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# Neurobehavioural effects of occupational exposure to organic solvents among construction painters

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ABSTRACT A cross sectional study of 101 construction painters was performed to investigate the relation between exposure to mixed organic solvents and changes in central nervous system function. Solvent exposure was estimated using questionnaire data to derive an exposure index (a measure of intensity of exposure) and to estimate the duration and frequency of exposure. Adverse effects on the central nervous system were assessed by self reported questionnaires and eight tests of a computer administered neurobehavioural evaluation system. Factor analysis of both measures of effect yielded factors both biologically plausible and in agreement with other empirical evidence. A consistent positive association was observed between most measures of exposure and the occurrence of neurotoxic symptoms, notably dizziness, nausea, fatigue, problems with arm strength, and feelings of getting "high" from chemicals at work. Associations with exposure were found with the neurobehavioural evaluation system tests of symbol digit substitution and digit span; however, no consistent pattern of effect on neurobehavioural function was observed. This pattern of the occurrence of neurotoxic symptoms without clear evidence of function deficit is consistent with the type 1 toxic central nervous system disorder as classified by the World Health Organisation.

Many industrial solvents have been shown adversely to affect the functioning of the central nervous system (table 1) and a variety of neurobehavioural tests have been widely used to evaluate the possible effects of these and other neurotoxic agents.[1] Many epidemiological studies have studied workers engaged in various painting operations as these workers have a potentially hazardous exposure to many different solvents. Exposure to solvent mixtures is of particular concern since existing threshold limit values (TLVs) for individual agents have been set on the assumption that exposure occurs to only one solvent at a time. The procedure for evaluating exposure to mixtures is simply to add the fractions of individual solvent exposure levels divided by the TLV for that solvent, the total should then be less than 1·0.[2] This method assumes that any effects are additive and may not provide adequate protection from possible synergistic or potentiating effects of solvent mixtures. It also assumes that similar health effects are occurring at comparable levels with respect to the substance TLV.

Various adverse effects on the nervous system have been documented.[3] Some studies of workers occupationally exposed to a variety of solvents have failed to show adverse effects on the central nervous system,[4–6] whereas others have shown an increase in subjective symptoms, including fatigue, irritability, loss of appetite, and sleep disturbances.[7–14] These symptoms frequently persist after exposure to solvents has ceased and after the excretion of solvent metabolites from body tissues would have been complete.

The most commonly documented deficit in neurobehavioural functioning is that of psychomotor performance, as measured by tests of dexterity and auditory and visual reaction time. Detrimental psychomotor effects have occurred after exposure to trichlorethylene, styrene, and solvent mixtures such as paint solvents and jet fuel.[7 10–24] Intellectual decline has been seen primarily in tests measuring perceptual organisation or visuoconstructive abilities.[7 15 25 26] Verbal intelligence, however, has seldom been impaired.[7 20] It is not clear to what extent chronic solvent exposure may affect verbal intelligence in a manner similar to that reported to follow chronic lead exposure[27]; however, vocabulary has been shown to be a stable measure of verbal ability and is perhaps the best single measure of general intelligence and it is relatively insensitive to the effects of neurotoxins.[28] Consistent evaluations of personality with special ref-

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Table 1 *Summary of epidemiological studies of chronic neurotoxic effects of solvents*

| *Exposure/population* | *Subjective symptoms* | *Visual/motor performance* | *Memory* | *Verbal concept formation* | *Mood* | *Reference* |
|---|---|---|---|---|---|---|
| Car painters | + | + | + | + | + | Hanninen *et al*[7] |
| Lacquerers | + | | | | + | Struwe *et al*[8] |
| Car painters | + | | | | | Husman[9] |
| House painters | + | + | + | + | + | Arlien-Soborg *et al*[10] |
| Spray painters | + | + | + | − | | Elofsson *et al*[11] |
| House painters | | + | − | | | Hane *et al*[15] |
| Solvent poisoned | − | + | + | − | | Lindstrom[16] |
| Viscose rayon | | + | + | − | | Harkonen[17] |
| Laminators | | + | − | − | | Harkonen *et al*[18] |
| Jet fuel exposed | | + | − | | | Knave *et al*[19] |
| Printers | | − | + | − | | Hanninen[26] |
| Steel workers | | + | | | − | Anshelm Olson *et al*[20] |
| Dry cleaners | | − | | | | Tuttle *et al*[4] |
| Viscose rayon | + | + | − | + | + | Hanninen[12] |
| Styrene exposed | | + | − | | | Lindstrom *et al*[21] |
| Methylene chloride | | − | − | | | Cherry *et al*[5] |
| Industrial painters | + | + | + | | | Anshlem Olson[13] |
| Toluene | | + | − | | | Iregren[22] |
| House painters | | + | + | | | Lindstrom *et al*[23] |
| Carbon disulfide | | − | − | | | Putz-Anderson *et al*[6] |
| Toluene | | − | − | + | | Cherry *et al*[24] |
| Solvent exposed | | + | − | | | Cherry *et al*[24] |
| Solvent exposed | + | + | − | + | + | Gregerson *et al*[14] |

+ = Adverse effect was observed.
− = Effect was tested for but not observed.

erence to mood have been undertaken in several studies[7 8 10 12 14] in which significant disturbances of affect have been reported.

The chronic disorders of the central nervous system which have been reported in association with exposure to solvents and other toxic agents have been classified into three major types in a scheme adopted by the World Health Organisation.[29] The earliest form of chronic toxicity (type 1) consists primarily of an increase in symptoms such as sleep disturbances, fatiguability, loss of interest in normal activities, psychomotor slowing, and complaints of diminished mental efficiency, such as difficulty in concentrating. More severe than the presence of symptoms alone, mild chronic toxic encephalopathy is characterised as either an organic personality or mood disorder (type 2a) or by deficits in neurobehavioural function (type 2b). Both frequently, but not necessarily, occur in the presence of type 1 symptoms. Recognition of mild intellectual and functional impairment at this stage is important since the disorder may progress to severe chronic toxic encephalopathy (type 3) in which the severe impairment of central nervous system function appears to be similar to other forms of dementia, such as Alzheimer's disease.

## Computerised neurobehavioural testing

To investigate mild chronic toxic encephalopathy, neurobehavioural tests of mood and psychomotor abilities, memory, perception, and verbal skills are used. Conventional neurobehavioural testing used in epidemiological research has been based primarily on tests used in the clinical setting and, as such, suffers from several practical drawbacks. These procedures require administration and scoring by an interviewer, introducing the potential for both random error due to variability in testing procedures and systematic error due to interviewer bias. Such errors can impair the ability to detect the subtle effects investigated in working populations. Computer administered behavioural tests ensure standardisation of administration, thus increasing test reproducibility. In addition, the use of computers allows for easy data handling and scoring, and the immediate reporting of results to participants which improves the level of interest of those being tested. This is particularly beneficial in follow up studies, where the quality of the study depends greatly on the continued willingness of the subjects to participate. Furthermore, interaction of the subject with the computer may be less personal, and therefore less threatening than interacting with an interviewer, thereby increasing motivation.

