Neuropsychological effects among workers exposed to organic solvents

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Juárez-Pérez CA, Aguilar-Madrid G, Sandoval-Ocaña J, Cabello-López A, Trujillo-Reyes O, Madrigal-Esquivel C, Wesseling C. Neuropsychological effects among workers exposed to organic solvents. Salud Publica Mex. 2019;61:670-677.
https://doi.org/10.21149/9800

Abstract

Objective. To assess neuropsychological performance among workers at a paint factory in Mexico City. **Materials and methods.** During 2004 and 2005 we assessed the neuropsychological performance of 208 workers who were exposed to organic solvents at a paint factory, mainly toluene and xylene. We categorized workers into low and high exposure groups using a cumulative index for toluene, based on times spent in different tasks. We evaluated cognitive and motor functions with 13 neuropsychological tests. **Results.** We found lower attention, longer time to complete the test β=5.5 (R^2=12.3%), and a lower score in the motor-cognitive test β=-15.7 (R^2=19.5%) in the high exposure group through multiple linear regression model analysis, with adjustment for age and education. **Conclusion.** Our results are similar to the ones reported in the literature, but the effects are less severe, probably due to lower exposure to organic solvents.

Keywords: occupational exposure; solvents; neuropsychological tests

Juárez-Pérez CA, Aguilar-Madrid G, Sandoval-Ocaña J, Cabello-López A, Trujillo-Reyes O, Madrigal-Esquivel C, Wesseling C. Efectos neuropsicológicos en trabajadores expuestos a disolventes orgánicos. Salud Publica Mex. 2019;61:670-677.
https://doi.org/10.21149/9800

Resumen

Objetivo. Evaluar el desempeño neuropsicológico de los trabajadores de una fábrica de pintura en la Ciudad de México. **Material y métodos.** Se evaluó el desempeño neuropsicológico de 208 trabajadores expuestos a disolventes orgánicos, principalmente tolueno y xileno, en una fábrica de pintura en la Ciudad de México durante 2004 y 2005. Se categorizaron en grupos de baja y alta exposición con un índice acumulado de tolueno con base en el tiempo empleado por actividad. Se evaluaron funciones motoras y cognitivas con 13 pruebas neuropsicológicas. **Resultados.** Se registró un tiempo más largo para completar la prueba β=5.5 (R^2=12.3%) y una puntuación baja en la prueba motor-cognitiva de β=-15.7 (R^2=19.5%) en el grupo de alta exposición en los modelos de regresión lineal múltiple, ajustados por confusores. **Conclusión.** Los presentes resultados son similares a los reportados en la literatura, aunque los efectos son menos graves, probablemente debido a la baja exposición.

Palabras clave: exposición ocupacional; solventes; pruebas neuropsicológicas

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Received on: June 7, 2018 • **Accepted on:** January 15, 2019
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More than thirty years of research assessing multiple domains and subdomains of the nervous system have confirmed the relationship between neuropsychological disorders and exposure to organic solvents (OS). These disorders were first studied in order to establish the diagnostic criteria for chronic solvent-induced encephalopathy (CSE).[1,2] Diminished attention, memory deficits, motor disabilities and affection disorders were identified as the most common characteristics of CSE.[2]

High-income countries have reported a reduction in the number of CSE cases due to the elimination of OS-related industrial processes.[3,4] A review found only weak and inconsistent associations between long-term human exposure to hydrocarbon solvents at or below occupational exposure limits and adverse neurobehavioral effects.[5]

Many industrial processes depending on OS have been transferred to low and middle-income countries with less stringent occupational health standards where there is little concern about OS-related diseases and health data is scarce. Since the early 1990s, only a handful of studies regarding OS exposure and neurotoxic effects in low and middle-income countries have been published, i.e. about a petrochemical complex in Brazil,[6] and more recently rubber workers in Iran[7] and printing workers in Hong Kong.[8]

In Mexico, trade agreements and economic globalization have contributed to increase the imports and production of OS from less than 1 million tons in 1987 to more than 66 million tons in 2013, and consequently the number of workers exposed to these chemical products has increased exponentially.[9] There is hardly anything known about solvent-induced neurotoxic effects in Mexico, except for a study that showed ototoxicity in workers from a paint factory.[10]

Therefore, the aim of this study was to assess the neuropsychological performance of workers from a paint factory in Mexico City, who were exposed to a mixture of organic solvents, mainly toluene and xylene.

