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Chronic Exposure to Solvents Among Construction Painters: Reductions in Exposure and Neurobehavioral Health Effects

Nancy Fiedler, Ph.D.[1,2], **Clifford Weisel, Ph.D.**[1,2], **Chizoba Nwankwo, Ph.D., M.P.H.**[3], **Howard Kipen, M.D., M.P.H.**[1,2], **Gudrun Lange, Ph.D.**[4], **Pamela Ohman-Strickland, Ph.D.**[2], and **Robert Laumbach, M.D., M.P.H., C.I.H.**[1,2]

[1]Rutgers University, Environmental & Occupational Health Sciences Institute, 170 Frelinghuysen Rd., Piscataway, NJ 08854

[2]Rutgers University School of Public Health, 683 Hoes Lane W., Piscataway, NJ 08854

[3]Merck & Company, Inc., Kenilworth, NJ USA

[4]Mount Sinai School of Medicine, Pain and Fatigue Study Center, 10 Union Square, New York, NY 10003

Abstract

Objective: To assess the neurobehavioral effects of lifetime solvent exposure by comparing the performance of painters and demographically comparable controls.

Methods: Performance of exposed painters (N=133) was compared to unexposed tapers, glaziers, or carpenters (N=78) on the following domains: motor/perceptual speed, visual contrast, attention, working memory/planning, and visual and verbal memory. Lifetime exposure was estimated with questionnaires, field measurements, and paint composition.

Results: After controlling for confounders, lifetime solvent exposure did not predict reduction in performance for overall domains of function. Lifetime solvent exposures predicted subtle alterations for individual tests of verbal learning, motor coordination, and visuospatial accuracy.

Conclusions: Concentrations of solvents in paints have steadily declined during the working lifetime of subjects in this study. Although reduced performance was observed on individual tests, these alterations were not consistent across tests and unlikely to be of clinical significance.

Keywords

Chronic Solvent Exposure; Painters; Neurobehavior

Almost 30 years following consensus definitions of chronic solvent encephalopathy (CSE) by the World Health Organization (WHO)(1) and the National Institute of Occupational Safety and Health (NIOSH)(2), the existence of this condition remains controversial due to

Corresponding Author: Nancy Fiedler, Ph.D.,Rutgers University, Environmental & Occupational Health Sciences Institute, 170 Frelinghuysen Rd., Piscataway, NJ 08854, Phone: (848) 445-6109, Fax: (732) 445-0130, nfiedler@eohsi.rutgers.edu.

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inadequate control of confounders (e.g., alcohol use), inconsistencies in the characterization of solvent exposures associated with CSE, and selection bias among study participants in cross-sectional studies.(3–6) Patients diagnosed with CSE present with irreversible signs of impairment that are observed in their performance on tests of neurobehavioral function.(7–9) As exposure to solvent mixtures has steadily declined in the developed world, fewer CSE cases are diagnosed.(10) Nevertheless, many workers continue to be chronically exposed to mixtures of organic solvents and even in the absence of clinically apparent CSE, some studies document subtle decrements in neurobehavioral performance. However, results are not uniform and study designs are typically cross-sectional with several factors (e.g., age, intelligence) in addition to solvent exposure that could explain solvent exposed and control subject performance differences.(6, 11, 12).

In spite of the inconsistencies in the literature, Baker(3) concluded that the majority of studies evaluating the neurobehavioral effects of solvent exposure found decrements relative to controls in short term memory and psychomotor function. Since Baker's review(3), Mikkelsen(13), and Meyer-Baron et al.(14) also reviewed studies, and highlighted the inconsistencies in relationships between exposure estimates and behavioral performance, but concluded that there was an overall dose-effect relationship. Unlike workers in more-controlled manufacturing settings, construction painters often work in highly variable settings with little documentation of historical solvent exposure(15). Although several studies among painters indicate significant behavioral decrements relative to controls for neurobehavioral functions such as reasoning, processing speed, concentration, memory, and motor/psychomotor coordination,(16–20) others show no effects even in the absence of protective equipment such as respirators to mitigate solvent exposure(21–24).

The goals of the present study were to address previous critiques of the literature by developing a more-comprehensive measure of solvent exposure, controlling for common confounders, and recruiting solvent-exposed workers at greater risk for neurotoxicity as a result of at least 10 years on the job(10). Thus, we compared performance on measures of cognitive, motor, and visual contrast sensitivity among solvent exposed construction painters and construction controls (i.e., tapers, glaziers, carpenters) all of whom had a minimum of 10 years on the job. In addition, as a predictor of neurobehavioral performance, we developed a metric of cumulative lifetime exposure that incorporated job duties, current and historical air concentrations of solvents in paint products and use of personal protective equipment.