A computer administered neurobehavioural evaluation system (NES) has been developed which has adapted tests of psychomotor function, memory, verbal abilities, and mood for the microcomputer.[30] The tests have been chosen on the basis of previous work done by Baker *et al*[27 31 32] and recommendations of an expert committee convened by the World Health Organisation (WHO) and the National Institute for Occupational Safety and Health (NIOSH).[33] The advent of this and similar systems has brought with it cautious optimism. While the obvious benefits are welcomed, concerns about their proper use have been aired, particularly regarding the reliability, validity,

standardisation of the test procedures, the development of reference values, and the generation of tests that are not merely extensions or revisions of existing procedures but which introduce new methods of evaluation which exploit the technical abilities of the computer.[34-36]

The reliability of four tests of the NES was investigated by administering and readministering them (with alternative versions when appropriate) at various intervals. Score stability was greatest after one day (r = 0·86–0·94), fell off slightly after 30 days (r = 0·84–0·90), and after 150 days was still high (r = 0·60–0·84).[37] Subjects' performance on four tests of the NES and five widely used standard tests which were judged to measure similar functions were compared in order to estimate the construct validity of the NES tests.[37] Overall, comparability was high with the best correlation between the manual and computer version of the symbol digit substitution task (r = 0·76)

## Potential confounding factors in the study of neurobehavioural functions

A careful assessment of potential confounders is essential for the proper epidemiological evaluation of neurobehavioural effects of toxic exposures.[28 38] In an occupational setting several factors in the population may vary; it is important, for example, to examine the nature of the relation between neurobehavioural functions and age, alcohol and drug intake, education, and other variables that may influence an individual's state of alertness.

### AGE

Psychomotor activity slows with age,[39 40] a factor which contributes to poorer performance on all timed tests. A decreased ability for abstract and complex reasoning is often present among older individuals; however, verbal skills, particularly those such as reading, writing, and vocabulary, are unaffected by aging.[41]

There is much evidence to show that a deficit in short term memory is associated with advancing age, with decrements having been linked to each of the components, registration,[42-44] storage,[45] and retrieval.[46 47] Normal aging does not appear to affect auditory memory span,[48-50] which may be primarily a test of attention rather than memory. Visually presented digits, however, have been associated with aging effects.[51] Lower digit scores result mainly from deficits in performing the "digits backward" subtest; this reflects the impairment of concentration and mental tracking. Older subjects also exhibit poorer performance on the Sternberg memory scanning test. Several studies have shown an increase in the memory scanning time (slope)[50] and often in the cognitive and motor processing time (intercept),[50 52] the latter due in part to the motor speed component of the intercept.

### ALCOHOL

The effects of alcohol consumption have been likened to those of aging[53] and may in fact serve as a model for the effects of other solvents. Effects on cognitive function, memory, and hand eye coordination may be seen with either acute alcohol intake[54-56] or chronic alcoholism.[57-59]

In studies of working populations, however, the role of alcohol in light or moderate social drinkers is more important and this is much less studied or understood. It is likely that there may be a continuum of effects on the brain[60 61] with evidence of no clear cut deficits among light drinkers,[62] some mild deficits reported by some among heavy social drinkers,[63-65] and more serious impairment among alcoholics and individuals suffering from Korsakoff's psychosis.[66] Parker *et al* reviewed several studies which associate social drinking with deficits primarily in visuospatial abilities, abstract thinking, and cognitive performance, but no clear evidence of impaired psychomotor functions or verbal abilities.[67]

### DRUGS

Many drugs in common use may affect the nervous system.[68] Aspirin has no effect on reaction time[69] and most drugs used in the treatment of psychological disturbances tend to have negligible effect on neurobehavioural testing,[70 71] although some change in performance has been documented in those treated with diazepam (Valium),[72] carbamezepine (Tegretol),[73] phenobarbitol,[74] and levodopa.[75]

Studies of the effects of chronic marijuana use have yielded equivocal results. Several researchers have found no observable change in function[57 76 77] whereas others have noted chronic personality and mood changes,[78 79] slowing on digit symbol substitution,[80] reduced memory storage efficiency,[81] and slowed visual processing.[82] The last functional deficits are seen primarily during and immediately after using marijuana.

### EDUCATION

Educational level is associated with several cognitive functions[28 83 84] although in many cases the reason for the association is not clear. Higher educational status often reflects higher innate intelligence or ability but subjects with more education may perform better on some tests because of a broader base of knowledge, such as a wider vocabulary, or because they are more accustomed to taking tests. The direction of the association is also undetermined: are

people brighter because they have more education or do they seek more education because they are brighter?

LEVEL OF ALERTNESS

Several factors affect neurobehavioural function primarily because of their effect on the general level of alertness. These include circadian rhythms and sleep patterns and drugs such as caffeine and nicotine.

The effects of diurnal variation on human performance are well documented.[85-87] Short term memory seems particularly vulnerable to increments in alertness and deteriorate while other cognitive and psychomotor functions are improving. Therefore, memory tasks are best performed in the morning,[88 89] whereas improvement is seen later in the day in tasks of reaction time,[90] vigilance, arithmetic calculation, card sorting, and letter cancellation.[88]

Individuals subjectively perceive the effects of caffeine as either increasing alertness or, often, nervousness.[91] At low doses, caffeine increases alertness and diminishes fatigue and improves reaction time; at higher doses, however, it increases the frequency of headache, tremors, and irritability.[92]

Studies of the effects of cigarettes on performance are relatively few. Some have reported deterioration in verbal rote memory[93] and incidental memory,[94] whereas others have noted an improvement in concentration[95] and some tasks of short term memory.[96]

## Methods

In April 1984 a cross sectional study of construction and maintenance painters exposed to solvents and dry wall tapers who were not exposed was performed to evaluate the neurobehavioural effects of long term exposure to mixed organic solvents.

SUBJECTS

A health survey was made available to all members of the Boston District Council of the International Brotherhood of Painters and Allied Trades (IBPAT) who were enrolled in the union's health and welfare plan—those who had been union members for more than one year. All eligible members were contacted by post by union officials and asked to call and make an appointment at an area hospital where the study was to be conducted. Follow up telephone calls were made by the union to encourage participation.