Materials and methods

This research project was registered and approved by the Ethics Committee of the High-Specialty Medical Unit from the *Centro Médico Nacional Siglo XXI* of the Mexican Institute of Social Security (*Instituto Mexicano del Seguro Social*, IMSS, in Spanish). The paint company agreed to grant workers a Monday as a day off, so they could attend the Occupational Health Research Unit for the examination. Transport was provided by the researchers and all participants signed an informed consent.

In this cross-sectional study we applied a neurobehavioral test battery to all workers from the production departments of a paint factory between June 21st 2004 and September 26th 2005. The participation rate in the study was 100%, but we excluded the only two female workers that attended the study, because of the low number of female participants, and three workers that presented alcohol breath on their test day. The final study population comprised 208 male workers. We used a validated questionnaire by means of a personal interview to collect sociodemographic data and occupational history, lifestyle behaviors (smoking, alcohol intake and recreational drug use), and neurological health (history of head trauma, neurological illness, psychiatric disorders and use of neuroleptic drugs).

Considering the effects of the different OS compounds which can have different clinical manifestations on both the central and peripheral nervous systems, we used a wide-ranging test battery, including tests from the World Health Organization's Neurobehavioral Core Test Battery (WHO-NCTB),[11] complemented with additional tests previously used in Latin America[12] and four questionnaires exploring neuropsychiatric symptoms. Before the start of data collection, we trained three psychologists to apply neurobehavioral tests according to a standardized protocol and two nurses to obtain the occupational history and apply the symptom questionnaires.

Workers were tested on the same day (Monday), after 48 hours without exposure to OS. Workers were asked not to drink alcoholic and caffeinated beverages 24 hours prior to the study and to rest properly. Moreover, examiners were blinded to participants' exposure status.

The tests assessed immediate auditory memory (digit span)—correctly repeated digits (score up to 28), associative memory (digit symbol)—symbols correctly drawn in 90 seconds (score up to 93), sustained attention (digit vigilance)—numbers correctly identified in one time, verbal fluency—number of words mentioned in 60 seconds, and visual-motor perception (trail making A)—time needed to complete the test. For immediate visual memory, Benton's test was applied; besides, the number of figures correctly selected (up to 10), and motor coordination hand-skill functions were also measured.[12] The WHO-NCTB measured the number of rotated pegboards. Moreover, Pursuit aiming II evaluated the motor speed, precision and stability functions.[12] Motor speed and coordination of finger tapping and hand strength of grip measured in kilograms were assessed. For affective evaluation, the Q-16 questionnaire, Brief Symptom Inventory (BSI),[12] Seppo Aro Questionnaire and Yoshitake Questionnaire were applied. Moreover, for statistical analysis the units of original measurement were used, either the

time or number of responses, as corresponding to each test.

We tested between three and four workers per day, from 8:00 am to 2:00 pm, with breaks between tests. The average test duration for individuals was 120 minutes. A comfortable setting was provided, as well as the necessary equipment and sufficient material for adequate development of the tests. All workers received the same information and motivation.[12]

During 2006 and 2007 we measured workers' exposure to 14 of the most used solvents in paint manufacture in the different departments of the factory. A subset of workers (n=134) carried Gillian gravimetric low-flux pumps at 1 to 500 milliliters/minute (±5%) intervals, during an 8 hour work day, with 4 or 5 continued collected samples for each worker. Adsorbent activated carbon tubes were sent to the IMSS Occupational Health Laboratory in Veracruz, Mexico, for gas chromatography analysis according to international standards. The results were reported in milligrams per cubic meter (mg/m^3). The average concentrations for specific jobs and specific work areas were assigned to the remaining 74 workers who did not participate in personal measurements according to job category, work shift and years worked in the corresponding job category.