Animal studies of single solvents found in paints and strippers such as toluene, methylene chloride, styrene, trichloroethylene, and xylene, only reveal neurobehavioral effects from chronic exposure when exposure levels are significantly higher than those typically found in industrial workplaces(25, 26). For example, trained pigeons' accuracy in response to a delayed match to sample task (DMS) was reduced following 1 to 2 weeks of daily exposure to 3000 parts per million (ppm) of toluene(27) while concentrations of 2000 to 4500 ppm of toluene resulted in impaired DMS performance for monkeys.(28) In contrast, the OSHA permissible exposure limit (PEL) for 8-hour time-weighted average exposure to toluene, in effect since 1971, is 200 ppm. Unlike the single-solvent exposures used in most animal studies, human studies of chronic solvent exposure evaluate neurobehavioral effects in

response to the mixtures of solvents to which painters and paint manufacturing workers have typically been exposed.(3, 13, 29, 30)

Among neurobehavioral tests found more frequently to differentiate solvent-exposed workers from controls, are those reflecting attention and processing speed (i.e., working memory) to include symbol digit substitution, reaction time, continuous performance, and serial digit learning.(20, 30–33) Furthermore, when decrements in verbal or visuospatial memory are observed among solvent-exposed workers, encoding or learning rather than recall often accounts for the difference in performance.(20, 34–37) These findings suggest disruption in the working memory processes of encoding and processing speed,(31) supporting a hypothesis of frontal lobe dysfunction that was validated in our functional imaging study.(38, 39) Though less frequently observed, decrements in verbal or visuospatial memory(40) have led others to hypothesize temporal lobe dysfunction in addition to frontal lobe dysfunction. Temporal lobe dysfunction, however, may only be seen among those with the highest lifetime dose and is more unlikely among workers with exposure during the past 25–30 years when solvent exposures have declined. Based on the preponderance of evidence suggesting slowing of information processing and poor encoding/learning, we hypothesized that solvent-exposed workers would exhibit significant reduction on tests of response speed, motor speed, attention, and working memory.

Method

Subjects:

Information indicating that we were recruiting workers from the construction trades for a health study was distributed at union meetings and through mailings to union members from the International Union of Painters and Allied Trades, District Council 9 in New York City and District Council 21 in Philadelphia and to dry wall/tapers and glaziers (District Council 21, Philadelphia) and carpenters (New Jersey). Subjects who contacted our office were screened with a standardized telephone interview for the inclusion/exclusion criteria. Subjects who reported any of the following conditions were not recruited to participate: history of head injury involving loss of consciousness for more than 30 minutes, significant neurologic disorders such as multiple sclerosis or seizure disorder; insulin dependent diabetes, other serious medical conditions such as kidney or liver disease, childhood history of learning disability, hospitalization for bipolar disorder or schizophrenia. Subjects who met the screening criteria were invited for a physical examination and neurobehavioral assessment. All study procedures and consent forms were reviewed and approved by the Institutional Review Board of Rutgers University. The consent form indicated the purpose of the study was to understand the effects of solvent exposure on learning and memory. All subjects were paid a stipend to compensate them for the time required to participate in the study. One-hundred and thirty-eight construction painters (exposed) and 96 tapers/glaziers/carpenters (controls) were recruited and scheduled for testing. All subjects had ≥ 10 years of work experience in their trade and were between the ages of 30 and 60. Two solvent-exposed subjects were excluded after testing because one did not complete the protocol and the second exposed subject had experienced loss of consciousness for more than 30 minutes that was not reported in the screening interview (Exposed N= 136). Likewise, 3 controls were

excluded for loss of consciousness (N=2) and insulin dependent diabetes (N=1) (Controls N= 93).

Measurement of Confounders:

The North American Adult Reading Test (NAART)(41) was converted to a Wechsler Adult Intelligence Scale – Revised (WAIS-R) Verbal intelligence quotient (VIQ) and was used as an estimate of pre-exposure verbal cognitive ability. For Spanish speaking subjects, the Word Accentuation Test (WAT),(42) a NAART-like Spanish test was used to estimate pre-exposure ability. To rule out acute effects of alcohol, an alcohol saliva test (Q.E.D. A150-STC Diagnostics, Bethlehem, PA) was administered to each subject prior to participation in the neurobehavioral study. To assess the usual overall quantity and frequency, peak quantity, and frequency of alcohol use during the past year, and peak quantity and frequency during periods in the subject's lifetime when use was significantly more or less than during the past year, a questionnaire was completed by the subject and reviewed by a nurse at the time of the screening physical examination.(35, 43) A similar questionnaire was used to quantify lifetime drug use (i.e., marijuana, inhalants, stimulants, sedatives, tranquilizers, psychedelics, cocaine, heroin). Due to the uncontrolled nature of most illicit drugs, frequency of use but not quantity was assessed during an interview administered by the nurse during the screening physical examination. A lifetime alcohol index was derived by multiplying the number of years of drinking by the quantity and frequency of alcohol use during the past year. If the subject reported periods of drinking a lot more or a lot less than during the past year, the quantity and frequency of this drinking pattern was subtracted from (less) or added to (more) the total years of drinking. Since peak exposure or periods of binge drinking may have more effect on neurobehavioral integrity than usual patterns of use, a separate peak index was calculated for the past year and for lifetime. A similar strategy was used to derive a separate index of lifetime drug use for each class of drugs. Current blood lead was assessed at the time of the physical examination and used in the statistical models evaluating the effects of chronic exposure to solvents.

