Neurobehavioral Changes of Shipyard Painters Exposed to Mixed Organic Solvents

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Abstracts: This study was conducted to evaluate neurobehavioral changes arising from occupational exposure to organic solvents among shipyard painters and to establish whether a dose-effect relation existed where there was any observed impairment of neurobehavioral performance by running the test of Simple Reaction Time (SRT), Symbol Digit Substitution (SD), and Finger Tapping Speed (FT) with a computer-assisted neurobehavioral test battery. The study group consisted of 180 shipyard painters and 60 reference workers. The workers answered a self-administered questionnaire on occupational, medical history, and demographic characteristics including age, work duration, education level, and quantity and frequency of alcohol and smoking, and performed three psychometric tests on the Korean Computerized Neurobehavioral tests. To estimate cumulative exposure level, samples of ambient air on 61 painters were analyzed using a gas chromatograph. Shipyard painters and the reference group showed significant differences in the results of test of SD, FT of dominant hand, and FT of non-dominant hand. The test results of SD of shipyard painters also showed significant difference by duration of work. This suggests that occupational exposure of organic solvent could induce neurobehavioral changes in the shipyard painters. Therefore an objective neurobehavioral test is recommended on evaluating neurobehavioral performance of long-term solvent-exposed shipyard workers.

Key words: Computer assisted neurobehavioral test, Shipyard painter, Organic solvents

Introduction

There is considerable evidence that long term occupational exposure to mixed organic solvents can cause a wide range of chronic central nervous system abnormalities^{1–8}. Behavioral manifestations of such damage include an increase in psychiatric symptoms, reported memory and concentration difficulties, and impairment of cognitive functioning as demonstrated by performance on neurobehavioral tests. In many cases these effects are subtle, occurring in the absence of overt clinical signs and only measurable by use of psychological test procedures.

There are many neurobehavioral tests and systems to assess

neurotoxic exposures in the workplace. World health organization (WHO) recommended neurobehavioral core test battery (NCTB) which consisted of digit symbol, digit span, Benton visual retention, pursuit aiming, simple reaction time, Santa Ana, and profile of mood states^{9, 10}. Letz and Baker developed the neurobehavioral evaluation system (NES) in the mid 1980s¹¹. The NES is a computer based testing system that incorporates the cognitive tests from NCTB and a number of other tests used in clinical neuropsychology. Letz's subsequent adaptation of the battery (the NES II) became the dominant testing system in 1990s^{12, 13}. Iregren *et al.*¹⁴ developed Swedish performance evaluation system (SPES), which was used for screening test for neurobehavioral disturbances of some neurotoxins^{15–18}. Recently, the behavioral assessment and research system (BARS) was used

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for the detection of neurotoxicity in non-mainstream human populations specifically people with limited education or literacy¹⁹⁻²¹).

The shipyard painters are exposed to many kinds of organic solvents and other neurotoxin such as lead which may be harmful to nervous system. In 1985 Valciukas *et al.*²² reported that neurobehavioral performance decreased in the shipyard painters compared with a control group, and found no significant correlations between performance test scores and duration of solvent exposure. In a study by Ruijten *et al.*²³, long-term exposure to xylene and other mixed organic solvents in shipyard spray painters caused impairment of simple visuo-motor performance and complex perceptual coding, and a relationship between effects on perceptual coding and the exposure index was demonstrated. Prevalence of neuropsychological symptoms among a cohort of dockyard painters was significantly increased compared with a non-painters^{24, 25}).

When planning human neurobehavioral research to detect exposure effects, the primary factor should be the chemicals to which the target subject is exposed. However, it is well known that Iregren and Letz's recommendation of the symbol digit, Simple Reaction Time, and tapping tests should be included in the core set of neurobehavioral tests¹⁶).

In Korea, Korean version of SPES (KCN; Korean Computerized Neuro-behavioral System version 2.1, ZNCSoft, Korea) has been widely used to detect neurobehavioral disturbance of workers exposed to various neurotoxin such as organic solvent and manganese²⁶⁻²⁸). Korean version of SPES consists of Korean written instruction and a simplified keyboard that have 10 buttons and several symbol keys (Fig. 1). We selected 3 tests from the Korean version of SPES to evaluate neurobehavioral performance of shipyard painters: Simple Reaction Time (SRT), Symbol Digit Substitution (SD), and Finger Tapping Speed (FT) in the battery were administered.

The objectives of the present study is to investigate neurobehavioral changes of shipyard painters compared with workers without organic solvent exposure, and to establish whether a dose-effect relation existed in where there was any observed impairment of neurobehavioral performance with a computer-assisted neurobehavioral test battery.