For every work shift we had one measurement of exposure which was used to assign workers' exposure levels. Then, a cumulative toluene exposure dose was estimated according to working years at the company (time-weighted average [TWA] × years working at the company). A low exposure group (group 1) was created with the first three quartiles and a high exposure group (group 2) with the one above the 75th percentile.

Since the company manufactured paints with lead oxides and some workers used leaded-glazed pottery, and as lead in blood has been associated with neuropsychological disorders and psychiatric symptoms,[13] we measured lead with an anodic voltameter (LeadCare) in capillary blood (micrograms per deciliter [μg/dl]) in a sample of workers.[13]

Statistical analysis was done with Stata v.10, which included descriptive analysis, mean differences, analysis of variance, and between proportions. Personal, sociodemographic and neuropsychiatric characteristics were considered as confounding variables (age, smoking, alcohol intake, drug use, neurologic diseases, level of education and lead exposure). Multiple linear regression models were constructed, considering 40 years of age as a cut-off point to contrast the two groups, given that cognitive decline was observed with age. A value of p <0.05 was considered as significant.

Results

The study included 208 workers from different production departments who completed the tests. Significant differences between categories were observed for mean values of age, education level, and time working at the company; for drug use, alcohol intake, head trauma and use of leaded pottery there were no differences (table I). Considering this, we evaluated the performance in each neurobehavioral test and neuropsychiatric symptom questionnaire by each work area and we did not find significant differences. We also analyzed job performance in subgroups with less or more than 10 years of employment, considering the cumulative dose and contrasted group one and two. The groups were similar in age, seniority at work and scholar achievements.

Toluene and xylene were present in all working areas, however the mean concentration in 80% of the working places was higher for toluene. Considering this and knowing that toluene (as well as xylene) is associated with neurotoxic effects,[14] we calculated the exposure related only to this substance. The 14 OS TWA concentrations were lower than the allowed values, but the highest toluene and benzene concentration surpassed this in 9 and 3 departments, respectively.

OS levels were lower than those permitted by the Mexican Official Norms (mean time weighted concentration-TWA) and United States Norms (TLV-TWA), which were very similar (table II). The average toluene weighted concentration in group one and group two was 5.65 and 21.14 mg/m^3, respectively. The cumulative index for toluene in the low exposure group was significantly lower than in the higher one (p <0.05). The means of 57% of the other 13 substances were higher in group 2, including xylene, as well as the means of 31% (table II).

Mean blood lead levels were not significantly different among users of leaded-glazed pottery (8.23 ± 6.2 μg/dl) and non-users (6.6 ± 3.7 μg/dl), and neither between the high (8.7 ± 3.8 μg/dl) and the low OS exposure groups (7.3 ± 5.9 μg/dl).

Regarding neuropsychological tests' results, we observed that 72% of the workers with high exposure to OS mixture had low performance, but the differences were only significant at 55%. The lowest performance was present in the following cognitive domains: associative memory (Digits and symbols), visual-motor perception (Trail making A), sustained attention (Digit vigilance), as well as in the cognitive motor-domain and motor coordination (Purdue pegboard, Grooved pegboard, Santa Ana and Pursuit aiming II). No differences in motor domain and neuropsychiatric symptoms tests were observed (tables III and IV).

Multiple linear regression models adjusted for age, education level and leaded-glazed pottery use showed that the higher exposure group had a lower performance in most of the neuropsychological tests; motor perception β=5.5 (p=0.04), motor speed β=-15.7 (p=0.02) and precision β=-16.4 (p=0.007) were statistically significant. Residuals analysis was performed for each model to corroborate that they fulfilled generalized linear models assumptions (table V). Other confounders were tested such as drug use, smoking, alcohol intake, traumatic brain injury, but they did not explain lower performance on any test—these confounders were categorized as present/absent and since they did not modified the model significantly, they were not included.