Of the 615 eligible subjects, 163 (26·5%) participated, including 118 painters and 45 "dry wall tapers." "Painters" included those who currently painted, used to paint (one retiree, one estimator), or who were dry wall tapers who performed painting operations part time. Dry wall tapers included only those who had no history of painting with solvent paints.

To determine the degree to which the study participants were representative of the union as a whole, a brief questionnaire was sent to each of the 452 nonrespondents to determine their reasons for not attending. In addition, the union payroll records of all 615 members were reviewed to determine the number of hours each individual worked in the year and the month before the study date. These data, as surrogates of exposure, were compared for those who attended the study, those who returned the questionnaire, and those who did neither.

MEASUREMENT OF CONFOUNDING FACTORS

In an attempt to control for the acute effects of consumption of neurotropic substances subjects were instructed to refrain from drinking alcohol for 24 hours before the testing session and from using caffeine and cigarettes for one hour before testing.

A comprehensive health questionnaire was administered to all subjects which assessed previous health problems, history or medication, and other potentially confounding factors such as alcohol and caffeine use. Immediately before testing, the subjects were administered a pretest questionnaire designed to evaluate transient conditions that could influence test performance—for example, physical injuries, recent alcohol and drug consumption, and sleep deprivation.

In addition, because lead is a potent neurotoxin and a potential exposure to painters, blood zinc protoporphyrin (ZPP), as an indicator of lead absorption, was measured using a portable haematofluorometer.[97] Individuals with ZPP concentrations above 50 $\mu$g/dl had blood lead (PbB) concentrations estimated as an additional measure of lead absorption.

MEASUREMENT OF EXPOSURE

A solvent history questionnaire was administered to all the participants which sought information regarding paint application rates and frequency by method (spray, roll, brush), respirator use, and ventilation. These data were incorporated into an exposure index (EI) and used to rank individuals as to their average lifetime paint use. The method for deriving the EI is described elsewhere.[98] The number of years worked as a painter and the number of weeks in the past year and days in the past month worked using solvent paints were also obtained from the questionnaire. The time of last exposure to solvents was also noted.

MEASUREMENT OF EFFECT

Trained interviewers administered a questionnaire to each subject which assessed the prevalence of neu-

rological symptoms rated on a five point scale (from "not at all" to "extremely"). The questionnaire was based in part on the Swedish "questionnaire 16"[99] and questionnaires used in previous field evaluations of neurotoxic effects of lead and organic solvents.[27 30]

Neurobehavioural performance was assessed with the NES. The testing procedure was explained by an interviewer and the subject was given the opportunity to familiarise himself with the computer. The subjects then proceeded to a room with eight personal computers separated by partitions. Two interviewers were present to monitor the session and to be available if questions or problems arose. All interactions between subject and interviewer were recorded in a log book. The NES testing session lasted about one hour.

The eight tests, chosen from the NES for use in this study, measured psychomotor performance (continuous performance test, symbol digit substitution, hand eye coordination); memory (digit span, pattern memory, Sternberg memory scanning test); verbal ability (vocabulary); and mood (mood scales) as described elsewhere.[30]

### DATA ANALYSIS

Data analysis was performed primarily on a microcomputer using the statistical package for the social sciences for the IBM PC/XT (SPSS/PC).[100] Regression analyses of the Sternberg memory scanning test were performed using Systat, a soft ware package for use on a microcomputer.[101]

Factor analysis techniques were used to provide appropriate groupings of neurobehavioural test results and, separately, symptom reports. Factor analysis is based on the assumption that underlying factors exist which can explain complex correlations among variables.[102] The steps in the factor analyses of the symptoms and the NES test results were as follows:

(1) Correlation matrices were generated. Pearson correlation was done for the NES test results; however, because the distributions of the symptoms were non-parametric, Spearman correlation was performed using the statistical analysis system (SAS)[103] on the IBM 4341 mainframe computer.

(2) Extraction of factors was done by principal components analysis. The number of factors generated was limited to those with eigenvalues greater than 1·00.

(3)Varimax rotation was performed to enhance the interpretability of the factors by minimising the number of variables with high loadings on a factor.

Multiple regression was used to investigate the relation between solvent exposure and both individual test results and factors of neurobehavioural function while controlling for potential confounders. The backward elimination technique was used, whereby all variables were entered into the equation, then sequentially removed if the probability of its F value was greater than 0·10.

## Results

### DEFINITION OF STUDY SAMPLE

Seven subjects were not tested; two because they spoke no English, one who had a broken arm, one who wore glasses, one who had pneumonia and was unable to complete his examinations, and two who refused to take the neurobehavioural tests although completing other aspects of the medical evaluations. Twenty four others were excluded from data analysis because they were women (1), had a previous diagnosis of alcoholism (6), were heavy chronic marijuana users (3), or spoke English as a second language (14). Thus 101 (86·3%) of the initial 117 painters and 31 (67·4%) of the 46 dry wall tapers were available for analysis.

Although the painters and dry wall tapers belonged to the same union and performed jobs of similar skill levels, the comparability of the two groups was questionable. The painters were older, slightly better educated, of higher socioeconomic status, and drank more alcohol than the dry wall tapers (table 2). Of more serious concern, however, is that there appears

Table 2 *Demographics of sample population*

| | *Painters (n = 101)* | | *Dry wall tapers (n = 31)* | | |
|---|---|---|---|---|---|
| | *Mean* | *Range* | *Mean* | *Range* | |
| Age | 42·8 | (19–66) | 37·9 | (26–51) | (p = 0·003)* |
| Years of school | 11·3 | (7–18) | 10·9 | (4–16) | |
| Vocabulary score (No correct of 25) | 16·4 | (4–24) | 17·9 | (9–25) | (p = 0·10) |
| Hollingshead index (parental SES)† | 53·7 | (15–77) | 58·3 | (37–77) | (p = 0·04) |
| Alcohol: | | | | | |
| Drinks/week | 13·6 | (0–105) | 9·6 | (0–58) | |
| Drinks/occasion | 2·9 | (0–14) | 2·7 | (0–8) | |
| Occasions/month | 16·0 | (0–75) | 9·6 | (0–30) | (p = 0·01) |
| Episodes of heavy drinking/month | 5·4 | (0–30) | 3·2 | (0–20) | (p = 0·09) |

*Two tailed *t* test.
†Hollingshead index: range 11–77, where higher score refers to lower SES.