Neurobehavioral Tests: (See Table 1)

Initially, simple training tests from the CANTAB battery (i.e., Big/Little Circle [BLC] and Motor screening [MOT]) were administered to provide training in following instructions (BLC) and motor speed (MOT) both of which are essential skills for completing the more complex tests of attention, working memory and planning, and visual memory. As recommended by Iregren and Letz,(44) the current study used the core tests of symbol digit, finger tapping, and simple reaction time to screen for cognitive and psychomotor dysfunction in response to chronic solvent exposure. Tests of attention, planning and working memory, and visual memory from the Cambridge Neuropsychological Test Automated Battery (CANTAB) were administered to assess the cognitive effects of chronic solvent exposure. Table 1 outlines neuropsychological tests administered, the cognitive domains assessed, and the outcome variables analyzed Table 1.

Visual Acuity and Contrast Sensitivity:

Some studies also suggest that a primary effect of chronic solvent exposure is reduced contrast sensitivity(51–58). The OPTEC model 1000 (Stereo Optical Co., Inc, Chicago, IL)

was used to assess near visual acuity prior to administration of the contrast sensitivity and other neurobehavioral tests. Subjects requiring correction for near visual acuity were required to wear their corrective lenses. The F.A.C.T. 101 Near Point Test (Stereo Optical Co., Inc., Chicago, IL) was administered to assess the effects of chronic solvent exposure on visual contrast sensitivity (Stereo Optical Co., Inc., Chicago, IL). A near visual acuity chart was placed in a calibrated holder at the 18” test distance position under normal office lighting. The progression of the high-quality sine-wave grating size changes in steps equal to one octave (i.e., a factor of two) between rows A, B, C, and D and half octave between rows D and E. The corresponding spatial frequencies were 1.5, 3, 6, 12 and 18 cycles per degree. The subject was shown a sample containing three patches and instructed that one shows the top of the lines (gratings) pointing to the left, the next shows the top of the lines pointing to the right and the third shows the lines pointing up. Occluding one eye, the subject then began with row A and proceeded from left to right (patches 1–9) stating which way they think the top of the lines point. If a response was incorrect, the subject was instructed to look at each patch to the left until a correct response was obtained and then encouraged to proceed to the right until one incorrect response was obtained. The last correct response was the score for that row (i.e., frequency). The same procedure was followed for rows B-E and the entire test was repeated for the subject’s other eye. The contrast score was determined for each of the five frequencies presented to each eye and scores were analyzed separately for each spatial frequency for each eye.

Solvent Exposure Index:

A cumulative lifetime exposure index was calculated in ppm years for any subject who had ever worked with solvent-based paints. Work duration, time spent performing specific job tasks (e.g., brush, roll, spray), and use of protective equipment were determined from a self–report questionnaire. Current distributions of solvent air concentrations were derived from personal air samples (OVM3500: 3M Company, St Paul, MN) worn by construction painters at the work site and field area samples collected during a series of week-long sampling programs during different seasons at New Jersey Department of Transportation and New York City Bridge Maintenance work sites. To take into account historical changes in exposure to solvents because of changes in paint composition, emission changes in paints from 1960 to the present were derived from several databases (e.g., Pub Med, Toxline, NIOSH) and from the impact of U.S. EPA regulations on VOC emissions. Similarly, historical and current protection factors associated with various protective equipment were also derived from several databases (e.g., OSHA, TOXLINE). Advances in exposure reconstruction techniques were used to develop a solvent exposure model for industrial painters using a Job Exposure Matrix to determine the time spent in activities for which exposure could occur and the distribution of air concentrations for those activities modified for changes in paint composition and protection factors for respirators over time. This exposure assessment determined the inhalation and dermal exposure for each subject exposed to solvent mixtures.