Table I
GENERAL CHARACTERISTICS OF MEXICAN WORKERS IN A PAINT FACTORY, DIVIDED BY EXPOSURE CATEGORIES. MEXICO CITY, 2004-2005

Variables	*Group 1** *n* *Mean (SD)*	*Group 2* *n* *Mean (SD)*	*p*
Age (years)	156 32.2 (8.0)	52 42.25 (8.3)	<0.001‡
Education level (years completed)	156 10.1 (2.1)	52 8.8 (2.6)	<0.001‡
Work seniority (years)	156 4.7 (5.6)	52 18.0 (8.6)	<0.001‡
Blood lead levels (μg/dl)	31 7.3 (5.9)	10 8.7 (3.8)	0.09§
Categorical variables	*n (%)*	*n (%)*	*p*
Drug use	155	49	
No	(75.5) 117	(85.7) 42	0.13#
Yes	(24.5) 38	(14.3) 7	
Alcohol intake	155	49	
No	(3.9) 6	(10.2) 5	0.09#
Yes	(96.13) 149	(89.8) 44	
Smoking	156	51	
No	(26.9) 42	(19.6) 10	0.30#
Yes	(73.1) 114	(80.4) 41	
Head trauma	156	52	
No	(50.6) 79	(53.8) 28	0.70#
Yes	(49.4) 77	(46.2) 24	
Use of PbLGCP&	156	51	
No	(32.7) 51	(31.4) 16	0.86#
Yes	(67.3) 105	(68.6) 35	

* Compacted group of the first three quartiles of the cumulative toluene index
‡ Student's *t* test
§ Mann Whitney U
# Chi squared test
& Leaded-glazed pottery; μg/dl: micrograms per deciliter

Discussion

Drawn from the results of the present work, it can be suggested that working populations with long-lasting high OS exposure time could have lower performance in the usual processing of information, i.e. the cognitive domain. A decrease in visual-motor perception was identified with Trail making test A, along with cognitive-motor alterations, where hand skills with speed and precision (Pursuit aiming II) showed a worse perfor-

Table II
WEIGHTED MEANS IN TIME OF 14 ORGANIC SOLVENTS AND CONCENTRATION LEVELS OF THE UNITED STATES AND MEXICAN STANDARDS. MEXICO CITY, 2004-2005

Organic solvent *Number of job positions with exposure to OS*	*TWMC* *Median (mg/m^3)* *[min-max]*	*TLV-TWA 2013* *(mg/m^3)* *[ppm]*
Toluene n=134	13.14 [1.1-495.9]	188.4 [20]
n-hexane n=48	3.38 [0.89-67.25]	176.24 [50.1]
Ethanol n=36	3.99 [0.86-16.4]	1884 [991.6]
Isopropanol n=54	4.41 [0.702-226.45]	491.5 [200.6]
Buthyl alcohol n=103	3.46 [0.63-58.92]	60.63 [16.22]
Acetone n=32	4.3 [1.17-165.46]	1187 [494.6]
Methyl-isobutyl-ketone n=105	6.64 [0.67-155.71]	204.83 [49.96]
Methyl-ethyl-ketone n=35	3.91 [0.69-123.97]	589.78 [200]
Ethyl acetate n=45	3.1 [0.81-22.3]	1441 [412]
Butyl acetate n=88	2.18 [0.68-52.04]	712.64 [150.6]
Benzene n=9	3.2 [0.801-30]	1.6 [0.5]
Xylene n=134	10.7 [1.67-112.96]	434.2 [100]
Methyl-n-amyl ketone n=12	4.2 [1.71-6.71]	233.5

TWMC: time weighted mean concentration
TLV-TWA: threshold limit value-time weighted average

Table III
Results of neuropsychological tests by cumulative exposure categories in Mexican workers from a paint factory. Mexico City, 2004-2005