Table 3 *Association between subjects' belief that they are sick from their job and neurotoxic symptom reports (among painters)*

| *Symptom* | *Mean value (adjusted for age and school)* | | |
|---|---|---|---|
| | *"Sick" (n = 26)** | *"Not sick" (n = 70)** | *p value* |
| Tired | 1·37 | 0·55 | 0·01 |
| Dizzy | 1·20 | 0·21 | 0·00 |
| Trouble concentrating | 1·64 | 0·17 | 0·02 |
| Confusion | 0·25 | 0·00 | 0·00 |
| Trouble remembering | 0·88 | 0·32 | 0·02 |
| Relatives notice trouble remembering | 0·58 | 0·18 | 0·06 |
| Have to make notes | 0·63 | 0·36 | 0·33 |
| Difficulty understanding meaning | 0·26 | 0·08 | 0·26 |
| Irritable | 0·98 | 0·44 | 0·10 |
| Depressed | 0·60 | 0·14 | 0·06 |
| Palpitations | 0·57 | 0·11 | 0·01 |
| Sleepy | 0·78 | 0·37 | 0·12 |
| Trouble falling asleep | 0·40 | 0·11 | 0·08 |
| Incoordination | 0·11 | 0·03 | 0·50 |
| Decreased leg strength | 0·16 | 0·00 | 0·06 |
| Decreased arm strength | 0·52 | 0·28 | 0·28 |
| Trouble grasping | 0·17 | 0·17 | 0·78 |
| Numb fingers | 0·37 | 0·21 | 0·16 |
| Numb toes | 0·01 | 0·07 | 0·44 |
| Headache | 0·66 | 0·51 | 0·60 |
| Nausea | 0·32 | 0·15 | 0·40 |
| Rash | 0·92 | 0·40 | 0·13 |
| Dryskin | 0·96 | 0·82 | 0·77 |
| Trouble driving | 0·58 | 0·24 | 0·21 |
| Perspire | 0·27 | 0·09 | 0·31 |
| Get "high" at work | 1·83 | 0·77 | 0·01 |
| Decreased tolerance to alcohol | 1·01 | 0·30 | 0·03 |

*Five of the 101 painters in the study did not respond to this question.
Symptoms scored as: 0 = "not at all"; 2 = "a little"; 3 = "moderately"; 4 = "quite a bit"; 5 = "extremely."

to be an inherent difference in the makeup of the two groups. Many dry wall tapers in the Boston District Council are French Canadians living and working in Boston on a temporary basis, whereas the painters are predominantly native to the Boston area. Because of the small number of eligible dry wall tapers and doubts about their comparability with the painters, all analyses reported will be internal comparisons within the group of painters.

### SELECTION BIAS

Subjects who were eligible but who did not participate in the study were sent a brief questionnaire regarding their reasons for not attending, as well as their percep-

Table 4 *Association between subjects' belief that they are sick from their job and NES test results (among painters)*

| *Test* | *Mean value (adjusted for age and school)* | | |
|---|---|---|---|
| | *"Sick" (n = 26)* | *"Not sick" (n = 70)* | *p value* |
| CPT: | | | |
| Mean RT | 414·25 | 417·37 | 0·82 |
| SD | 68·71 | 74·36 | 0·29 |
| Symbol digit: latency | 2·70 | 2·95 | 0·56 |
| Hand eye: RMSE | 1·73 | 1·98 | 0·11 |
| Pattern memory: | | | |
| % Correct | 0·72 | 0·68 | 0·43 |
| Latency | 8·88 | 9·19 | 0·85 |
| Digit span: | | | |
| Forward | 6·57 | 6·19 | 0·42 |
| Backward | 5·34 | 5·14 | 0·99 |
| Sternberg memory scanning: | | | |
| Intercept | 499·66 | 512·04 | 0·91 |
| Memory scanning time | 64·97 | 75·17 | 0·52 |
| Vocabulary: No correct | 17·27 | 17·51 | 0·37 |
| Mood: | | | |
| Tension | 7·87 | 5·62 | 0·01 |
| Anger | 4·85 | 2·30 | 0·01 |
| Fatigue | 9·14 | 7·44 | 0·03 |
| Depression | 4·34 | 2·62 | 0·01 |
| Confusion | 6·08 | 4·23 | 0·08 |

CPT = Continuous performance test.

Table 5 *Union payroll record review*

| | *Tested* | *Returned questionnaire* | *Non-respondents* | *Total* |
|---|---|---|---|---|
| Painters: | | | | |
| No | 118 (28·9%) | 59 (14·4%) | 232 (56·7%) | 409 |
| Age | 41·7 | 43·7 | 40·0 | 41·0 |
| Hours in past year | 1549·4 | 1467·5 | 1403·0 | 1452·4 |
| Hours in past month | 106·1 | 103·9 | 101·6 | 103·1 |
| Dry wall tapers: | | | | |
| No | 45 (21·8%) | 30 (14·6%) | 131 (63·6%) | 206 |
| Age | 39·5 | 36·9 | 36·3 | 37·1 |
| Hours in past year | 1279·1 | 1508·7 | 1351·9 | 1357·7 |
| Hours in past month | 76·0 | 121·5 | 126·2 | 114·5 |

tion of their health status. Of 452 questionnaires sent out, 89 (20%) were returned. Twenty one (24%) were not experiencing health problems; however, most gave reasons unrelated to the state of their health.

To assess further the comparability of the study sample with the entire group of eligible subjects, each was asked the following question either at the time of testing or on the posted questionnaire: "Do you think that you are getting sick from your job?" Overall, about twice as many among the study sample answered "yes." Furthermore, this difference was seen only among the painters (28·8% *v* 13·5%); 12·2% of tapers who participated in our study answered by comparison with 16·7% of non-participating tapers contacted by post only.

Among those who participated in the study, there was a significant association between the response to this question and the age and education of the subject. Perhaps due to cultural differences, younger ($p = 0·04$) and better educated ($p = 0·08$) subjects were more likely to state that they believed they were getting sick from their job. To compare individuals who said they believed they were getting sick from their work, multiple regression analyses were performed for each symptom and test variable on age, school level, and whether they thought they were getting sick from work (1 = yes, 0 = no). There was a significant difference in the mean values of the number of symptom reports between those who believed they were getting sick from their jobs and those who did not. Among the neurobehavioural tests, however, a difference existed only with the results of the mood scales (tables 3, 4).

The results of the review of union payroll records (table 5) showed that the study sample, those who posted in the questionnaire, and those who did not participate at all were of similar age and had worked about the same number of hours in both the previous year and the previous month. The small difference in the number of hours worked in the past year among the groups of painters is due to the higher number of retirees among the non-respondents.