Subjects and Methods

The exposed subjects comprised 180 shipyard painters employed by a shipyard in Ulsan, Korea. There were 60 groups that consisted of 3 cases whose ages were close to 1 randomly selected safety inspector who did not exposed to

Fig. 1. Keyboard of Korean version of Swedish performance evaluation system.

organic solvent in a shipyard. The painters were exposed to mixed organic solvents during their working of spray painting, mixing of paint, and painting by brush. The study subjects represented 51% of all those painters employed by a shipyard. Twenty-six percent were unwilling to take part in the study and 23% were excluded due to pre-set exclusion criteria, namely educational level below 9 yr, previous head injury, alcohol or drug dependency, or existing disease affecting the nervous system. The painters included in exposure group did not change the job duties up to the study. The study was carried out with their informed consent.

A questionnaire was administered prior to testing. The questionnaire consisted of occupational, medical history, and demographic characteristics including age, work duration, education level, and quantity and frequency of alcohol and smoking. All the exposed subjects had an exposure-free time of at least 48 h. Before a test day, the subjects were asked to sleep their usual duration and not to drink any alcoholic beverages in the evening before the test day. The subjects were given the amount of US \$35 (approximately 120% of their wage for working an equivalent time) as an incentive. A trained examiner administered the test of Simple Reaction Time, Symbol Digit Substitution, and Finger Tapping Speed in the battery.

Simple Reaction Time is a visuo-motor speed test that measures how fast a subject responds to a visual stimulus by pressing a button²⁹). Data are recorded as individual reaction times over the presentation of nine blocks of 8 trials each. The time interval between the blocks is 30 s. The mean and standard deviation of the response latencies (in msec) over the last 6 blocks are used as the dependent measures for this task. Shorter reaction time indicates better neuropsychological performance. Symbol Digit Substitution

Table 1. Demographic characteristics of the shipyard painters and controls

Characteristics	Painters (n=180)	Controls (n=60)	p
Age (yr)	43.9 ± 8.0	44.0 ± 6.2	0.920
30–39	54 (30.0%)	18 (30.0%)	
40–49	96 (53.3%)	32 (53.3%)	
50–59	30 (16.7%)	10 (16.7%)	
Education (yr)	12.6 ± 2.9	13.9 ± 2.0	0.000
Work duration (yr)	16.5 ± 9.0	16.1 ± 10.5	0.775
Smoking (Pack · yr)	12.9 ± 9.8	13.0 ± 16.1	0.964
Absolute alcohol consumption (g/wk)	86.5 ± 110.4	84.0 ± 133.8	0.896

is widely used and sensitive tests to detect central nervous system damage regardless of its etiology in human behavioral neurotoxicity research³⁰). The test presents nine symbols, each paired with a number between 1 and 9 in matrix. After five presentations of the symbols and digits together, the symbols are presented alone and a subject asks to respond with corresponding digits. Mean response latency (in sec) is recorded. A shorter latency indicates better neurological performance. This test is a measure of incidental memory and is recorded in terms of number of incorrect responses. Finger Tapping Speed test is a test of motor speed and coordination²⁹). An examinee is instructed to press a button as many as possible in 30 s. This occurs with the dominant hand and subsequently the non-dominant hand.

For exposure assessment two sources of information were used. One is a direct field exposure measurement, and the other is information from job descriptions included in the questionnaire. The direct field exposure measurement was done in April 2003. Randomly selected 61 out of 180 shipyard painters were given three passive dosimeters (3M 3500 Organic vapor Monitors) to collect volatile organic compounds in the personal breathing zone during 3 separate work days. Subjects were instructed to attach the dosimeters to the lapel or pocket of their shirt taking care that the dosimeter was exposed to the air all the times. The dosimeter were analyzed by NIOSH Method 1500 for hydrocarbon extraction from charcoal using 1.5 ml of carbon disulfide containing 50 µg/ml of bromofluorobenzene as an internal standard. The samples were analyzed by gas chromatography HP 5890II mass (Hewlett Packard, USA) and gas chromatography mass spectrometry HP6890/5973N (Hewlett Packard, USA). Mixed organic solvent exposure index (En) was a sum of each current solvent level divided the threshold limit value (TLV) of the American Conference of Governmental Industrial Hygienists (ACGIH)³¹).

En = $\sum Ci/TLVi$, where Ci = concentration of each solvent, TLVi = TLV of each solvent

A cumulative exposure index (CEI) was calculated from: a sum of the products of exposure duration and mixed solvent exposure index. Exposure duration was working duration of painting job expressed in years.

CEI = En × exposure duration (year)

Exposure duration in years was once more used as a surrogate for dose. The subjects were structured into 3 exposure groups (< 10 yr, 10–20 yr, > 20 yr).

Data were analyzed by SPSS 10.0 for Windows. Student *t*-test was used for a simple comparison of the neurobehavioral performance between the exposed and control groups. To ascertain and control of confounding factors multiple regression analysis and the analysis of covariance were used.