Neuropsychological tests	*Group 1** *n* *Mean (SD)*	*Group 2‡* *n* *Mean (SD)*	*p§*
Cognitive	156	52	
Benton (figures chosen correctly)	8.4 (1.5)	8.1 (1.3)	0.20
Digits and symbols (correct items)	48.2 (9.8)	42.8 (8.9)	<0.001
Total digit span (correct sequences added)	9.9 (2.5)	9.2 (2.3)	0.04
Verbal fluency (number of words)	155	48	
Naming animals	19.2 (5.2)	18.1 (5.9)	0.21
Words with the letter "F"	9.7 (3.8)	9.8 (4.5)	0.86
Trail making A (sec)	153 43.0 (14.75)	51 52.7 (17.6)	<0.001
Digit vigilance (length time)	155 172.8 (33.5)	51 189.7 (34.0)	0.001
Cognitive-motor	156	52	
Purdue pegboard, dominant hand (time in seconds)	15.9 (2.1)	15.3 (1.6)	0.06
Purdue pegboard, non-dominant hand (time in seconds)	14.9 (1.8)	14.2 (1.6)	0.009
Grooved pegboard and slots, dominant hand (time)	58.7 (7.4)	62.9 (6.8)	<0.001
Grooved pegboard and slots, non-dominant hand (time)	66.6 (9.5)	71 (11.1)	0.003
Santa Ana (total number rotated pegs)	81.6 (12.1)	77.2 (10.5)	0.009
Pursuit aiming II	156	52	
Sum of correct and incorrect points (speed)	239.1 (40.5)	207.7 (37.3)	<0.001
Proportion of correct points (precision)	0.95 (0.05)	0.95 (0.09)	0.90
Motor	156	52	
Grip strength, dominant hand (kg)	38.4 (7.4)	36.9 (5.5)	0.18
Grip strength, non-dominant hand (kg)	36.4 (6.7)	35.5 (6.5)	0.38
Finger tapping dominant hand	48.8 (6.5)	48.4 (6.4)	0.67
Finger tapping non-dominant hand	44.6 (5.6)	44.34 (4.8)	0.78
Stability in nine holes	155	52	
Number of times edge was touched, dominant hand	109.7 (45.1)	100.2 (43.2)	0.20
Time duration touching edge (sec), dominant hand	129 9.8 (5.6)	24 11.2 (6.4)	0.30
Number of times edge was touched, non-dominant hand	156 115.6 (41.0)	52 113.4 (45.5)	0.75
Time duration touching edge (sec), non-dominant hand	129 12.6 (6.1)	24 13.8 (6.3)	0.40

* Group 1: low exposure (5.65 mg/m^3)
‡ Group 2: high exposure (21.14 mg/m^3)
§ Student's *t* test

mance compared with the low exposure group. Age also contributed to diminish these functions, whereas higher education level increased them as expected, and this provides certainty that the observed effects are true. Although the remaining multiple linear regression models did not show significant differences between the groups, the group with the highest accumulated exposure consistently performed worse (table V).

The diversity of processes where OS were used poses a challenge and limits extrapolation of the results. Therefore, we considered comparing our results with studies carried out in factories which produce solvent-

Table IV
MEAN SCORE OF FATIGUE, STRESS AND NEUROPSYCHIATRIC SYMPTOMS IN MEXICAN WORKERS FROM A PAINT FACTORY. MEXICO CITY, 2004-2005

Questionnaires	*Group 1* *n* *Mean (SD)*	*Group 2* *n* *Mean (SD)*	*P**
Brief Symptom Inventory (BSI)			
Somatization symptoms	156 0.29 (0.34)	52 0.34 (0.37)	0.40
Obsessive-compulsive symptoms	156 0.51 (0.41)	52 0.47 (0.36)	0.52
Interpersonal sensitivity	156 0.47 (0.60)	52 0.41 (0.4)	0.53
Depression symptoms	156 0.32 (0.48)	52 0.36 (0.34)	0.70
Anxiety symptoms	156 0.49 (0.48)	52 0.39 (0.46)	0.22
Hostility symptoms	156 0.42 (0.58)	52 0.32 (0.37)	0.27
Phobic anxiety symptoms	156 0.28 (0.33)	52 0.29 (0.34)	0.85
Paranoia symptoms	156 0.74 (0.58)	52 0.71 (0.50)	0.68
Psychosis symptoms	156 0.45 (0.47)	52 0.40 (0.40)	0.48
Additional symptoms	156 0.39 (0.46)	52 0.39 (0.36)	0.96
BSI total score	156 4.4 (3.7)	52 4.0 (2.9)	0.54
Stress (Seppo Aro)	156 7.8 (5.3)	52 8.4 (5.8)	0.51
Fatigue (Yoshitake)	156 4.4 (3.9)	52 4.3 (3.8)	0.85
Neuropsychiatric symptoms Q-16 (frequency)	156 3.0 (2.7)	52 3.3 (2.9)	0.52

* Student's test
Group 1: low exposure (5.65 mg/m^3)
Group 2: high exposure (21.14 mg/m^3)

based paints or industrial painters by the similarity of mixtures to which workers are exposed: toluene, xylene, n-hexane, benzene and acetone.