Analysis of personal air space revealed 3 broad classes of VOC compounds associated with paint emissions were present: aromatic compounds, acetates and ketones. The highest concentrations were observed for individuals involved in spray painting (mean/maximum

personal concentrations) 410±240/800ppm, 2.7±70/690ppm and 0.8±38/270ppm, respectively, intermediate exposure concentrations for rolling painting 6.7±4.6/13ppm, 0.9±70/5.9ppm and 0.3±6.9/7.6ppm, respectively, and the lowest for brush painting 0.8±0.8/2.4ppm, 0.2±3.6/0.8ppm and 0.2±3.6/1.2ppm, respectively. Wearing of respirators was assumed to decrease the exposure based on reported efficiencies according to type of respirator, dust mask 0% efficient, half-face chemical cartridge (before 1990 65%, after 1990 90%), full-face chemical cartridge (before 1990 75%, after 1990 98% and supplied-air respirator (before 1990 90%, after 1990 99.9%). The percentage of painters who reported wearing respirators almost all of the time increased from 1980 to 2000 and with the painting type: from a low for brushing (14% in 1980–1984) to rolling to high for spraying (62% in 2000–2005). The lifetime exposure index for each subject incorporated self-reported lifetime painting activities, current and historical estimates of solvent air concentrations from paints of differing composition and during various work activities, self-report of protective equipment used, and the protection factor associated with use of the protective equipment. Lifetime exposure index for each subject is expressed in parts per million years. Details of the exposure modeling and exposure index calculation are included in Wang et al.(59)

Procedure

All subjects were scheduled for testing in the morning to control for circadian rhythm effects on neurobehavioral testing. Testing occurred on a weekend day or during periods of unemployment to eliminate acute exposure to solvents on the day of testing. After signing informed consent, subjects were administered the alcohol saliva screening test to rule out alcohol use on the day of testing. All alcohol saliva tests were negative. Subjects had a fasting blood draw for routine blood chemistry and current blood lead. Subjects were given breakfast and rotated through stations to complete the screening physical examination, neurobehavioral testing, psychiatric interview, and exposure history interview. A trained technician administered tests at each station in a quiet, individual room. The technician administered instructions for the neurobehavioral tests and assured that subjects understood the test prior to commencing test administration. The solvent exposure questions were read by the technician to the subject and answers were recorded on the computer by the technician. A nurse administered the screening physical examination including height and weight for each decade of life since the age of 18, review of the medical questionnaire, alcohol questionnaire, and administration of the drug use questionnaire. Medical questionnaire responses were augmented by the study nurse who followed up on any reported symptom or diagnosis with further documentation as appropriate. These questionnaire responses were subsequently reviewed by an occupational physician internist (co-author: HK) as a final check for any diagnoses warranting follow-up or exclusion from the study. Based on this procedure, subjects included in the study were assumed to have normal neurologic function. For the day of the examinations, subjects were asked to get a good night’s sleep and to abstain from alcohol and sedating medications (e.g., antihistamines) 24 hours prior to participation. They were also sent the medical questionnaire, symptom questionnaire (Orebro Q-16),(60) and alcohol questionnaire to be completed prior to their appointment.

Statistics:

Analyses were conducted within each behavioral domain to examine differences between exposed and controls where only those recruited as exposed with some reported solvent exposure (n= 133) and controls with no solvent exposure (n= 78) were included. Specifically, a Multivariate Analysis of Variance (MANOVA) with Hotelling's T statistic was conducted on each set of measures to examine whether group status (i.e., exposed vs. control) had an effect on the outcomes. Analyses of variance (ANOVAs) for individual measures within each domain were also conducted. A follow-up MANOVA was conducted, adjusting for age, race (white/black/other), current blood lead, estimated verbal IQ, lifetime marijuana use rank, lifetime cocaine use rank and lifetime alcohol use rank. Note that in the latter three cases, rank was used because of the extreme skew of the values; the extreme values would too strongly influence parameter estimates and render those and other estimates unstable. These covariates were chosen as confounders because, in the case of the former four, they differed significantly by group status or, in the case of the latter three, they have historically been considered to be confounders for the outcomes under consideration. Finally, within each behavioral domain, the continuous effect of exposure was examined (using ranks), adjusting for age, race (white/black/other), current blood lead, estimated verbal IQ, lifetime marijuana use, lifetime cocaine use and lifetime alcohol use.

Results:

Subject Characteristics (See Table 2):

Based on the results of the solvent exposure index, an additional 3 construction painters were excluded because their exposure index value was 0 while 15 controls were excluded because they had an exposure index value >0. Solvent exposure ranged from a minimum of 0.95 to 5942.24 ppm years and were skewed to the right with approximately 4 orders of magnitude difference between the lowest and highest exposure percentile.(59) Table 2 displays the demographics for the final subject groups (Exposed = 133; Controls = 78). Controls were slightly but significantly older than the exposed subjects, but the groups were similar in level of education and gender (one exposed was female). Although of similar educational background, exposed subjects had significantly lower estimated cognitive verbal ability than controls. Compared to controls, exposed subjects were significantly less likely to be Caucasian (Chi square = 9.92 p = 0.007) (Exposed: Caucasian: 74%; African American: 17%; Other: 9%; Controls: Caucasian: 91%; African American: 1%; Other: 8%). Exposed had significantly higher current blood lead concentrations, but the groups did not differ in lifetime alcohol, marijuana, or cocaine use Table 2.

