

## Cognitive Impairment and Peripheral Neuropathy by Mixed Organic Solvents in Spray Painters Working in a Shipbuilding Industry

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**Background** : Exposure to organic solvents becomes a common problem to workers of heavy industries in Korea. A number of volatile organic solvents which are frequently used in painting can cause various derangements of the nervous system, especially cognitive impairments and peripheral neuropathy. **Methods** : This study was carried out on 190 workers as a control group who had never been exposed to organic solvents and on 674 spray painters with long-term exposure to organic solvent mixtures. The major components of organic solvent mixtures were determined. All subjects underwent neurological examination as well as routine physical check-up after completing questionnaires on general, musculoskeletal, neuropsychiatric and neurological systems. Subjects with abnormal findings on neurological examination related with the exposure of organic solvent mixtures took further neuropsychological and neurophysiological tests. **Results** : The prevalence rates of cognitive impairments and of peripheral neuropathy in the exposed group were significantly higher than the control group (9.5% vs 2.1% and 2.1% vs 0%, respectively). High exposure group (more than 2.64 of cumulative exposure index, CEI) showed also higher prevalence of cognitive impairments and of peripheral neuropathy than low exposure group (cognitive impairments; 12.3% vs 6.4%, peripheral neuropathy; 2.3% vs 1.8%). Most common cognitive impairments were attentional deficit, and abnormal sense on the extremities or face was most common symptom of the peripheral nervous system. **Conclusions** : This study is the first large-scale, case-control study extensively evaluating cognitive impairments and peripheral neuropathy related with volatile organic solvent mixtures in spray painters working in a shipbuilding industry in Korea. The results show that the prevalence rates of cognitive impairments and of peripheral neuropathy are relatively low, but clearly related with the exposure extent of organic solvents.

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**Key Words** : Mixed organic solvents, Prevalence rate, Cognitive impairment, Peripheral neuropathy

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**In Soo Joo, M.D.** 1995 0.14% ,  
Department of Neurology, .  
Ajou University School of Medicine, 16% .  
Wonchon-dong, San 5, Paldal-ku, .  
Suwon, 442-721, Korea (carbon disulfide, CS<sub>2</sub>)가  
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dimethyl formamide), TCE(trichloroethylene), 2-bromopropane 가 .<sup>2</sup>

가 .<sup>3</sup>

가 (cognitive difficulties scale, CDS)<sup>15</sup>

가 38

(malingering)

가 7

(coordination),

가 가

.<sup>6</sup>

가

.<sup>7</sup>

.<sup>8</sup>

.<sup>9</sup>

encephalopathy) 가 ,<sup>10-11</sup>

(toxic

가 27

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Dantec Counterpoint

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Oh <sup>16</sup>

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FID, Hewlett Packard 5890 series , U.S.A.)

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1996 7 2 7 16

**Table 1.** Demographic characteristics of the study groups

Characteristics	Control Group		Exposed Group	
	(n=190)	LE*(n=348)	HE†(n=326)	
Sex†				
Male	187 (98.4%)	324 (99.4%)	296 (85.1%)	
Female	3 (8.0%)	2 (0.6%)	52 (14.9%)	
Age (year)†	39.7 ± 8.1 <sup>§</sup>	39.5 ± 8.2	42.4 ± 7.0	
Education (year)†	10.1 ± 2.0	10.0 ± 2.1	9.1 ± 2.4	
Duration of exposure (year)	-	9.5 ± 5.5	12.5 ± 3.6	
Alcohol consumption (bottles)	1.9 ± 2.3	2.1 ± 3.0	1.6 ± 3.1	
Smoking (pack-year)	10.2 ± 10.2	10.3 ± 12.6	9.5 ± 12.4	