Paint industry has been transformed since the end of the 1960's and has gradually decreased exposure levels to OS mixtures.[4,15] Despite this decline, Orbaek and colleagues observed a decrease in memory, difficulties in concentration, fatigue, as well as feeling of internal tension and hostility in an exposed group, pointing out the presence of a neurasthenic syndrome.[4] Similar results were found by Elofsson and colleagues in which painters also had significant differences in performance of speed of perception, manual skills and memory, among other tests.[16] Even so, we did not find any differences in neuropsychological symptoms (table IV). In addition, Jung-Der and Jong-Dar identified more acute and chronic central nervous system symptoms in the category of higher OS exposure among workers in paint factories from Taiwan.[17]

Thus, decrease in the performance of only three tests (14%) of 21, including emotional disorders in our study, is slightly lower than the proportion of lower performance tests found by Son-Yen *et al*—three (21%) out of 14 in Taiwan.[8] Also in that study, the exposure determined lower performance in continuous pattern matching and memory performance,[8] whereas in our study these changes were related to the lower cognitive performance across domains (Trail making) and cognitive-motor (Pursuit aiming II) related to greater exposure. Similar to our results, Colvin and colleagues, and Kishi and colleagues studied industrial painters exposed to similar mixtures at moderate concentrations; a decrease in the performance in various neuropsychological tests was observed as well as poor performance on vocabulary, block design, digit span, and Santa Ana motor coordination test, along with two subcategories of the profile of mood status. Moreover, multiple linear regression models adjusted for age, education level and alcohol intake showed an association with OS mixture exposure, along with motor, memory and attention tests which are similar to ours in the cognitive-motor Pursuit aiming test.[18,19]

Our results were very similar to those in which cognitive deficiencies were evaluated, particularly regarding lesser cognitive performance and decreased immediate memory.[20,21] It is likely that concentrations below the allowed limits produce slight neuropsychological alterations in the cognitive sphere with no neuropsychiatric alterations.[22-24] About these supposition, it is necessary to conduct further research in populations with low OS exposure. Perhaps most of our observations were due to a greater OS mixture exposure in the recent past at U.S. capital enterprises, as flexibility in the compliance with standard limits allowed in Mexico was common. Besides we have to mention that differences between studies, despite similar OS mixtures exposures, are probably due to different OS concentrations, exposure estimation methods, and misclassification of exposure, as well as healthy worker bias and use of different neuropsychological tests.

One limitation of the study is the lack of OS exposure historical data from the company, which makes it difficult to quantify intensity and cumulative exposure time more precisely for each OS and different mixtures. Although there are biomarkers for organic solvents exposure such as phenyl mercapturic acid (benzene), mercapturic acid (toluene) and methyl hippuric acid

Table V
Multiple linear regression models for neuropsychological tests by exposure groups adjusted for age, education level, and use of leaded glazed pottery in Mexican workers from a paint factory. Mexico City, 2004-2005

