A total of 98 controls were selected randomly from office workers at the same laboratory to comprise the unexposed group, and they were matched for sex, age, and educational degree. The study was approved by the ethics committee of the TUMS, and the participants gave written informed consent.

A questionnaire consisting of demographic characteristics, occupation, and medical history was administered prior to the neurobehavioral tests.

The subjects' neurobehavioral performance tests were conducted by a trained technician. The tests were performed in a silent environment and took 45 minutes per subject. The neurobehavioral core test battery (NCTB) has been widely used to detect neurobehavioral disturbances of workers exposed to many neurotoxins, such as organic solvents. Three tests from the NCTB (a Simple Reaction Time [SRT] test, a Purdue Pegboard Test, and a Benton Visual Retention Test [BVRT]) were selected to evaluate the pharmaceutical laboratory staff's neurobehavioral performance.[10]

An SRT test is a visual and motor speed test that measures the mean reaction time of responses to 64 visual stimuli, which are given at random intervals of 1–10 seconds. The time between the presentation of each stimulus and the pressing of a button was measured, as were the mean and SD of response latencies (in milliseconds).

A Purdue Pegboard Test is one of manual dexterity and requires rapid hand–eye coordination. The instrument consists of a board with two parallel rows that have 25 holes in each row. The subject's task was to fit the board's pegs correctly into its holes as fast as possible. Measurement was taken as fast as possible within a 25-second time limit.

A BVRT measures short-term visual memory. The test consists of 10 drawing cards that have to be recognized. The first card, which contains a pattern to be memorized, is shown for 10 seconds. Thereafter, a second card is shown that contains four patterns, one of which is identical to the pattern presented previously. The number of correct retentions was scored. A higher score means a better performance by the subject.

The concentration of organic solvents was measured using the NIOSH method. Personal air sampling was performed by first check multi gas detector for VOCs with a flow rate of 0.9 L/min (made by Ion Science in the UK) and calibrated with a standard kit sensor. The airborne concentrations of four solvents are listed in Table 1.

Table 1: Airborne concentrations (ppm) of organic solvents

Solvents	Concentration (ppm)	TLV-TWA (ppm)
Ethyl acetate	43	400
Chloroform*	25	10
Methanol	60	200
Acetone	250	500

*Shows that concentration of chloroform is more than the threshold limit value (TLV)

The data were analyzed by SPSS version 22. Associations between categorical variables were assessed using a Chi-square test, and the normality of continuous variables was checked by a one-sample Kolmogorov–Smirnov test and histogram. As all variables were distributed normally, a Student's t-test was used to compare continuous variables between the exposed and non-exposed groups. Multiple linear regression was used for assessing the relations of the different variables with the neurobehavioral scores. Significant level was considered at 0.05.

Results

There were no significant differences between the exposed and unexposed groups in terms of the demographic (age, sex) and occupational characteristics (job category, educational degree, and duration of exposure), as shown in Table 2.

Significant differences between the exposed and unexposed groups were found in the SRT, Purdue Pegboard, and BVRT tests. The subjects in the exposed group showed poorer performances than those in the unexposed group in all of the employed tests (Table 3).

A multiple regression analysis was performed to assess the effect of the demographic and occupational characteristics on the neurobehavioral performance tests. Independent variables consisted of exposure, age, sex, educational degree, and duration of exposure. Although solvent exposure had a significant effect in the SRT and BVRT tests, it did not affect the results of the Purdue Pegboard Test in this regression (Table 4).

Table 2: Characteristic of exposed and unexposed group

Variables	Exposed group (N=73)	Unexposed group(N=94)	P.V
Age (mean±SD)	22.1±2.5	22.2±2.6	0.72*
Duration of exposure(mean ±SD)	3.83±1.4	3.7±3.2	0.68*
Gender, N (%)			0.08**
Male	36(49.3%)	59(62.8%)	
Female	37(50.7%)	35(37.2%)	
Jobcategory, N (%)			0.30**
Student	55(75.3%)	64(68.1%)	
Office worker	18(24.7%)	30(31.9%)	
Educational degree, N (%)			0.08**
PhD	56(80%)	64(68.1%)	
Others	14(20%)	30(31.9%)	

*T-test, ** Chi square test

Discussion

Our study was conducted on laboratory staff from the TUMS, Faculty of Pharmacy. A statistically significant difference in neurobehavioral performance was detected between the workers exposed to organic solvents and their controls by the neurobehavioral tests.

