Neuropsychological performance of journeymen painters under acute solvent exposure and exposure-free conditions

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Abstract

Journeymen painters were evaluated with a comprehensive battery of neuropsychological tests and compared to demographically similar nonexposed controls. For painters, a cumulative exposure to solvents was estimated from a structured interview that derived an index based on lifetime exposure and exposure in the past year. Painters were tested either shortly after having painted or after an exposure-free interval. Significant between-group differences were found on a cluster of tests measuring learning and memory. Within the painter group, scores on the learning and memory tests were significantly related to the interaction of condition and exposure. That is, those painters who were tested soon after painting and who also had a higher overall lifetime exposure, performed worst on tests of learning and memory. These results are consistent with the view that neuropsychological function—particularly learning and memory—may be compromised in active workers with a history of chronic solvent exposure. Furthermore, both the chronicity of solvent exposure, as well as the acuteness of the exposure, are significant factors in cognitive performance. (*JINS*, 1997, *3*, 269–275.)

Keywords: Neuropsychology, Organic solvents, Memory, Painters, Exposure

INTRODUCTION

For well over a century, exposure to organic solvents has been linked to decrements in cognitive function such as decreased attention and memory, as well as behavioral changes such as depression and anxiety (see Hartman, 1995). Studies evaluating the effects of solvents on human cognitive function can be divided into three categories: chamber studies, clinical research studies, and field studies.

Chamber studies expose healthy volunteers to controlled, short-term doses of a solvent (e.g., xylene) or a mixture of solvent. Typically, participants are placed in a chamber for several hours and incremental doses of solvent are introduced into the chamber. Participants provide feedback concerning somatic symptoms, and complete a brief battery of cognitive tests. Chamber studies have demonstrated the presence of neurasthenic symptoms (e.g., headache, fatigue), mood changes, and cognitive decrements (e.g., decreased digit span) that follow or vary with the intensity of solvent dose (Gamberale & Hultengren, 1972; Gamberale et al., 1978; Savolainen et al., 1979; Mølhave et al., 1986; Echeverria et al., 1989). These studies provide a convincing demonstration that solvents may cause, at least transiently, psychiatric, somatic, and cognitive disturbances.

Clinical research studies assess patients who have presented to an occupational medicine setting because of adverse health effects related to chronic long-term exposure or to an acute overexposure. While patients may not be exposed at the time of testing, the majority of studies find significant deficits on a wide range of cognitive measures, particularly on tests assessing learning and memory (Hane et al., 1977; Lindstrom, 1980; Gregersen et al., 1984; Ekberg et al., 1986; Morrow et al., 1989, 1990, 1993; Baker, 1994). Many early studies contained methodological flaws (e.g., lack of control group, failure to adjust for IQ), but

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recent studies that have controlled for confounding variables have found evidence of solvent-related cognitive deficits (Morrow et al., 1990).

Finally, field studies focus on workers who are currently, or acutely, exposed to solvents in their occupation, but have not sought treatment for physical or cognitive problems. These studies typically find workers report a predominance of symptoms such as headaches and dizziness, but tests of neuropsychological function often fail to differentiate significantly solvent-exposed from nonexposed workers (Maiz-lish et al., 1985; Triebeg et al., 1988; Parkinson et al., 1990; Bleeker et al., 1991; Spurgeon et al., 1994).

One question that has received little attention is the relationship between current, or acute exposure, and ongoing chronic exposure. That is, does the reaction to an acute exposure differ depending on one's past history of exposure? A chamber study by Bælum and colleagues looked at acute exposure to toluene in persons with and without a prior occupational history of solvent exposure (Bælum et al., 1985). Forty-three printers occupationally exposed to mixtures of organic solvents were compared to 43 unexposed controls. Printers and controls were divided into two groups: Half were exposed to 100 ppm of toluene; the other half to clean air for a period of 6.5 hr. Overall, participants exposed to toluene reported more fatigue, headaches, and feelings of intoxication in comparison to participants exposed to clean air. Acutely exposed participants also had lower scores on psychometric tests (e.g., perceptual speed). More importantly, those who were also chronically exposed in their occupation as printers showed a tendency to manifest a greater sensitivity (lower scores on two tests) while acutely exposed. In a similar study, Iregren (1986) exposed 26 spray painters to toluene in a chamber and measured somatic symptoms and performance on four psychometric tests. The 26 workers were composed of 14 with a high number of preexposure symptoms-headaches, eye irritation present before the controlled exposure—and 12 with a low number of preexposure symptoms. Findings demonstrated more local irritation for those painters with preexposure symptoms. However, no significant performance differences were found for the psychometric tests.