Neurobehavioral Results (see Table 3):

Hypothesis 1: Relative to controls, exposed subjects will show significant decrements on screening neurobehavioral tests, (i.e., latency and accuracy of symbol digit substitution, reaction time for simple and choice reaction time and finger tapping).

This hypothesis was partially confirmed. After adjusting for confounders, 5- choice reaction time was significantly slower for exposed (t = 3.97; df = 1, 204; p = 0.05) and simple reaction time approached significance (t = 2.75; df = 1, 204; p = 0.10) with exposed

responding more slowly than controls. Finger tapping with alternating hands was significantly worse for exposed relative to controls (t = 3.89; df = 1, 204; p = 0.05). No other comparisons were significantly different after adjustment for confounders.

Hypothesis 2: Relative to controls, exposed subjects will show significant reduction in tests of attention and working memory but comparable performance on tests of visual memory.

Hypothesis 2 was also partially confirmed. Although the adjusted MANOVA was not significantly different for tests of attention (i.e., intra-extra dimensional shift, match to sample, simple and 5-choice reaction time and rapid visual processing) (T = 1.18; df = 10, 186; p = 0.31), several individual tests within this domain were significantly worse for exposed subjects relative to controls. As indicated previously, tests of simple and choice reaction time were slower for exposed relative to controls. In addition, exposed subjects made significantly fewer correct responses on the match to sample test than controls after adjustment for confounders (t = 5.17; df = 1, 204; p = 0.02). As hypothesized, the adjusted multivariate analysis of variance (MANOVA) with Hotelling's T statistic revealed no overall significant difference for measures of visual memory (T = 0.33; df = 10, 187 = 0.97). Individual analyses of variance controlling for confounders found no significant differences for individual tests of visual memory (i.e., delayed match to sample, paired associate learning, pattern recognition memory, spatial recognition). Contrary to the hypothesis, the adjusted MANOVA was also non-significant for tests of working memory (T = 0.88; df = 7, 190; p = 0.52) (Stockings of Cambridge, spatial span, spatial working memory). Individual adjusted analyses revealed that Stockings of Cambridge approached significance with exposed's ability solving problems with a minimum number of moves poorer than controls (t = 3.04; df = 1, 205; p = 0.08). Finally, for a measure of verbal memory, exposed remembered significantly fewer word/name associations than controls after a delay of 30 minutes (t = 5.48; df = 1, 205; p = 0.02).

Multiple regression analyses did not reveal a significant effect of solvent exposure for the domains of attention (F = 1.20 df = 10, 186; p = 0.30), visual memory (F = 1.03; df = 10, 187; p = 0.42) or working memory (F = 0.94; df = 7, 190; p = 0.48). However, multiple regression analyses of individual variables revealed results similar to adjusted analyses of variance with significant effects of solvent exposure rank for alternating finger tapping (F = 4.64; df = 1,222;, p = .03), total correct for match to sample (F = 6.32; df = 1,222; p = .01), and delayed verbal memory (F = 5.83; df = 1,223; p = .02). A marginal effect for solvent exposure rank was detected for problems solved with a minimum number of moves on the Stockings of Cambridge test (F = 2.84; df = 1,223; p = .09). For each of these individual tests, solvent rank was negatively associated with performance. However, solvent exposure rank was not a significant predictor for simple or choice reaction time after controlling for confounders.

Hypothesis 3: Relative to controls, exposed subjects will show significant decrements in visual contrast sensitivity in the mid-range but not the low (1.5) or high (18) cycles per degree (cpd) spatial frequencies.

Subjects whose near visual acuity was > 20/40 were excluded as were subjects who reported drinking > 2 alcoholic beverages per day every day. In addition, subjects who reported a history of glaucoma, cataracts, eye infections, corrective eye surgery, detached retina, insulin dependent or non-insulin dependent diabetes, or metal shavings in the eye were excluded. Thus, the subsequent analyses were performed with 53 exposed and 42 controls. Contrary to the hypothesis, no significant differences were noted between exposed and controls in visual contrast sensitivity for any spatial frequency (i.e., 1.5 to 1.8 cycles per degree) (data not shown). Moreover, the solvent exposure index was not a significant predictor of visual contrast at any spatial frequency. Results were also non-significant for all spatial frequencies when analyses were performed with adjustment for confounders.