## MEASURES OF EXPOSURE

Several measures of exposure were available for use in this study: estimates of duration (years painting with solvent paints), frequency (weeks worked with solvents in past year, days worked with solvents in past month), and amount (exposure index for lifetime and past year, where index is a weighted average of gallons per year available for inhalation). In addition, in regression analyses of symptom reports, a term indicating whether a subject had worked in the past month was used (1 = yes, 0 = no), as the questionnaire sought to determine the presence of symptoms in the past month. Similarly, in regression analyses of the tests of neurobehavioural function, an indicator of work within the past year was included because the potential reversibility of chronic effects could obscure an association if analysis did not distinguish those who had not been exposed within the past year (table 6).

## MEASURES OF EFFECT

### *Neurotoxic symptoms*

Of the 105 study participants, 101 (96·2%) reported

Table 6 *Solvent exposure among painters*

| | *All painters (n = 101)* | *Exposed in past year (n = 90)* | *Exposed in past month (n = 80)* |
|---|---|---|---|
| Years as painter | 17·99 (10·84) | 18·04 (10·69) | 18·19 (10·66) |
| Weeks in past year | 30·60 (11·28) | 34·34 (17·13) | 36·19 (10·66) |
| Days in past month | 13·34 (11·28) | 14·97 (10·88) | 16·84 (10·07) |
| Exposure index: | | | |
| Lifetime | 28 728·00 (median) | 29 238·60 (median) | 30 357·00 (median) |
| Past year | 24 303·40 (median) | 26 910·20 (median) | 28 175·10 (median) |

Table 7 *Frequency of self reported neurotoxic symptoms (n = 101)*

| | *Not at all* | *A little* | *Moderately* | *Quite a bit* | *Extremely* |
|---|---|---|---|---|---|
| Tired | 71 | 16 | 6 | 4 | 0 |
| Dizzy | 78 | 13 | 3 | 1 | 2 |
| Trouble concentrating | 86 | 6 | 4 | 2 | 0 |
| Confused | 94 | 2 | 1 | 0 | 0 |
| Trouble remembering | 82 | 5 | 9 | 1 | 0 |
| Relatives notice trouble remembering | 88 | 4 | 5 | 0 | 0 |
| Have to make notes to remember | 84 | 7 | 3 | 3 | 0 |
| Trouble understanding meaning of magazines, books, etc | 93 | 2 | 2 | 0 | 0 |
| Irritable | 77 | 12 | 5 | 3 | 0 |
| Depressed | 89 | 2 | 4 | 2 | 0 |
| Palpitations | 88 | 7 | 2 | 0 | 0 |
| Seizures | 96 | 0 | 0 | 1 | 0 |
| Sleepy | 82 | 6 | 7 | 2 | 0 |
| Trouble falling asleep | 90 | 3 | 2 | 2 | 0 |

neurotoxic symptoms (table 7). Because it was thought that the scale of effect is approximately linear, with the largest difference being between the symptom not being present at all and any presence of it, the numerical scale used is 0, 2, 3, 4, 5 corresponding to "not at all, a little, moderately, quite a bit, and extremely." The frequency of any presence of a symptom ranged from 1% (seizures) to 28% (dry skin).

To determine possible patterns of symptoms or symptom clusters within this group of painters, factor analysis was performed on 19 of the 27 symptoms questioned. Several were not included because of low prevalence (confused, trouble understanding meaning of things read, seizures, incoordination, decreased leg strength, numb toes, and perspiration) whereas others were to be examined as separate symptoms ("high" at work, decreased tolerance to alcohol).

Principal component analysis yielded eight factors with eigenvalues greater than 1·0. Factor loadings—that is, the correlation between a symptom and a factor, generated after varimax rotation—are presented in table 8. The cumulative variance of the sample explained by these eight factors was 68·6%. Other factor analyses were performed in which the number of factors was set to range from five to nine. In these the clusters identified in table 8 remained essentially intact.

Scores for each of the factors were determined for each subject by weighting each component symptom by its factor score. These weighted scores correlated highly with the simple arithmetic mean of the symptoms in each factor. Therefore, for ease of interpretability, an individual's score for a factor was calculated as the unweighted mean of the symptoms included in that factor.

Since the symptom clusters determined by factor

Table 8 *Factor analysis of symptoms*

| | *Factor loadings* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *Factor 1* | *Factor 2* | *Factor 3* | *Factor 4* | *Factor 5* | *Factor 6* | *Factor 7* | *Factor 8* |
| Tired | 0·76 | 0·04 | −0·09 | 0·02 | 0·02 | 0·12 | 0·31 | 0·02 |
| Irritable | 0·72 | 0·13 | 0·18 | −0·02 | 0·25 | 0·00 | −0·11 | −0·11 |
| Depressed | 0·75 | 0·05 | 0·09 | 0·23 | 0·05 | −0·05 | −0·10 | 0·05 |
| Sleepy | 0·47 | 0·11 | −0·31 | 0·00 | −0·21 | 0·24 | 0·42 | 0·01 |
| Trouble remembering | 0·19 | 0·80 | −0·02 | −0·03 | 0·04 | 0·13 | 0·08 | 0·16 |
| Relatives notice | 0·31 | 0·77 | 0·29 | 0·03 | 0·08 | −0·03 | −0·04 | −0·08 |
| Have to make notes | −0·16 | 0·84 | −0·05 | 0·09 | −0·04 | −0·04 | −0·06 | −0·13 |
| Decreased arm strength | 0·26 | 0·02 | 0·55 | 0·09 | 0·11 | 0·37 | −0·22 | 0·35 |
| Trouble grasping | −0·06 | 0·06 | 0·77 | 0·03 | −0·06 | −0·07 | 0·09 | 0·00 |
| Headache | 0·11 | −0·06 | −0·06 | 0·83 | 0·14 | −0·01 | −0·20 | 0·00 |
| Nausea | 0·13 | 0·16 | 0·18 | 0·61 | 0·17 | 0·06 | 0·32 | −0·27 |
| Dizzy | 0·02 | 0·06 | 0·15 | 0·61 | 0·28 | 0·05 | 0·15 | 0·17 |
| Trouble concentrating | 0·02 | 0·24 | −0·31 | 0·24 | 0·45 | 0·03 | 0·16 | 0·07 |
| Trouble falling asleep | 0·08 | −0·12 | 0·05 | 0·04 | 0·78 | 0·20 | 0·12 | −0·23 |
| Palpitations | 0·21 | 0·19 | −0·12 | 0·09 | 0·63 | −0·24 | −0·20 | 0·26 |
| Rash | 0·04 | 0·01 | 0·10 | 0·00 | 0·04 | 0·87 | −0·03 | 0·02 |
| Trouble driving | 0·00 | −0·05 | 0·16 | 0·03 | 0·07 | −0·07 | 0·76 | 0·18 |
| Numb fingers | −0·04 | −0·05 | 0·04 | 0·00 | −0·05 | 0·05 | 0·19 | 0·88 |
| Dry skin | 0·20 | 0·08 | 0·58 | 0·19 | −0·05 | 0·27 | 0·36 | −0·04 |
| Eigenvalue of each factor | 3·43 | 1·86 | 1·61 | 1·46 | 1·34 | 1·21 | 1·13 | 1·00 |
| Cumulative variance explained | 0·18 | 0·28 | 0·36 | 0·44 | 0·51 | 0·57 | 0·63 | 0·69 |