The previous studies raise the possibility that persons with prior, ongoing exposure, may develop more serious adverse health effects after an acute exposure. However, both studies did a very limited assessment of cognitive function and focused mainly on tests of motor speed.

The present study assessed neuropsychological function in journeymen painters who were tested either after an acute exposure (within 48 hours of painting), or after an exposurefree interval (no exposure for at least 5 days). Both groups of painters were compared to demographically similar nonexposed controls. Participants were administered a comprehensive battery of neuropsychological tests designed to assess various cognitive domains (e.g., memory, spatial skills). In addition, painters completed a questionnaire specifically developed to assess use of solvent-based paints over the lifetime (Fidler et al., 1987a).

METHOD

Research Participants

This study evaluated 38 journeymen painters and 36 nonexposed control participants. All of the painters were members of the International Brotherhood of Painters and Allied Trades and were recruited from the roster of active members in the Local 6 union. Painters were assigned to two groups: those who had painted in the previous 48 hours (acute condition, N = 20), and those who had not painted for at least 5 days (free condition, N = 18).

Over 60% of nonexposed control participants were recruited from two local unions: United Food and Commercial Workers (Local 326) and Bakery Drivers (Division of International Brotherhood of Teamsters, Local 485). The remaining control participants were recruited through advertisement. None of the control group worked with solvents in the home or on the job.

All participants were paid for their participation, and informed consent was obtained prior to testing. There were no significant differences between the painters and control subjects in age [M (SD) = 38 (6.2), and 35 (10.6) years,respectively, p = .15 or education [M (SD) = 12.9 (1.4), and 13.3 (1.7) years, respectively, p = .17]. All painters were male and 88% of the controls were male. Ethnic membership was 92% and 84% White for the painters and controls, respectively; the remaining participants were African American. The median household income was equivalent for both painters and controls (\$30,000-\$40,000). Information on current and past alcohol use was obtained with the Structured Clinical Interview for DSM-III-R (Spitzer et al., 1989). Detailed information on psychiatric symptomatology for the painters is presented elsewhere (Condray et al., 1995). There were no significant differences between the groups for lifetime diagnosis of alcohol abuse/dependence ($\chi^2 = 1.9, p =$.16) or drug abuse/dependence ($\chi^2 = 1.6, p = .20$). The average number of drinks daily for the past month was also ascertained. No significant differences in the average number of daily drinks were noted between painters (1.1) and controls (.6; df = 2,36; p = .17).

A comparison between journeymen painters in the acute and free conditions revealed no differences in age [*M* (*SD*) = 37 (6.8) vs. 39 (5.3) years, respectively; p = .25], education [*M*(*SD*) = 13.2 (1.5) vs. 12.5 (1.1) years, respectively; p = .12], or lifetime alcohol ($\chi^2 = .08$, p = .76) or drug use ($\chi^2 = 1.1$, p = .27). There was, however, a higher number of mean daily drinks for painters in the free condition as compared to the acute condition [*M*(*SD*) = 2.3 (3.2) vs. .27 (.46), p = .02, respectively].

Neuropsychological Assessment

Subjects completed a comprehensive battery of standardized neuropsychological tests measuring learning and memory, visuospatial skills, psychomotor speed and manual dexterity, attention and mental flexibility, and general intelligence. The battery included tests from the Pittsburgh Occupational Exposures Test battery (POET; Ryan et al., 1987), as well as additional neuropsychological measures. In previous studies, the POET battery has been shown to discriminate exposed from nonexposed persons (Ryan et al., 1988; Morrow et al., 1989).

Five Verbal subtests and four Performance subtests from the Wechsler Adult Intelligence Scale–Revised (WAIS–R; Wechsler, 1981) were administered according to the standard instructions. The Visual Reproductions subtests from the Wechsler Memory Scale–Revised (WMS–R, Wechsler, 1987) was given, along with the Stroop Color–Word Interference Test (Golden, 1978). Memory and learning were assessed with a verbal paired-associate learning test, a symbol paired-associate learning test, incidental recall of the symbols from the WAIS–R Digit Symbol Substitution Test, and the Recurring Words Test. Administration and scoring procedures for the learning and memory measures are provided in Ryan et al. (1987). Participants also completed the Grooved Pegboard (Rourke et al., 1973) and the Trail Making Test (Reitan, 1992).

In order to assess psychiatric symptomatology as a control variable, participants completed the Symptom Checklist 90–Revised (Derogatis, 1983). This self-report inventory asks subjects to indicate how much they have been distressed by 90 different problems (e.g., feeling sad) over the past month. Nine subscales are coded, as well as a General Severity Index (GSI). The GSI was used as an index of general psychiatric symptomatology.