Discussion

Overall multivariate analyses for the domains of attention, working memory, and visual memory did not support that exposed subjects exhibited a consistent pattern of impaired neurobehavioral function in any domain. Although several previous studies reported reduced visual contrast sensitivity as an indicator of solvent induced neurotoxicity(51, 55–58), the current study also did not reveal any significant differences in contrast sensitivity at any spatial frequency. This discrepancy among studies may be explained by differences in solvent exposures and in some cases less control for other factors known to affect visual contrast sensitivity (e.g., alcohol use, diabetes).(55, 58) Therefore, in contrast with the conclusions of previous reviews(13) the current study did not reveal an association between chronic solvent exposure and indicators of either cognitive, motor, or visual contrast function.

Although overall analyses were not significant, further exploration of individual cognitive tests revealed that increasing solvent exposure predicted compromised encoding and recall of new information (verbal paired association learning), reduced accuracy under time pressure (match to sample), and motor incoordination (alternating finger tap). Among the individual test results, performance was consistently worse for solvent exposed participants on all trials of the verbal memory task, suggesting that encoding was poor initially, and thus, led to significantly fewer items recalled after a delay. For matching of complex figures, the participants must maintain attention to detail while under time pressure. Solvent exposed participants achieved a response speed similar to controls but their accuracy was compromised, suggesting that they may have sacrificed accuracy for speed and/or had difficulty maintaining accurate details of the complex images.

In our previously reported functional imaging study among a subset of our participants, we observed lower activation in the dorsolateral prefrontal cortex and cingulate. These lower neural activation patterns may partially explain the working memory aspects of compromised verbal associative memory and accuracy in matching complex figures observed in the present study. For example, satisfactory performance on a verbal memory task requires successful encoding and maintenance of information within the working memory system prior to longer term storage of the memory trace. However, because results for tests of working memory were not consistent across all or even a majority of working memory tests administered, these relatively minor performance differences, particularly for

the verbal associative memory task, may be attributable to the observed differences in estimated verbal intelligence between the exposed and control participants. Although verbal ability was a covariate in our statistical analyses, reading tests provide only an estimate of pre-exposure verbal ability and statistical control is less than an ideal approach to manage pre-exposure group differences.

Learning from previous studies, our study carefully controlled for a suite of confounders to include alcohol, marijuana, and cocaine use, blood lead, verbal IQ, age and race, all of which are known to affect behavioral performance. Moreover, we developed a comprehensive lifetime exposure index that included self-report of work activities and use of protective equipment from 1985 to 2005 and recruited workers who had spent a minimum of ten years in their occupations. Estimates of exposure were then modified by current and historical solvent air concentrations from field measurements and an extensive search of industrial, governmental, and academic databases.(59) In addition, our solvent exposure index predicted reduced neural activation (fMRI) during a working memory task, thereby substantiating the predictive validity of our exposure assessment method against a biological measurement of cognitive performance.(39) Nevertheless, any exposure index based on historical recall is subject to inaccuracies and recall bias that could result in random misclassification. In addition, a cross sectional study design introduces error because we can only estimate pre-exposure abilities with current vocabulary or reading examinations and educational attainment. These study limitations generally reduce the power to find consistent results.

Typical workplace air concentrations of solvents and emission of solvents from paint products have steadily declined over the past 20 years.(59) Although our study documented some associations between the solvent exposure index and individual measures of behavioral performance, these associations reflected relatively small differences and were not seen across all measures within a domain. In addition, many solvent exposed participants reported using protective equipment when at most risk for high exposure such as during spray painting activities. Thus, the current neurobehavioral results provide some reassurance that solvent exposed workers are not experiencing clinically significant alterations in the cognitive domains previously of concern such as attention and memory. Moreover, visual contrast sensitivity, as an early and sensitive indicator of solvent induced deficits was also not affected among our industrial painters. When comparing the current sample of workers to those in studies of workers diagnosed with chronic solvent encephalopathy (CSE), workers with CSE were exposed to solvent mixtures for 5 – 10 years at or near occupational exposure limits and as might be expected, these workers had more severe and diffuse neurobehavioral deficits than those seen in the present study(7, 8, 10) Similarly, reductions in solvent emissions from paint products have been accompanied by significant reductions in Finnish cases of CSE (e.g., 5–10 per year in a working population of 2.5 million).(8)

In conclusion, improvements in use of protective equipment and reductions in solvent concentrations have occurred during the working lifetime of our participants. The current study made significant efforts to address previous criticisms of cross sectional studies to include assessment and control of known confounders, a more detailed historical assessment of solvent exposure, and a comprehensive battery of neurobehavioral tests that reduce the

cultural biases of some previous test batteries used in the original literature on chronic solvent encephalopathy. Because relatively few subclinical effects were detected and several potential confounders had to be included in the analysis, future cross sectional studies using a similar study design are unlikely to be informative with regard to the question of solvent encephalopathy at current exposure concentrations in developed countries.