\*Low exposure group (CEI<2.64), †High exposure group (CEI ≥ 2.64), ‡p<0.05

§Mean ± Standard deviation

**Table 2.** TWA/TLV\* of each solvents in solvent mixture and exposure index of solvent mixtures (Em)†

Solvents	TWA	TLV	Overexposure frequency (%)‡
	Mean ± SD (minimum-maximum)		
Acetone	1.19 ± 10.83 (0.00-156.85)	750	
Butyl acetate	0.35 ± 1.21 (0.00-9.97)	150	
Benzene	0.08 ± 0.49 (0.00-4.98)	10	
1-Butanol	1.44 ± 6.10 (0.00-61.0)	50C <sup>§</sup>	2 (0.5)
2-Butanol	0.08 ± 0.62 (0.00-7.51)	100	
2-Ethoxy ethyl acetate	0.21 ± 1.11 (0.00-14.09)	5	3 (0.8)
Ethyl acetate	0.32 ± 1.44 (0.00-12.64)	400	
Ethyl benzene	4.04 ± 11.91 (0.00-110.10)	100	1 (0.3)
2-Ethoxy ethanol	0.14 ± 0.40 (0.00-4.57)	5	
Ethyl(2-, 3-, 4-) toluene	2.69 ± 8.46 (0.00-108.01)	-	
Hexane	0.04 ± 0.79 (0.00-15.71)	50	
Isobutyl alcohol	0.05 ± 0.24 (0.00-1.61)	50	
Isopropyl alcohol	0.03 ± 0.20 (0.00-2.06)	400	
Methyl butyl ketone	0.08 ± 1.07 (0.00-18.87)	5	2 (0.5)
2-Methoxy ethanol	0.09 ± 0.35 (0.00-4.60)	5	
Methyl ethyl ketone	0.08 ± 0.72 (0.00-12.91)	200	
Methylisobutylketone	0.50 ± 2.02 (0.00-21.84)	50	
Propyl benzene	1.19 ± 3.81 (0.00-25.57)	-	
Styrene	0.10 ± 0.50 (0.0-5.62)	50	
Trichloroethylene	0.06 ± 0.77 (0.00-14.25)	50	
Trimethylbenzene	1.99 ± 5.41 (0.00-54.40)	25	6 (1.5)
Toluene	1.74 ± 7.24 (0.00-102.62)	100	1 (0.3)
Xylene (m-, o-, p-)	16.58 ± 56.48 (0.00-480.48)	100	15 (3.8)
Em	0.44 ± 1.05 (0.00-10.20)	1	41 (10.3)

\*TWA (Time Weighted Average concentration, ppm)/TLV (Threshold Limit Value, ppm)

†Em (Exposure index of solvent mixtures) = Xn/TLVn, where Xn is the time-weighted concentration of the nth solvent and TLVn is the threshold limit value for that solvent

‡Sample number = 398

§Ceiling value (ppm)

(cumulative exposure index, CEI)

3.

17

CEI

SPSS 7.0

2.64

2.64

ANOVA)

(oneway

2

**Table 3.** Results of cognitive impairments on neuropsychological test

Cognitive impairment	Control Group	Exposed Group	
	(n=190)	LE*(n=326)	HE†(n=348)
minimal to mild (1.5-2SD)	1	13	22
moderate to severe (>2.SD)	3	8	21
Total‡	4 (2.1%)	21 (6.4%)	43 (12.3%)

\*Low exposure group (CEI<2.64), †High exposure group (CEI ≥ 2.64), ‡p<0.05

**Table 4.** Cognitive impairments of the exposed group on neuropsychological test

Cognitive domains	Exposed Group		
	Total (n=674)	LE* (n=326)	HE† (n=348)
Attention	48 (7.1)‡	14 (4.3)	34 (9.8)
mild	19 (2.8)	8 (2.5)	11 (3.2)
severe	29 (4.3)	6 (1.8)	23 (6.6)
Memory	46 (6.8)	15 (4.6)	31 (8.9)
mild	21 (3.1)	7 (2.2)	14 (4.0)
severe	25 (3.7)	8 (2.4)	17 (4.9)
Psychogenic disorder	36 (5.3)	10 (3.0)	26 (7.5)
mild	11 (1.6)	3 (0.9)	8 (2.3)
severe	25 (3.7)	7 (2.1)	18 (5.2)
Executive function	22 (3.3)	6 (1.8)	16 (4.6)
mild	13 (1.9)	4 (1.2)	9 (2.6)
severe	9 (1.3)	2 (0.6)	7 (2.0)
Visuoconstructive function	10 (1.5)	2 (0.6)	8 (2.3)
mild	4 (0.6)	1 (0.3)	3 (0.9)
severe	6 (0.9)	1 (0.3)	5 (1.4)
Intellectual decline	1 (0.1)	0 (0.0)	1 (0.3)

\*Low exposure group (CEI<2.64), †High exposure group (CEI ≥ 2.64)

‡Number of person (%)

p = 0.05

2.

1. 864 (40.3%), 190 (22%), 326 (37.7%), 57 (7%), 807 (93%), 41 (39.5%), 398 (10.3%), 6 (1.5%), 15 (3.8%), 41 (10.1%), 12.5 (9.1%), 9.5 (10.0%), 348 (40.3%), 17ppm (17%), 4ppm 3ppm, (ethyl benzene), (ethyl toluene), (xylene), (ethyl acetate), 2-ethyl acetate, (toluene), 2-ethyl acetate, (trimethylbenzene), (methyl butyl ketone), (Em)

(Table 2).

(Table 1).