Exposure Index

For painters, a solvent history questionnaire was administered that computed an index of exposure over the lifetime and the past year. The questionnaire derives an overall index based on method of painting (spraying, rolling, brushing), application rate, frequency, ventilation, and use of protective equipment (see Fidler et al., 1987a). Research with this exposure questionnaire has shown a positive association between increasing exposure and neurasthenic symptoms (Fidler et al., 1987b), as well as mood and performance on a symbol-digit test (Baker et al., 1988). We modified the exposure questionnaire somewhat in that we obtained estimates of exposure based on gallons per week as opposed to gallons per year to make it easier for subjects to reconstruct their painting history. Examination of material safety data sheets for the painters demonstrates typical exposures were to the aromatic solvents (e.g., toluene, xylene, mineral spirits).

Because many paints still have a lead base, venous blood samples were also drawn to determine current blood lead levels. Lead levels were determined using atomic absorption spectrophotometry conducted by Central Laboratory Service, Inc., which is affiliated with the University of Pittsburgh Medical Center.

Data Analysis

To determine whether an acute exposure is more detrimental in painters with higher past exposure a hierarchical regression analysis was performed within the painter group. Summary z scores were computed for the individual neuropsychological tests (with higher scores indicative of better performance) and an average z score was calculated for the five neuropsychological domains. Because our primary theoretical question was whether an acute exposure was more detrimental in persons with a higher exposure index, an exposure term was computed as the interaction between the quantitative exposure index and dummy variable representing condition (acute vs. free). Two models were tested; the first used the exposure index over the lifetime, and the second used the exposure index over the past year. Independent variables were age, education, psychiatric symptomatology (GSI), number of drinks per day, the exposure interaction term, and blood lead level. Separate regressions were run for each neuropsychological domain. For each of these five cognitive domains, age, education, SCL-90-R index, and number of drinks per day were entered on the first step in order to control for their contribution. The exposure interaction term and blood level were entered on the second and third steps, respectively.

In order to determine whether journeyman painters have significant reductions on standard neuropsychological measures, and if the differences are confined to certain cognitive domains, a multivariate analysis procedure was used to examine performance between painters and nonexposed controls on each of the five neuropsychological clusters. To control for multiple comparison procedures, neuropsychological tests were grouped into five domains (confirmed by correlation). The omnibus F was computed for each cluster and, if significant, univariate F levels were examined for the individual tests in that cluster. Comparison of groups for individual variables were conducted using t tests.

RESULTS

Between-Group Analyses

Findings demonstrated that painters and nonexposed controls were comparable in age and education, but painters had significantly lower scores on the majority of cognitive tests. However, statistically significant group differences were found only for the cluster of learning and memory tests [F(67,6) = 2.48, p = .03]. Within the learning and memory cluster, significantly poorer scores were seen on the individual tests of verbal paired-associate learning, symboldigit paired associate learning, incidental memory, recurring words, and delayed recall of verbal paired associates. Table 1 presents means and standard deviations for each test, and the associated *p* values derived from the univariate analyses.

Psychiatric symptomatology was significantly higher for the painters as compared to controls (t = 2.49; df = 2,36;

Table 1. Test results for five neuropsychological clusters

	Painters $(N = 38)$	Controls $(N = 36)$	
Learning and Memory			
Verbal Paired Associate Learning	22.3 (7.4)	26.8 (7.4)**	
Delayed Verbal Learning	6.2 (2.5)	8.0 (2.1)**	
Symbol Paired Associate Learning	19.3 (5.6)	22.1 (5.2)*	
Delayed Symbol Learning	5.6 (1.6)	6.0 (1.4)	
Recurring Words	43.1 (2.4)	44.3 (2.0)*	
Incidental Recall	6.7 (2.2)	7.6 (1.5)*	
Spatial			
WAIS-R Block Design	10.6 (2.4)	10.5 (2.8)	
WAIS-R Picture Arrangement	9.8 (2.2)	9.6 (2.6)	
WAIS-R Picture Completion	10.4 (1.9)	9.9 (2.6)	
WMS-R Visual Reproductions	34.8 (4.2)	35.4 (3.4)	
WMS-R Visual Reproductions Delay	27.5 (8.5)	28.8 (8.8)	
Attention			
WAIS-R Digit Span	9.9 (2.4)	10.0 (2.3)	
WAIS-R Digit Symbol	9.4 (2.4)	10.5 (1.9)	
Trails A	27.8 (11.0)	24.1 (7.4)	
Trails B	66.0 (22.9)	60.3 (26.3)	
Stroop Color-Word Interference	35.4 (9.0)	39.2 (9.3)	
Motor Speed			
Grooved Pegboard Dominant	67.2 (9.1)	65.3 (9.8)	
Grooved Pegboard Nondominant	74.4 (9.4)	71.7 (14.2)	
General Intelligence			
WAIS-R Information	9.5 (2.5)	10.4 (2.1)	
WAIS-R Similarities	9.8 (2.4)	9.9 (1.9)	
WAIS-R Comprehension	9.1 (1.9)	9.6 (2.1)	
WAIS-R Arithmetic	10.5 (2.6)	10.4 (2.5)	