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Table 1:

Neurobehavioral tests, domains, and variables

Test Descriptions	Domains	Variables
Attention		
Symbol Digit (45) •Match 9 numbers to 9 symbols from key; 6 sets of digit symbol pairs presented (1 practice set; 5 trials);	Sustained attention, visuo-motor coordination	Average response latency per trial (sec.)
Matching to Sample Visual Search (46) • Match the sample pattern within a series of 2, 4, or 8 patterns	Attention	Average latency of response for correct match (ms) Total correct
Rapid Visual Information Processing (46) • Digits 2–9 appear one at a time at 100 digits/minute; detect target odd or even sequences	Sustained attention	Probability of hit (correct response) Probability of false alarm (incorrect response) Sensitivity to target (accuracy)
Simple & 5-choice Reaction Time (RT) (46) • Touch a dot on screen as soon as it appears in center (simple RT) or one of five lcoations (5-choice RT)	Attention, vigilance, psychomotor speed	Response latency
Intra-Extra dimensional set shifting (computerized Wisconsin card sort) (46) • Paired abstract patterns in 2 to 4 boxes; subject determines the rule and selects the box that follows the correct rule; stimuli and rules are manipulated; 9 stages are presented	Attention, flexibility of attention	Total errors adjusted* Total trials adjusted* Stages completed *adjusted for stages not attempted
Working Memory & Planning		
Spatial Working Memory (46–48) • Search a series of boxes for a blue token; never appears in same box twice; 2–8 boxes with tokens;	Visual Working Memory	Between errors: revisit box where token found Within errors: revisit box found empty Double errors: within and between error Strategy: number times search starts with same box (higher score = worse strategy)
Spatial Span (46–49) • A series of white boxes light up one at a time. After a tone, subject repeats the pattern presented	Visual Working Memory	Span length: longest sequence recalled Total Errors: number of incorrect boxes selected
Stockings of Cambridge (computerized Tower of London) (46–48) • Reconstruct a pattern of balls using the least amount of moves possible	Planning and executive function	Number of problems solved in minimum moves
Visual Memory		
Simultaneous & Delayed Matching to Sample (50) • Match the sample pattern among 4 choices presented after 0 – 12 sec. delay	Visual memory	Total correct across all delays, Mean correct latency across all delays (ms)
Paired Associations Learning (50) • 6 boxes contain different patterns displayed for 3 sec. each; subject matches target pattern to correct original location on screen; reminders for incorrect responses; 2–8 patterns;	Visuospatial memory, episodic memory, and learning	Total errors adjusted* Mean errors to success: total errors/ successful stages completed Patterns correct located after 1st trial across all stages completed Stages completed: overall success * adjusted for stages not attempted
Pattern & Spatial Recognition Memory (50) • 12 visual patterns presented one at a time; Subject selects correct pattern in paired comparisons with a novel pattern; • 5 spatial locations presented one at a time; correct spatial location when familiar and novel locations are paired	Visual Memory	Number of correct patterns; Average correct response latency (ms) Number correct spatial locations Average correct response latency (ms)
Verbal Memory		
Paired Associate Learning (45) • Three letter names (e.g. Ken) paired with occupations (16 pairs); subject matches names with occupations; 3 trials of pairs given	Verbal memory	Number of correct responses after 30 minute delay

Test Descriptions	Domains	Variables
Attention		
Motor		
Finger Tapping Test (45) • Right and left hand taps for 20 seconds; 2 trials/hand	Response speed and coordination	Average number of taps each hand

Table 2:

Demographic Comparisons of Exposed and Controls

Variable	Controls (N=78) Mean (S.E.)	95% CI	Exposed (N=133) Mean (S.E.)	95% CI
AGE*	46.76 (0.88)		44.39 (0.60)	
YRS ED	12.70 (0.14)		12.64 (0.13)	
LIFETIME SOLVENT EXPOSURE ppm-years	0.0		500.92 (70.31)	
VERBAL Cognitive Ability (VIQ) **	100.00 (0.77)	98.48–101.53	93.76 (0.88)	92.02–95.50
BLOOD LEAD LEVELS **	2.51 (0.10)	2.30–2.71	5.95 (0.37)	5.22–6.69
LIFETIME ALCOHOL USE	18776 (2237.6)	14320–23231	22081 (3217.3)	15715–28446
RANK LIFETIME ALCOHOL USE	111.51 (6.19)	99.18–123.84	100.29 (5.53)	89.35–111.23
LIFETIME MARIJUANA USE	1377.6 (424.38)	532.56–2222.6	1298.6 (274.5)	755.58–1841.6
RANK OF LIFETIME MARIJUANA	105.44 (6.57)	92.35–118.52	106.33 (4.98)	96.48–116.18
LIFETIME COCAINE USE	163.5 (47.21)	69.50–257.5	307.86 (126.52)	57.58–558.13
RANK OF LIFETIME COCAINE USE	110.03 (5.87)	98.35–121.7	103.64 (4.37)	94.99–112.29