**Table 5.** Results of symptom questionnaire on the peripheral nervous system

Symptoms	Control Group	Exposed Group	
	(n=187)	LE* (n=324)	HE† (n=296)
Abnormal sense‡	78(41.7)§	226(69.8)	226(76.4)
Muscle weakness‡	27(14.4)	132(40.7)	152(51.4)
Decreased visual acuity‡	105(56.1)	229(70.7)	219(74.0)
Hearing disturbance‡	56(29.9)	184(56.8)	198(66.9)
Olfactory disturbance‡	12( 6.4)	73(22.5)	99(33.4)
Dizziness‡	32(17.1)	142(43.8)	133(44.9)
Sexual disturbance‡	20(10.7)	110(34.0)	129(43.6)
Urination problem‡	16( 8.6)	65(20.1)	75(25.3)
Defecation problem‡	38(20.3)	109(33.6)	117(39.5)
Sweating problem‡	17( 9.1)	100(30.9)	109(36.8)

\*Low exposure group (CEI<2.64), †High exposure group (CEI ≥ 2.64), ‡p<0.05

§Number of person (%)

**Table 6.** Results of nerve conduction study(NCS)

Findings	Control Group	Exposed Group
	(n=12/190)*	(n=124/674)
Normal	9	65
Abnormal	3	59
Carpal tunnel syndrome	3	32
Tardy ulnar nerve palsy	1	19
Peripheral polyneuropathy†	-	13
Median motor neuropathy	-	3
Ulnar sensory neuropathy	1	1
Bilateral ulnar neuropathy†	-	1
Combined	2	10

\* Subjects taken NCS/Total subjects of each group

† Peripheral neuropathy caused by mixed organic solvents

mative data)<sup>18</sup>  
 , 가  
 4 (2.1%), 21 (6.4%),  
 43 (12.3%)  
 가 가 (Table 3).  
 가 (38%)  
 (49%)  
 가 .  
 , (atten-  
 tional deficit)가 48 가  
 7.1% , 가 46  
 (6.8%), (psychogenic disturbance)가 36  
 (5.3%), (executive dysfunction)가  
 22 (3.3%), - (visuoconstructive  
 dysfunction) 10 (1.5%)  
 (Table 4).

가  
 (methyl-  
 hippuric acid) 0.49 g/g creatinine ,  
 ,  
 (mandelic acid)  
 (hippuric acid) 0.04 g/g creatinine,  
 0.56 g/g creatinine .  
 가 .  
 3.  
 864 가  
 가  
 84 ( 6 , 29 ,  
 47 ) . 2  
 82 ( 9.7%)  
 . 42.2 ±  
 5.9, 43.6 ± 6.4 , 44.1 ± 5.6 ,  
 9.0 ±  
 2.7, 8.7 ± 2.4 , 8.0 ± 2.6  
 .  
 (based on 'cut-off' score or nor-



(n-hexane),<sup>28</sup>  
MBK),<sup>29</sup>

(methyl-n-butyl ketone,  
(carbon disulfide)<sup>30</sup>

가

가

가

41.7%

72.9%가

가

가

가

가

가

가

가

3

59

3

가

45 19  
14

<sup>31</sup>

2.1% 가

8 (2.3%) , 6 (1.6%)

가 가

가

<sup>32</sup>

<sup>33</sup>

가 40

## REFERENCES

1. . 95 : 1996:227-257
2. : , 1997;9-42.
3. Elofsson SA, Gamberale F, Hindmarsh T, Iregren A, Isaksson A, Johnsson A, et al. Exposure to organic solvents. A cross-sectional epidemiologic investigation on occupationally exposed car and industrial spray painters with special reference to the nervous system. *Scand J Work Environ Health* 1980;6:239-272.
4. Baker EL, Fine LJ. Solvent neurotoxicity: The current evidence. *J Occup Med* 1986;28:126-129.
5. Maizlish NA, Langolf GD, Whitehead LW, Fine LJ, Albers JW, Goldberg J, et al. Behavioral evaluation of workers exposed to mixtures of organic solvents. *Br J Ind Med* 1985;42:579-590.
6. Edling C, Ekberg K, Ahlberg G, Alexandersson R, Barregard L, Ekenvall L, et al. Long term follow up of workers exposed to solvents. *Br J Ind Med* 1990;47:75-82.
7. Linz DH, de Garmo PL, Morton WE, Wiens AN, Coull BM, Maricle RA. Organic solvent induced encephalopathy in industrial painters. *J Occup Med* 1986;28:119-126.
8. Lolín Y. Chronic neurological toxicity associated with exposure to volatile substances. *Human Toxicol* 1989;8:293-300.
9. Kukull WA, Larson EB, Bowen JD, McCormick WC, Teri L, Pfanschmidt ML, et al. Solvent exposure as a risk factor for Alzheimer's disease: A case-control study. *Am J Epidemiol* 1995;141:1059-1071.
10. Cheon YH. Toxic encephalopathy in a worker to organic solvents; A case report. *Korean J Occup Med* 1991;3:216-219.
11. Kang SK, Rhee KY, Chung HK, Lee YJ. A case of demyelinating lesion in central nervous system due to organic solvents. *Korean J Occup Med* 1992;4:110-117.
12. Lee SH, Yoon NK, Lee JY, Suh SK. Psychiatric symptoms of workers exposed to organic solvents. *Korean J Preventive Med* 1992;25:1-12.
13. Lee DH, Park IG, Kim JH, Lee YH, Kang SG, Kim DH. Neurobehavioral changes according to cumulative exposure of complex organic solvents. *Korean J Preventive Med* 1995;28:386-397.
14. Sakong J, Chung JH, Lee HY. Interrelation of neuropsychiatric symptom and neurobehavioral test among workers exposed to organic solvents. *Korean J Occup Med*