*p < .05; **p < .01.

p = .01). However, correlations between the GSI and the neuropsychological domains (*z* scores) showed low and non-significant correlations, ranging from -.02 on the Attention factor to -.21 for the Intelligence factor.

Within-Group Analyses

The exposure index for solvent paints in this sample ranged from 117 to 5374 (median 715). This exposure level is somewhat higher than the exposure reported by Fidler et al. (1987a) in their group of painters (a median of 552 when converted to gallons/week). This is consistent with the fact that the painters in that study averaged 30.6 weeks of painting over the past year as compared to 37.1 weeks for the painters in this study. Age was not a surrogate for exposure, since the correlation between age and the exposure index was small and nonsignificant (r = .07).

The results of the hierarchical regression are presented in Table 2. For the Learning and Memory cluster, there was a significant interaction between lifetime exposure to solvents and exposure condition (acute *vs*. free) in which the subject was tested. The interaction term was significant after having controlled for the age and education, as well as level of psychiatric symptomatology and number of drinks

Table 2.	R^2 changes for each cluster at each step		
of the hierarchical regression analysis			

	Demographic	Career Exposure Index by Condition (acute/free)	Lead (µg/dl)
Learning and Memory	.147	.118*	.011
Spatial	.170	.060	.035
Attention	.253*	.018	.001
Motor Speed	.180	.015	.004
General Intelligence	.199*	.018	.002

Demographic = age, education, SCL-90-R global index, number or drinks/ day. *p < .05.

per day. The findings show that having a longer lifetime exposure *and* being acutely exposed at the time of testing was associated with significant reductions on tests of learning and memory (p = .02). A similar, but marginal relationship, was noted for the Spatial cluster (p = .12).

For the second model, which used exposure in the past year as opposed to lifetime career exposure, the results were virtually identical (data not shown). That is, the interaction term of exposure by condition was significant for the Learning and Memory domain (p = .02). The similarity of the two models is not surprising as exposure over the lifetime and the past year was highly correlated (r = .87).

Our original goal was to investigate whether performance on cognitive tests was influenced by lifetime career exposure and acuteness of exposure. However, in order to determine whether lifetime exposure or the exposure condition (acute/free) separately accounted for a significant proportion of the variance in performance on the memory and spatial clusters, we reran the regression analyses entering first the demographic variables and then separately the exposure index and the condition term. We did not add the two separate exposure terms into the original model, as they are not independent of the interaction term. There was no significant independent contribution of the two separate exposure terms (all ps > .10).

DISCUSSION

This study reports findings for a group of chronically exposed journeymen painters. The first objective of the study was to evaluate the relationship between ongoing and acute exposure to organic solvents. To that end, we assessed painters either shortly after having worked with solvent-based paints or after an interval when they had not painted for several days. An exposure free interval of at least 5 days was chosen to assure clearance of solvents from the body. The results indicate that scores on the memory tests—after controlling for the effects of age, education, psychiatric symptomatology, and drinks per day—were influenced by the lifetime dose of solvent exposure and having been acutely exposed at the time of testing. That is, painters who had

more exposure to solvents over the career *and* who were recently exposed prior to the assessment were more likely to have reductions in memory and learning as well as poorer spatial skills. When the analysis was repeated using exposure over the past year, the results were virtually the same. Current blood lead level did not significantly add to the model. Although the relationship to the spatial tests failed to reach statistical significance, we would not discount the finding, as it may reflect our small sample size and correspondingly limited statistical power.

Our results, demonstrating that painters with higher past exposure are more sensitive to the acute effects of solvent exposure during learning and memory performance, are consistent with the "neural sensitization" model suggested by Iris Bell (Bell, 1994). This model, based on data from both animal and human studies, proposes that intermittent chemical exposures over time may produce changes in the brain, particularly limbic structures, such that there is a heightened reactivity—both cognitively and physically—to subsequent chemical exposures. While we cannot determine past intermittent exposures for the painters, our findings confirm the notion that higher past solvent exposure increases the risk for cognitive decrements during acute exposures.