A variety of such tests are available for evaluating neurotoxic effects on worker populations exposed to neurotoxins. The NCTB, which is recommended by WHO, is simple, inexpensive, not tiring, free from cultural bias, and easy to administer.[10]

Earlier studies have found neurobehavioral performance deficiencies in workers exposed to organic solvents. These studies have shown that SRT and BVRT tests can be affected by exposure to solvents.[8,11-14]However, the Purdue Pegboard Test was not affected by exposure to solvents in multiple regression models. Similar studies have found no significant correlation between some of the neurobehavioral performance tests and solvent exposure.[15,16]

Subjects with conditions affecting the CNS (neurologic or psychiatric disease, alcohol consumption, smoking habit, etc.) were excluded from the study in an effort to control the confounding factors. The diagnosis of a neurobehavioral deficiency due to occupational exposure has been developed in the absence of any other etiological factor.

A person's age and the duration of their exposure are known as important factors that affect neurobehavioral performance. In regard to removing the effects of these factors, participants with similar ages and durations of exposure were chosen. It is also known that the results of neurobehavioral performance tests are influenced by educational level and computer experience.[17]A simple keyboard was used for the SRT tests, in which participants needed to press only one button and the involved groups did not differ significantly by

Table3: Neurobehavioral performance tests in exposed and unexposed groups (Mean ±SD)

Neurobehavioral tests	Exposed group (N=73)	Unexposed group (N=94)	P.V
SRT	361.09±65.88	343.50±35.62	0.042
Purdue pegboard	10.55±1.47	11.02±1.41	0.036
BVRT	8.51±0.76	9.35±0.73	0.000

Table4: Multiple regression analysis of neurobehavioral tests

Variables	SRT		Purdue Pegboard Test		BVRT	
	B*	P.V	B	P.V	B	P.V
(Constant)	335.436	0.000	11.883	0.000	9.721	0.000
Solvent exposure	15.270	0.044	-0.381	0.115	-0.822	0.000
Age	0.417	0.765	-0.042	0.303	-0.011	0.603
Gender	-6.552	0.414	-0.069	0.770	-0.133	0.277
Duration of exposure	-3.042	0.209	0.034	0.631	-0.020	0.588
Job	12.372	0.628	0.287	0.702	0.143	0.712
Educational degree	2.224	0.919	-0.371	0.565	-0.041	0.903
R^2	0.037		0.038		0.259	

*B is regression coefficient

educational degree. Thus, it can be assumed that our selection criteria were appropriate.[18]

The measurements of exposure to some of the organic solvents—such as chloroform—in the laboratory were more than the threshold limit value (TLV). Although it has been assumed that low exposure to organic solvents cannot cause chronic CNS effects, the lower performances of the exposed workers indicate functional impairments of the CNS.

In this study, only three tests of the NCTB were performed. Consequently, the deficiencies of neurobehavioral tests could not be covered exactly. Also, it was not possible to exclude the potential effects of other chemical substances present among the laboratory workers.

Workers exposed to solvents are at risk of developing chronic CNS diseases. The first step to preventing organic solvent–induced chronic CNS diseases is the regular monitoring of exposure by ambient air measurements. In addition, bio monitoring is strictly needed.

Neurobehavioral tests are used for assessing the relation between exposure and effect, and they also provide a guide for establishing standards in the control of workplace exposure. In an occupational setting, these tests are useful in periodic follow-ups on exposed workers for determining the degree of any functional impairments and detecting subclinical occupational illnesses.

Conflict of Interest

The authors declare that They have no conflict of interest.