- 1997;9:49-60.
15. McNair D, Khan R. Self-assessment of cognitive deficits. In Crook T, Ferris S, Bartus R. *Assessment in geriatric psychopharmacology*. New Canaan, CN: Mark Powley & Assc., 1983:137-143.
  16. Oh SJ. *Clinical electromyography*; Nerve conduction studies. 2nd ed. Baltimore: Williams & Wilkins, 1993;39-77, 447-478.
  17. Jang JY, Lee SY, Kim JI, Park JB, Lee KJ, Chung HK. Application of biological monitoring to the quantitative exposure assessment for neuropsychological effect by chronic exposure to organic solvents. *Int Arch Occup Environ Health* 1999;72:107-114.
  18. 김희정, 김희정, 김희정, 김희정. K-WAIS : 74, 1992:105-170.
  19. Andrews LS, Snyder R. Toxic effects of solvents and vapors. In Amdur MO, Doull J, Klaassen CD. *Casarett and Doull's toxicology: The basic science of poisons*. 4th ed. New York: Pergamon Press, 1991;681-722.
  20. Maizlish NA, Fine LJ, Albers JW, Whitehead L, Langolf GD. A neurological evaluation of workers exposed to mixtures of organic solvents. *Br J Ind Med* 1987;44:14-25.
  21. World Health Organization. *Environmental health; Chronic effects of organic solvents on the central nervous system*. Copenhagen: WHO, 1985.
  22. Cherry N, Hutchins H, Pace T, Waldron HA. Neurobehavioral effects of repeated occupational exposure to toluene and paint solvents. *Br J Ind Med* 1985;42:291-300.
  23. Morrow LA, Robin N, Hodgson MJ, Kamis H. Assessment of attention and memory efficiency in persons with solvent neurotoxicity. *Neuropsychologia* 1992;30:911-922.
  24. Flodin U, Edlng C, Axelson O. Clinical studies of psychoorganic syndromes among workers with exposure to solvents. *Am J Ind Med* 1984;5:287-295.
  25. Sato A, Endoh K, Kaneko T, Johanson G. A simulation study of physiological factors affecting pharmacokinetics behaviour of organic solvent vapours. *Br J Ind Med* 1991;48:342-347.
  26. Vliet CV, Swaen GMH, Volovics A, Slangen JJM, Meijers JMM, Boorder TD, et al. Exposure-outcome relationships between organic solvent exposure and neuropsychiatric disorders: Results from a Dutch case-control study. *Am J Ind Med* 1989;16:707-718.
  27. Bleecker ML, Bolla KI, Agnew J, Schwartz BS, Ford DP. Dose-related subclinical neurobehavioral effects of chronic exposure to low levels of organic solvents. *Am J Ind Med* 1991;19:715-728.
  28. Towfighi J, Gonatas NK, Pleasure D, Copper HS, McCree L. Glue sniffer's neuropathy. *Neurology* 1976;26:238-243.
  29. Allen N, Mendell JR, Billmaier DJ, Fontaine RE, O'Neill J. Toxic polyneuropathy due to methyl n-butyl ketone; An industrial outbreak. *Arch Neurol* 1975;32:209-218.
  30. Seppäläinen AM. Neurophysiological findings among workers exposed to organic solvents. *Acta Neurol Scand* 1982;Suppl(92):109-116.
  31. Silverstein BA, Fine LJ, Armstrong TJ. Occupational factors and carpal tunnel syndrome. *Am J Ind Med* 1987;11:343-358.
  32. Ehyai A, Freeman FR. Progressive optic neuropathy and sensorineural hearing loss due to chronic glue sniffing. *J Neurol Neurosurg Psychiatry* 1983;46:349-351.
  33. Mitchell ABS, Parsons-Smith BG. Trichloroethylene neuropathy. *Br Med J* 1969;1:422-423.