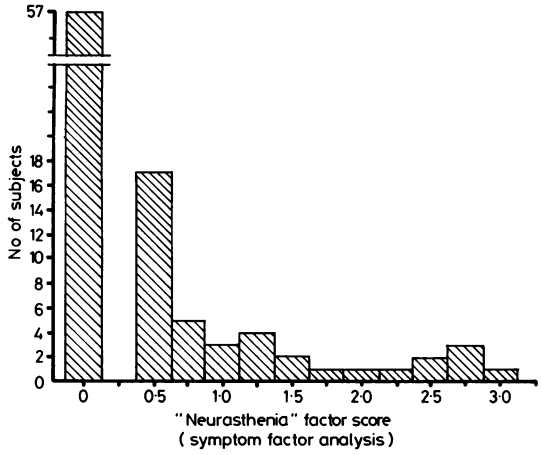


Fig 1 *Frequency distribution of "neurasthenia" symptoms (tired, irritable, depressed, sleepy) based on factor analysis using Spearman correlation matrix.*

analysis generally correspond to patterns of symptoms seen clinically, they were named accordingly: neuraesthenia (factor 1), memory problems (factor 2), arm strength and coordination difficulties (factor 3), a complex of headache, nausea, and dizziness (symptoms characteristic of acute solvent intoxication (factor 4)), and a complex of problems associated with anxiety (factor 5). The distribution of one of these factors ("neuraesthenia") is presented in fig 1. Factors 6, 7, and 8 consisted of only one symptom: rash, trouble when driving, and numb fingers, respectively.

*Neurobehavioural evaluation system*

A summary of the results of each of the eight NES tests administered is presented in table 9. A Pearson correlation matrix was generated among the NES parameters and the factor matrix produced by varimax rotation (table 10) showed four distinct factors, which correspond to assessments of mood, hand eye error, memory, and psychomotor speed. These factors accounted for 64·8% of the total variance of the sample.

So that all the test results would share a common scale, they were converted into Z scores. Then, like the symptom factors, the unweighted arithmetic mean of the components of each factor was calculated and used as an individual's score for that factor. The scores of three of the factors (mood, error, speed) were multiplied by −1 so that, for all four factors, a higher score implies better performance. The distribution of the factor relating to memory problems is presented in fig 2.

*Association of neurobehavioural test performance and exposure to solvents confounding factors*

Several potential confounding factors were included as independent variables in all the regression analyses of NES tests and symptoms. These included age, level of schooling, vocabulary score (as a surrogate of general level of intelligence), chronic alcohol intake (drinks/occasion), and parental socioeconomic status (Hollingshead index).[104] Vocabulary scores and Hollingshead index were initially included in analyses of symptoms; however, because no association was seen in any of these analyses, they were eliminated from further investigations of symptoms.

Because of the large number of known potentially confounding factors, it would be impractical to attempt to control for them all. Several factors were not included in regression analyses since they were found to be unassociated with exposure terms. These were recent alcohol and caffeine intake, subjects' percep-

Table 9 *Neurobehavioural evaluation system (NES): results of 101 painters*

| *Test* | *Parameter* | *Mean* | *SD* | *Median* | *Range* |
|---|---|---|---|---|---|
| Continuous performance test | Mean RT (msec) | 389·20 | 41·25 | 387·68 | 301·67–510·41 |
| | SD (msec) | 71·21 | 16·85 | 69·87 | 35·11–113·62 |
| | Non-responses (min 2–5) | 0·36 | 0·85 | 0·00 | 0·00–6·00 |
| | False positives (min 2–5) | 1·49 | 1·92 | 1·00 | 0·00–14·00 |
| Symbol digit | Mean latency/symbol (msec) (best 2 of 4 trials) | 2·92 | 0·74 | 2·78 | 1·84–6·28 |
| Hand eye coordination | Log of root mean squared error (best 2 of 4 trials) | 1·95 | 0·51 | 1·83 | 1·27–3·96 |
| Digit span | Forward | 6·26 | 1·32 | 6·00 | 4·00–9·00 |
| | Backward | 5·13 | 1·42 | 5·00 | 3·00–8·00 |
| Pattern memory | Per cent correct | 0·69 | 0·17 | 0·72 | 0·21–1·00 |
| | Mean latency (msec) | 9·04 | 2·77 | 8·56 | 4·42–17·22 |
| Sternberg memory scanning | Intercept (msec) | 452·19 | 121·16 | 449·40 | 182·80–893·40 |
| | Slope: set size (msec) | 71·86 | 40·41 | 64·65 | 0·90–190·30 |
| Vocabulary | No correct of 25 | 16·37 | 4·08 | 17·00 | 4·00–24·00 |
| Mood | Tension | 6·27 | 3·47 | 5·50 | 0·00–15·00 |
| | Depression | 3·27 | 2·68 | 2·00 | 0·00–12·00 |
| | Anger | 3·01 | 2·75 | 3·00 | 0·00–11·00 |
| | Fatigue | 7·95 | 3·45 | 8·00 | 0·00–17·00 |
| | Confusion | 4·57 | 2·85 | 4·00 | 0·00–14·00 |

Table 10 *Factor analysis of neurobehavioural tests factor loadings: varimax rotation*

| | *Factor 1 Mood* | *Factor 2 Error* | *Factor 3 Memory* | *Factor 4 Psychomotor speed* |
|---|---|---|---|---|
| Tension | 0·87 | 0·04 | 0·12 | −0·09 |
| Depression | 0·75 | 0·05 | −0·01 | −0·05 |
| Anger | 0·77 | 0·18 | −0·15 | −0·22 |
| Fatigue | 0·77 | −0·11 | −0·12 | 0·16 |
| Confusion | 0·62 | 0·07 | −0·26 | 0·20 |
| Hand eye error | 0·00 | 0·60 | −0·24 | 0·00 |
| CPT non-responses | 0·02 | 0·80 | −0·07 | 0·19 |
| CPT false positive | 0·16 | 0·82 | −0·02 | −0·04 |
| Digit span: | | | | |
| Forward | −0·07 | −0·02 | 0·81 | −0·21 |
| Backward | 0·02 | −0·10 | 0·84 | −0·01 |
| Pattern memory | −0·01 | −0·33 | 0·56 | 0·09 |
| CPT (mean RT) | −0·05 | −0·15 | 0·04 | 0·87 |
| CPT (SD) | 0·02 | 0·21 | −0·03 | 0·85 |
| Symbol digit latency | 0·08 | 0·43 | −0·44 | 0·53 |
| Eigenvalues for each factor | 3·32 | 2·75 | 1·68 | 1·32 |
| Cumulative variance explained | 0·24 | 0·43 | 0·55 | 0·65 |

CPT = Continuous performance test.

tion of fatigue, amount of sleep the previous night, subjects' assessment of how hard they tried on the tests, and handedness. Zinc protoporphyrin level was not included because no one had a significantly raised level.