References

1. Meyer-Baron M, Kim EA, Nuwayhid I, Ichihara G, Kang SK. Occupational exposure to neurotoxic substances in Asian countries - challenges and approaches .Neurotoxicology2012;33:853-61.doi:10.1016/j.neuro.2011.12.012

2. Jin CF, Haut M, Ducatman A. Industrial solvents and psychological effects. ClinOccupEnviron Med 2004;4:597-620.

3. Takebayashi T, Omae K, Ishizuka C, Nomiyama T, Sakurai H. Cross sectional observation of the effects of carbon disulphide on the nervous system, endocrine system, and subjective symptoms in rayon manufacturing workers. Occup Environ Med 1998;55:473-9. doi:10.1136/oem.55.7.473

4. Sancini A1, Caciari T1, Chighine A1, Gioffrè PA1, Andreozzi G1, Sacchi L, et al. Workers of the printing industry and hepatic damage. Ann Ig2014;26:321-9. doi:10.7416/ai.2014.1992

5. Gade A, Mortensen EL, Bruhn P. "Chronic painter's syndrome". A reanalysis of psychological test data in a group ofdiagnosed cases, based on comparisons with matched controls.ActaNeurolScand1988;77:293-306. doi:10.1111/j.1600-0404.1988.tb05913.x

6. Daniell W, Stebbins A, O'Donnell J, Horstman SW, Rosenstock L. Neuropsychological performance and solvent exposure among car body repair shop workers. Br J Ind Med 1993;50:368-377. doi:10.1136/oem.50.4.368

7 El Hamid Hassan AA, El MoezElnagar SA, El Tayeb IM, El HalimBolbol SA. Health hazards of solvents exposure among workers in paint industry. Open Journal of Safety Science and Technology 2013;3:87-95.

8. Aminian O, Hashemi S, Sadeghniiat-Haghighi K, Shariatzadeh A, NaseriEsfahani AH. Psychomotor effects of mixed organic solvents on rubber workers.Int J Occup Environ Med 2014;5:78-83.

9. Herpin G, Gauchard GC, Vouriot A, Hannhart B, Barot A, Mur JM, et al. Impaired neuromotor functions in hospital laboratory workers exposed to low levels of organic solvents. Neurotox Res 2008;13:185-96. doi:10.1007/BF03033502

10 Anger WK, Cassitto MG. Individual-administered human behavioral test batteries to identify neurotoxic chemicals. Environ Res 1993;61:93-106. doi:10.1006/enrs.1993.1053

11. Colvin M, Myers J, Nell V, Rees D, Cronje R. A cross-sectional survey of neurobehavioral effects of chronic solvent exposure on workers in a paint manufacturing plant. Environ Res 1993;63:122-32. doi:10.1006/enrs.1993.1134

12. Reinvang I, Borchgrevink HM, Aaserud O, Lie V, Malt UF, Nakstad P, et al. Neuropsychological findings in a non-clinical sample of workers exposed to solvents. J NeurolNeurosurg Psychiatry 1994;57:614-6.doi:10.1136/jnnp.57.5.614

13. Lee CR, Jeong KS, Kim Y, Yoo CI, Lee JH, Choi YH. Neurobehavioral changes of shipyard painters exposed to mixed organic solvents. Ind Health 2005;43:320-6.

14. Song H, Yu IT, Lao XQ. Neurobehavioral effects of occupational exposure to organic solvents among male printing workers in Hong Kong. Arch Environ Occup Health 2015;70:147-53. doi:10.1080/19338244.2013.828676

15. National Toxicology Program..Final report on carcinogens background document for formaldehyde.Rep CarcinogBackgr Doc 2010. 512 p.Report No.: NO1-ES-35505.

16. Seeber A, Bruckner T, Triebig G. Occupational styrene exposure and neurobehavioural functions: a cohort study with repeated measurements.Int Arch Occup Environ Health 2009;82:969-84. doi:10.1007/s00420-008-0382-5

17. Letz, R. Use of computerized test batteries for quantifying neurobehavioral outcomes. Environ Health Perspect1991;90:195-8. doi:10.2307/3430868

18. Edling C, Anundi H, Johanson G, Nilsson K. Increase in neuropsychiatric symptoms after occupational exposure to low levels of styrene. Br J Ind Med 1993;50:843-50. doi:10.1136/oem.50.9.843