* $p < .05$

** $p < .0001$

Table 3:

Neurobehavioral Means, Standard Error and 95% Confidence Intervals

	Controls (N=78)		Exposed (N=133)	
Variable	**Mean (S.E.)**	**95%CI**	**Mean (S.E.)**	**95%CI**
Screening Tests				
Symbol Digit (latency)	22.03 (0.37)	21.30–22.76	22.97 (0.41)	22.17–23.77
Simple Reaction Time * (latency)	333.79 (8.64)	316.58–351	357.07 (6.77)	343.68–370.45
5-Choice Reaction Time ** (latency)	353.76 (6.68)	340.46–367.07	386.83 (6.62)	373.73–399.92
Attention				
Intra-Extra Dimensional Shift				
Total Errors Adjusted	24.46 (2.06)	20.36–28.57	30.46 (2.99)	24.54–36.38
Total Trial Adjusted	93.58 (3.47)	86.67–100.49	103.5 (5.13)	93.36–113.65
Stages Completed	8.62 (0.09)	8.44–8.79	8.36 (0.12)	8.12–8.60
Match to Sample				
Total Correct **	46.78 (0.16)	46.46–47.10	46.18 (0.16)	45.87–46.49
Latency	2147.9 (82.49)	1983.6–2312.1	2288.5 (81.14)	2128–2449
Rapid Visual Processing				
Sensitivity to Target	0.90 (0.01)	0.88–0.91	0.88 (0.01)	0.87–0.89
Probability of Hit	0.62 (0.02)	0.57–0.66	0.57 (0.02)	0.54–0.61
Probability of False Alarm	0.01 (0.00)	0.01–0.02	0.19 (0.00)	0.01–0.03
Working Memory				
Spatial Working Memory				
Between Errors	29.51 (2.22)	25.09–33.93	31.96 (1.91)	28.19–35.73
Within Errors	2.65 (0.51)	1.64–3.67	3.02 (0.43)	2.16–3.87
Double Errors	1.47 (0.32)	0.83–2.11	1.80 (0.30)	1.21–2.40
Strategy	32.87 (0.62)	31.63–34.12	33.68 (0.50)	32.70–34.66
Spatial Span				
Span Length	5.74 (0.15)	5.44–6.04	5.77 (0.11)	5.56–5.99
Errors	12.95 (0.67)	11.61–14.29	13.54 (0.58)	12.39–14.69
Stockings of Cambridge				
Problems Solved in Minimum Moves *	7.99 (0.20)	7.59–8.39	7.41 (0.17)	7.08–7.74
Visual Memory				
Delayed Match to Sample				
Total Correct All Delays	24.81 (0.38)	24.04–25.57	24.43 (0.28)	23.87–24.99
Mean Correct Latency All Delays	3397 (100.79)	3196.3–3597.7	3637.7 (85.17)	3469.3–3806.2
Paired Associate Learning				
Total Errors Adjusted	14.33 (1.72)	10.90–17.77	17.64 (1.56)	14.56–20.72
Mean Errors to Success	1.71 (0.17)	1.38–2.04	2.13 (0.16)	1.81–2.45
First Trial Memory Score	19.06 (0.43)	18.22–19.91	18.59 (0.31)	17.98–19.20
Stages Completed	7.96 (0.03)	7.90–8.02	7.94 (0.03)	7.89–7.99
Visual Memory Cont–d				

Variable	Controls (N=78) Mean (S.E.)	95%CI	Exposed (N=133) Mean (S.E.)	95%CI
Pattern Recognition Memory				
Number Correct	19.67 (0.34)	18.99–20.35	19.17 (0.26)	18.65–19.68
Latency	2248.9 (64.91)	2119.6–2378.1	2271.8 (53.49)	2166–2377.7
Spatial Recognition Memory				
Number Correct	15.95 (0.24)	15.47–16.42	15.46 (0.22)	15.03–15.89
Latency	2312.7 (73.07)	2167.2–2458.2	2715.1 (103.4)	2510.5–2919.6
Motor Skill				
Finger Tapping *-alternating (#taps)	196.1 (5.93)	184.28–207.91	173.34 (4.25)	164.92–181.75
Verbal Memory				
Associate Learning				
Delayed Recall **(#correct)	2.58 (0.28)	2.02–3.14	1.63 (0.17)	1.30–1.97

Note:

* p<0.10;

** p <0.05