Domain Neuropsychological tests	Higher exposure			Age >40			Education level			PbLGCP*		
	b	CI 95%	p	β	CI 95%	p	β	CI 95%	p	β	CI 95%	p
Cognitive Digits and symbols, R^2=24.5%	-0.74	-3.7, 2.3	0.63	-6.0	-9.0, -2.9	<0.001	1.4	0.83, 1.94	<0.001	-2.6	-5.1, -0.1	0.04
Trail making A, R^2=12.3%	5.5	0.19,10.8	0.042	4.3	-1.1, 9.8	0.12	-1.7	-2.7, -0.64	0.002	0.75	-3.7, 5.2	0.74
Digits, R^2= 2%	-0.34	-1.2, 0.53	0.44	-0.60	-1.5, 0.3	0.2	0.1	-0.06, 0.26	0.23	-0.45	-1.2, 0.3	0.23
Digit vigilance, R^2=8.3%	9.2	-2.5, 20.9	0.12	6.4	-5.5, 18.3	0.3	-3.4	-5.5, -124	0.002	0.26	-9.4, 10	0.96
Verbal fluency, Animals, R^2=2%	-0.5	-2.4, 1.5	0.63	-0.50	-2.4, 1.5	0.62	0.40	0.05, 0.74	0.025	-0.73	-2.3, 0.8	0.36
Benton, R^2=15%	0.29	-0.18, 0.7	0.22	-0.76	-1.2, -0.3	0.002	0.16	0.08, 0.25	<0.001	-0.51	-0.9, -0.1	0.01
Cognitive-motor Pegs and slots dominant hand (manual skills), R^2=10%	1.6	-1.1, 4.3	0.24	4.7	2.0, 7.4	0.001	-0.25	-0.7, 0.2	0.31	0.09	-2.1, 2.3	0.93
Pegs and slots Non-dominant hand (manual skills), R^2=10%	1.1	-2.3, 4.5	0.52	6.3	2.9, 9.8	<0.001	-0.43	-1.1, 0.2	0.17	-0.07	-2.9, 2.7	0.96
Pursuit aiming II, R^2=19.5%	-15.7	-28.9, -2.5	0.02	-24.0	-37.4, -11	0.001	3.4	0.9, 5.8	0.007	-7.4	-18.4, 3.5	0.18
Correct points, R^2=21%	-16.4	-28.2, -4.6	0.007	-18.2	-30.2, -6.1	0.003	3.6	1.5, 6	0.001	-9.4	-19.3, 0.37	0.06
Santa Ana, R^2=5.4%	-1.7	-5.8, 2.3	0.40	-4.5	-8.7, -0.40	0.032	0.45	-0.3, 1.2	0.24	-2.9	-6.2, 0.52	0.1

* PbLGCP: uses leaded glazed pottery

(xylene), their unique measurement could mislead to an imprecise exposure assessment. In Mexico, no single or repeated measurements of organic solvents in the work environment or their biomarkers are made during the working life of workers.

Moreover, exposure underestimation is possible, as we had no access to previous exposure data of workers with longer seniority, therefore we assumed that the measured OS exposure behaved similarly all the time. Furthermore, we consider that in our study healthy worker bias could be present because three years before, personnel who had been working at the company for the longest time were fired. We also have to mention that the population was young, with mean age of 32 years, which probably contributed to underestimating the observed effect.

Conclusion

There is evidence of neurotoxic effects associated with low OS exposure; however, it is difficult to compare studies' results, since the evaluation criteria, the use of neuropsychological tests and the diagnostic criteria are not homogeneous, despite the efforts made to standardize these tests by the WHO. Thus, we recommend a comprehensive assessment of the neuropsychological performance of all domains and subdomains in order to reduce bias and control confounders.[3,12]

Finally, we conclude that incipient findings are relevant because some deficiencies or impairments in some tests could have occurred even at OS exposure limits below Mexican occupational norms. This study provides information about the usage of early detection tools and suggests that occupational norms regarding OS exposure limits should be revisited in order to prevent health damages and to apply epidemiologic surveillance in workers at risk.

Funding

Source of financial support: The Miguel Alemán AC Foundation and the Mexican Ministry of Health Fund

for Medical Research Promotion (FOFOI-IMSS): FP-2003/109.

Acknowledgements

To the Miguel Alemán AC Foundation, the Mexican Ministry of Health and the Mexican Institute of Social Security. Cuauhtémoc Arturo Juárez Pérez is an Irving Selikoff International Scholar of the Mount Sinai School of Medicine (grant 1 D43 TW00640 from the Fogarty International Center of the National Institutes of Health).

Declaration of conflict of interests. The authors declare that they have no conflict of interests.

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