The demographic data revealed no significant difference between the shipyard painters and controls on the demographic variables except education level. The mean age of shipyard painters was 43.9, and that of control was 44.0. The control group had more educated than shipyard painters ($p=0.000$). The mean work duration of shipyard painters was 16.5 yr, and that of controls was 16.1 yr (Table 1).

Xylene, methyl isobutyl ketone (MIBK), ethylbenzene, 1-butanol, 2-methoxyethanol, cyclohexane, trimethylbenzene, toluene, and other several organic solvents were detected. The airborne concentrations of top 10 organic solvents were listed in Table 2.

The concentrations of all organic solvents were below their TLVs of ACGIH.

Results

Multiple regression analysis was performed to assess the effect of the demographic characteristics on neurobehavioral performance. Independent variables comprised exposure, age, duration of education, alcohol intake amount (ethanol g/wk), and tobacco smoking amount (packs/yr). Exposure

Table 2. Airborne concentrations (ppm) of top 10 organic solvents

	GM	GSD	Range	TLV
Xylene	22.70	4.10	1.6–591.2	100
MIBK	10.04	3.09	1.0–404.2	50
Ethylbenzene	8.26	3.54	ND–160.8	100
1-Butanol	7.34	4.41	0.3–154.5	50
2-Methoxyethanol	6.43	2.90	0.4–85.2	100
Cyclohexanone	5.78	7.59	0.2–182.9	300
Trimethylbenzene	3.71	3.95	0.2–57.0	15
Toluene	3.70	2.75	ND–58.0	100
N-Butylacetate	3.30	4.67	ND–160.8	150
2-Butoxyethanol	1.25	1.73	0.6–2.6	25

GM: geometric mean, GSD: geometric standard deviation, ND: not detected, TLV: threshold limit value.

Table 3. Multiple regression analysis of neurobehavioral tests (n=240)

Variable	SRT			SD			FTSD			FFTSN		
	β	p	R ²	β	p	R ²	β	p	R ²	β	p	R ²
Exposure	–3.98	0.742		–524.43	0.0000		3.09	0.145		3.64	0.000	
Age (yr)	–0.55	0.432		26.52	0.000		–0.20	0.000		–0.08	0.0301	
Education (yr)	–0.49	0.415	0.016	–413.31	0.000	0.178	–0.07	0.317	0.093	–0.02	0.122	0.162
Smoking	0.72	0.137		2.43	0.677		–0.02	0.666		–0.05	0.354	
Alcohol	–0.05	0.313		–0.34	0.546		–0.01	0.085		–0.01	0.091	
Constant	319.8	0.000		2591.75	0.000		67.81	0.000		55.55	0.000	

β : regression coefficient, SRT: Simple Reaction Time, SD: Symbol Digit Substitution, FTSD: Finger Tapping Speed of dominant hand, FFTSN: Finger Tapping Speed of non-dominant hand.

Table 4. Results of neurobehavioral test of study subjects before and after controlling age and education

Tests	Unadjusted mean $\pm$ S.D.			Adjusted mean (S.E.)		
	Painters (n=180)	Controls (n=60)	p	Painters (n=180)	Controls (n=60)	p
SRT (msec)	297.2 $\pm$ 70.0	292.2 $\pm$ 95.0	0.671	296.0 (5.9)	295.8 (10.9)	0.992
SD (msec)	3,233.2 $\pm$ 998.9	2,693.8 $\pm$ 711.8	0.000	3,156.6 (67.7)	2,691.6 (124.3)	0.000
FTSD (No. of taps/10 sec)	62.6 $\pm$ 8.2	66.4 $\pm$ 9.7	0.000	63.0 (0.6)	65.5 (1.2)	0.046
FTSN (No. of taps/10 sec)	55.9 $\pm$ 8.0	60.2 $\pm$ 9.7	0.000	56.1 (0.7)	60.3 (1.2)	0.003

S.D.: standard deviation, S.E.: standard error, SRT: Simple Reaction Time, SD: Symbol Digit Substitution, FTSD: Finger Tapping Speed of dominant hand, FTSN: Finger Tapping Speed of non-dominant hand.

group had a significant effect on the results of SD and FT of non-dominant hand. Age had a significant effect on those of SD and FT of dominant hand. However duration of education had a significant effect only on the result of SD. On the contrary alcohol intake amount and tobacco smoking amount did not affect any neurobehavioral performance (Table 3).

Simple comparison of the results of neurobehavioral performance between shipyard painters and controls showed

significant differences in the tests of SD, FT of dominant hand, and FT of non-dominant hand. These significant differences between groups were sustained though significance levels became slightly weak despite controlling the confounding factor such as age and education level by the analysis of covariance (Table 4).