The correlation matrix of potential confounders and exposure terms (table 11) shows that, not surprisingly, age is strongly correlated with duration of exposure (r = 0·79). For this reason, duration was not used as an indicator of exposure, since its association with neurobehaviour cannot be distinguished from that of age.

*Neurotoxic symptoms: regression analyses*

The relation between solvent exposure and neurotoxic symptoms was investigated for four measures of exposure (lifetime and past year exposure indices and number of weeks in the past year and days in the past month using solvent paints). Multiple regressions (backward elimination) were performed for each of the symptoms and the symptom factors separately. Initially, each analysis included the following potential confounding variables in the model: age, ed-

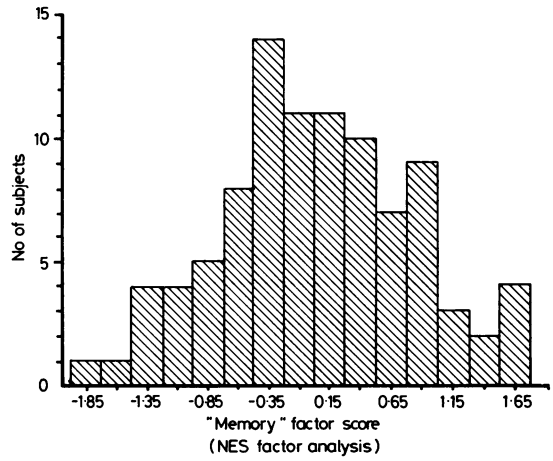


Fig 2 *Frequency distribution of "memory" factor (performance on NES tests: digit span (forward and backward), pattern memory) based on factor analysis using Pearson correlation matrix.*

Table 11 *Correlation matrix of potential confounder and exposure terms*

| | *Age* | *School* | *Vocab* | *HI* | *Alcohol* | *Years as painter* | *Weeks* | *Days* | *EI:life* | *EI:year* |
|---|---|---|---|---|---|---|---|---|---|---|
| Age | 1·00 | −0·51** | −0·10 | 0·42** | −0·25* | 0·79** | −0·06 | −0·15 | −0·12 | −0·11 |
| Years of school | | 1·00 | 0·50* | −0·40** | 0·09 | −0·44** | −0·01 | 0·04 | 0·02 | 0·06 |
| Vocabulary score | | | 1·00 | −0·23 | −0·01 | −0·05 | 0·12 | 0·08 | 0·00 | 0·08 |
| Hollingshead index† | | | | 1·00 | −0·04 | 0·34** | 0·00 | −0·10 | −0·19 | −0·13 |
| Alcohol consumption | | | | | 1·00 | −0·21 | 0·09 | 0·11 | 0·15 | 0·24 |
| Years as painter | | | | | | 1·00 | 0·17 | 0·04 | −0·05 | −0·01 |
| Weeks worked in past year | | | | | | | 1·00 | 0·68** | 0·22 | 0·42** |
| Days worked in past month | | | | | | | | 1·00 | 0·20 | 0·37** |
| Exposure index: lifetime | | | | | | | | | 1·00 | 0·77** |
| Exposure index: past year | | | | | | | | | | 1·00 |

*p < 0·01; **p < 0·001.
†Higher score indicates lower socioeconomic status of painter's parents.

Table 12 *Multiple regressions (backward elimination) of symptoms. Addition of exposure term to model with age, school, alcohol, work status. p value of regression coefficient**

| | *EI: lifetime* | *EI: past year* | *Weeks in past year* | *Days in past year* |
|---|---|---|---|---|
| Tired | – | – | + | – |
| Irritable | + | – | + | + |
| Depressed | – | – | + | + |
| Sleepy | + | + | + | 0·01 |
| Trouble remembering | + | + | + | + |
| Relatives notice trouble remembering | + | – | + | + |
| Have to make notes | + | + | + | – |
| Decreased arm strength | – | – | + | 0·08 |
| Trouble grasping | 0·02 | 0·02 | + | – |
| Headache | – | – | + | – |
| Nausea | 0·09 | 0·08 | + | + |
| Dizzy | 0·02 | 0·03 | 0·03 | 0·08 |
| Trouble concentrating | + | + | + | + |
| Trouble falling asleep | + | + | 0·03 | + |
| Palpitations | 0·09 | + | + | – |
| Rash | + | + | + | + |
| Driving | + | + | 0·03 | + |
| Numb fingers | + | 0·04 | + | + |
| Dry skin | – | – | + | + |
| Perspire | + | + | + | – |
| Get "high" at work | 0·01 | + | – | + |
| Decreased tolerance to alcohol | + | + | + | + |
| Factors: | | | | |
| Neurasthenia | – | – | + | 0·10 |
| Memory | + | + | + | – |
| Arm strength | + | + | + | + |
| Acute intoxication | + | 0·04 | + | + |
| Anxiety | 0·08 | + | + | + |

*p Value listed only if <0·1.
"+" Signifies positive association between exposure and occurrence of symptom.
"–" Signifies negative association.
EI = Exposure index.