The second objective was to determine if there were differences between the painters and healthy controls on standard tests of neuropsychological function. Related to this, we wanted to ascertain if there was a differential pattern of impairment across cognitive domains. The results show that painters have lower scores on the majority of tests, but significant groups differences were found only on measures of learning and memory. Scores on tests tapping spatial ability, attention and mental flexibility, general intelligence, and motor speed did not demonstrate significant between group differences. The poorer performance on the learning and memory measures-lower scores were particularly apparent on tests of verbal learning-was fairly consistent across the individual memory tests. Painters learned fewer verbal paired associates, and remembered less information following a delay interval. They also learned fewer symbol-digit pairs, had poorer incidental recall, and recalled less on a recurring words test.

Prior studies have been inconsistent in demonstrating significant differences between solvent-exposed and nonexposed painters on cognitive measures. In a study of Dutch painters, Hooisma et al. (1993) found no reliable evidence of cognitive differences between young and old painters and similarly matched controls. They did, however, report a relationship between certain exposure indices (e.g., nonprotected spray painting) and performance on both visuomotor and memory measures in older painters. Triebeg et al. (1988) also found no consistent differences between house painters and matched controls. In contrast, a study of shipyard painters found significant differences between painters and controls for three out of four cognitive measures (Valciukas et al., 1985). Moreover, persons with chronic exposure plus current symptoms scored significantly poorer than asymptomatic painters. Studies by Baker and colleagues, which

also assessed journeymen painters with the same exposure index as in the present study, found fairly consistent associations between symptoms and neuropsychological performance and exposure variables (Fidler et al., 1987b; Baker et al., 1988).

Discrepancies across painter studies are probably due to a number of factors, including the composition of the sample, differences in solvent exposure history, test selection, and computation of exposure indices. Test selection may be particularly important. In the present study we used a fairly extensive battery of tests with an emphasis on complex tests of learning and memory. The World Health Organization Neurobehavioral Core Test Battery, often used by researchers in the field, includes only one memory test, the Benton Visual Retention Test, recognition form (Cassitto et al., 1990). We would suggest that when assessing exposed populations, particularly in field studies of subjects with no cognitive complaints, the test battery should focus on tests of complex verbal and nonverbal learning that include encoding and retrieval of novel information.

Learning and memory are the chief complaints of patients with solvent encephalopathy and have routinely been documented in clinical research studies (Linz et al., 1986; Mikkelsen et al., 1988; Morrow et al., 1990, 1991; Baker, 1994, 1995; Morrow, 1994). This has led to the suggestion that solvents may be particularly detrimental to mesial temporal areas (Ryan et al., 1988). Consistent with this, temporal lobe demyelination has been documented for a worker with long-term chronic exposure (Gatley et al., 1991), and functional imaging studies of toxic encephalopathy patients have shown the highest percentage of abnormalities in the temporal lobes (Morrow et al., 1990; Callender et al., 1993). Delays in the P300 component of the event-related potential—linked to hippocampal and limbic activity—have also been observed in solvent-exposed patients (Morrow et al., 1992). Our findings of significant memory decrements are in line with the hypothesis that chronic organic solvent exposure may be particularly detrimental to those areas of the brain that support encoding and retrieval of new information, namely the mesial temporal areas. However, the deficits on the paired-associate tests may reflect problems with encoding and strategies for organization, which would suggest frontal-diencephalic pathways may also be compromised (Wheeler et al., 1995). At this point, future studies are needed to address the role of specific brain sites that may be altered due to acute and chronic solvent exposure.

There is no doubt that chronic long-term exposure to high levels of organic solvents (e.g., glue sniffing) can result in significant neuropsychological impairment and alterations to the CNS (Rosenberg et al., 1988). However, there is still controversy regarding whether low-to-moderate levels of exposure can produce significant neuropsychological impairment—especially in persons who do not report adverse health effects (Rebert & Hall, 1994). The present study is important in that we have documented significant reductions on standardized learning and memory tests in solventexposed painters. Part of the reason for our findings may be the sensitivity of the tests—that is, the use of complex pairedassociate learning measures. The fact that reductions were noted on tests of learning and memory is in line with the notion that solvents may have a particular affinity for mesial temporal areas of the brain. Moreover, the finding of an interaction between the overall lifetime exposure and acuteness of exposure demonstrates that persons with higher past exposure are at risk for a more adverse reaction (i.e., poorer memory) to an acute exposure. While the exact mechanism responsible for this phenomenon is unknown, future studies will need to address both the prior history as well as the acuteness of solvent exposure.

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