In another multiple regression analysis all results of neurobehavioral performance were not affected by cumulative solvent exposure index obtained by the direct

Table 5. Results of neurobehavioral test of shipyard painters by duration of work adjusted for age and education

Tests	< 10 yr (n=48)	10–20 yr (n=41)	> 20 yr (n=91)
SRT (msec)	297.8 (20.4)	297.9 (11.2)	292.3 (11.6)
SD (msec)	2,972.1 (282.5)	3,033.8 (155.1)	3,452.4 (160.7)*
FTSD (No. of taps/10sec)	64.8 (2.3)	63.9 (1.3)	61.3 (1.3) [#]
FTSN (No. of taps/10 sec)	57.6 (2.4)	56.3 (1.3)	55.2 (1.3)

*, P<0.05, [#], P=0.052, S.E.: standard error, SRT: Simple Reaction Time, SD: Symbol Digit Substitution, FTSD: Finger Tapping Speed of dominant hand, FTSN: Finger Tapping Speed of non-dominant hand.

field exposure measurement of current exposure and duration of exposure (The result of tests was not presented).

However, when 'duration of exposure in year' was used as a measure of 'dose', the test results of SD between the group with exposure years < 10 and the group with exposure years > 20 were significantly different after controlling for age and education level by the analysis of covariance. Those of FT of dominant hand were different between the two groups through not significantly (Table 5).

Discussion

During the last two decades, the use of computers in psychological testing has steadily increased, motivated by the ambition to reach higher levels of resource efficiency and a higher degree of uniformity in test administration and scoring than is possible with traditional procedures. Computer-assisted systems also have been developed to provide interpretive test reports. The combination of computer and psychological tests has led to a compilation of systems with automatic test interpretation.

Iregren and Letz recommended that the core set of tests should include the symbol digit, Simple Reaction Time, and finger tapping tests¹⁶. So we adopted 3 tests of KCN to assess the neurobehavioral performance of shipyard painters.

Age is the strongest factor of neurobehavioral performance^{1, 29, 32, 33}. To remove the effect of age on neurobehavioral performance we matched age of painters and controls. As duration of education also was known to affect neurobehavioral performance^{9, 29, 32, 34}, we excluded workers whose educational level was below 9 yr to reduce the effect of education level on neurobehavioral performance. However, duration of education still had effect on the result of SD according to the results of multiple regression analysis in our study.

The results of our study are consistent with the previous studies of Valciukas *et al.*²² and Ruijten *et al.*²³ who reported

neurobehavioral changes of shipyard painters. However, we can find no significant correlations between neurobehavioral performance and cumulative exposure index. Considering of the test results of neurobehavioral performance, damage of central nervous system with or without abnormal motor speed and coordination was suspected in shipyard painters who were chronically exposed to mixed organic solvents.

Alcohol intake amount did not affect any of neurobehavioral performance, this was consistent with the previous study of Paker *et al.*³⁵. Tobacco smoking amount also did not affect any of neurobehavioral performance, this was consistent with the study of Andersson and Hockey³⁶.

Affinity to computer was known to affect the results of neurobehavioral test³⁷, so we used a simplified keyboard that had 10 buttons and several symbol keys to reduce the effect of affinity to computer. This keyboard was proved to be suitable all kinds of subjects regardless of familiarity to computer on the performance of computerized neurobehavioral tests³⁸.

The shipyard painters were exposed to mixed organic solvents such as xylene, MIBK, ethylbenzene and so on, the geometric concentrations of each organic solvent were below TLVs of ACGIH. At first we used cumulative exposure index as 'dose' of organic solvents, however, there was no correlation between cumulative exposure index and neurobehavioral performance. It means cumulative exposure index is not a suitable measure of chronic exposure effect of organic solvents on neurobehavioral performance, but a measure of current exposure, and cumulative exposure index also did not reflect the extent of internal dose of current and past exposure that could have a biological effect on the exposed workers. A direct field measurement is useful only for identifying the kinds and levels of organic solvents for this study. As Spurgeon *et al.*³⁹ have used exposure duration as 'dose' of exposure, the painters were structured into 3 exposure groups (< 10 yr, 10–20 yr, > 20 yr). The test results

of SD between the group with exposure years < 10 and the group with exposure years > 20 were significantly different after controlling the confounding factors by the analysis of covariance. Though the significance level was slightly low, those of FT of dominant hand were also different between the group with exposure years < 10 and the group with exposure years > 20. These means there is a week dose-effect of organic solvents on neurobehavioral performance.

Certain limitations exist with this study. First, we performed only 3 tests of KCN, so we could not evaluate various functions of central nervous system. Second, we did not consider the effects of other neurotoxic substance that could be exposed during working such as lead. The possibility of neurobehavioral changes due to lead could not be rule out.

In summary, occupational exposure of organic solvent could induce neurobehavioral changes in the shipyard painters. Therefore an objective neurobehavioral test is recommended on evaluating neurobehavioral performance of long-term solvent-exposed shipyard workers.

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