Table 13 *Multiple regressions analysis of NES tests and factors. p Value of regression coefficient**

| | *Age* | *School* | *Vocabulary* | *Alcohol†* | *HI‡* | *Status§* | *R-squared* |
|---|---|---|---|---|---|---|---|
| CPT: | | | | | | | |
| Mean RT | | 0·02 | | 0·07 | | | 0·10 |
| SD | | | <0·01 | <0·01 | | | 0·17 |
| Non-resp | | | 0·03 | | | | 0·05 |
| False pos | | | <0·01 | | | | 0·07 |
| Symbol digit: latency | <0·01 | | <0·01 | 0·05 | | | 0·44 |
| Hand eye: | | | | | | | |
| RMSE | <0·01 | | 0·01 | | | | 0·16 |
| Digit span: | | | | | | | |
| Forward | <0·01 | | <0·01 | | <0·01 | 0·03 | 0·26 |
| Backward | 0·01 | | <0·01 | | | 0·05 | 0·21 |
| Pattern memory: | | | | | | | |
| % Correct | | | <0·01 | | | | 0·09 |
| Latency | | 0·09 | | | | | 0·03 |
| Sternberg memory scanning: | | | | | | | |
| Intercept | 0·09 | | | | | | 0·03 |
| Slope (memory scanning time) | | | <0·01 | | | | 0·16 |
| Mood: | | | | | | | |
| Tension | 0·09 | | | | | | 0·03 |
| Depression | 0·05 | | | | | | 0·04 |
| Anger | 0·08 | | | | | | 0·03 |
| Fatigue | | | | | | | |
| Confusion | | | <0·01 | | | | 0·12 |
| Factors: | | | | | | | |
| Mood | | | | | | | |
| Memory | 0·01 | | <0·01 | | | | 0·23 |
| Speed | | <0·01 | | <0·01 | | | 0·22 |
| Error | 0·04 | | <0·01 | | | | 0·14 |

*p Value listed only if <0·1.
†Alcohol: drinks/occasion.
‡HI: Hollingshead index (parental SES).
§Work status: indicates whether worked in past year (1 = yes, 0 = no).
CPT = Continuous performance test.

ucation level, chronic alcohol consumption rate, and an indicator of whether an individual worked with solvent paints in the past month. Of all the symptoms evaluated, none was significantly ($p < 0.05$) associated with age. Only depression was positively associated with level of education ($p = 0.06$). Only skin problems ($p = 0.02$) and trouble driving home from work ($p = 0.06$) were associated with whether an individual had worked in the past month. When the symptoms were clustered, the factor for acute intoxication (headache, nausea, and dizziness) was positively associated ($p = 0.01$) with working in the past month. Increased chronic alcohol consumption was positively associated with the occurrence of a variety of symptoms (tired, dizzy, nausea, trouble driving, trouble falling asleep, increased perspiration, numbness in fingers, and tendency to get "high" from chemicals at the worksite, and the factor for acute intoxication). In all cases the total variance explained by the confounder variables in the model was relatively small ($R^2 = 0.03$ to $0.18$).

Further regression analyses were then performed whereby each exposure term was added separately to a model which included terms for age, schooling, and alcohol consumption. Generally, increased exposure was associated with increased symptom reporting. Particularly strong associations were observed between the exposure index and symptoms of rash ($p = 0.09$) and trouble driving ($p = 0.07$) and the cluster of symptoms of acute intoxication ($p = 0.04$). Similar associations were noted with exposure frequency measures (table 12).

*Neurobehavioural evaluation system: regression analyses*

As with the investigation of the symptoms, the relations between solvent exposure and the results of the NES were explored using backward elimination regression analyses. Analyses of the test measures and the factors derived from them included several potential confounders in each model: age, education level, vocabulary score, Hollingshead index, chronic alcohol consumption, and an indicator of whether an individual had worked with solvent patients in the past year (table 13).

The most consistent finding was the relation of vocabulary test score (used as a surrogate of verbal intelligence) with tests of other neurobehavioural functions. Better performance on ten of the 17 measures, with at least one measure from each test administered, was seen with higher vocabulary score.

Age was also found to be associated with tests of several neurobehavioural functions. Higher age was related to poorer performance of psychomotor abilities (symbol digit latency, hand eye score, and Sternberg intercept, which measures both cognitive encoding and motor processing time) and short term memory (forward and backward digit span). Older

Table 14 *Multiple regression analysis of NES tests and factors. p value of regression coefficient**

| | *EI: lifetime* | *EI: past year* | *Weeks in past year* | *Days in past year* |
|---|---|---|---|---|
| CPT: | | | | |
| Mean RT | +** | + | + | − |
| SD | − | − | + | − |
| Non-resp | − | − | − | − |
| False pos | − | − | − | − |
| Symbol digit: latency | + | + | 0·04 | + |
| Hand eye: RMSE | − | − | − | − |
| Digit span: | | | | |
| Forward | − | − | 0·03 | + |
| Backward | + | + | + | + |
| Pattern memory: | | | | |
| % correct | − | − | − | − |
| Latency | − | − | − | − |
| Sternberg memory scanning: | | | | |
| Intercept | − | − | + | + |
| Slope (MST) | + | − | − | − |
| Mood: | | | | |
| Tension | 0·10 | + | + | + |
| Depression | + | − | + | + |
| Anger | + | + | + | + |
| Fatigue | + | + | + | 0·08 |
| Confusion | + | + | − | − |
| Factors: | | | | |
| Mood | + | + | + | + |
| Memory | − | + | + | + |
| Speed | − | − | + | − |
| Error | − | − | − | − |

*p Value listed only if $< 0.1$.
"+" Signifies association between higher exposure and poorer performance on NES tests.
"−" Signifies association between higher exposure and better performance on NES tests.
CPT = Continuous performance test.

Table 15 *Pearson correlations between symptom factors and NES tests and NES factors*

| | *Symptom factor* | | | | | *Individual symptoms* | | |
|---|---|---|---|---|---|---|---|---|
| | *1* | *2* | *3* | *4* | *5* | *6* | *7* | *8* |
| CPT: | | | | | | | | |
| Mean RT | 0·04 | 0·26* | 0·04 | −0·11 | −0·09 | 0·03 | 0·03 | −0·23 |
| SD | 0·03 | 0·01 | −0·07 | −0·09 | −0·03 | 0·03 | 0·02 | −0·17 |
| Non-resp | −0·05 | 0·03 | −0·13 | −0·18 | −0·02 | −0·09 | 0·00 | −0·03 |
| False pos | −0·05 | −0·02 | −0·06 | −0·03 | −0·01 | −0·06 | −0·02 | 0·05 |
| Symbol digit: latency | 0·07 | 0·11 | −0·07 | −0·01 | −0·15 | −0·07 | 0·17 | −0·15 |
| Hand eye: error | −0·05 | 0·00 | 0·21 | 0·00 | −0·07 | −0·05 | −0·04 | −0·01 |
| Digit span: | | | | | | | | |
| Forward | −0·06 | 0·19 | 0·06 | 0·01 | 0·24 | 0·07 | −0·15 | 0·13 |
| Backward | 0·06 | 0·24 | −0·02 | 0·18 | 0·14 | 0·10 | 0·01 | 0·23 |
| Pattern memory: | | | | | | | | |
| % Correct | 0·07 | 0·20 | −0·09 | 0·13 | 0·15 | 0·10 | 0·02 | 0·11 |
| Latency | −0·06 | −0·21 | −0·05 | −0·10 | −0·17 | 0·00 | −0·09 | −0·14 |
| Sternberg memory scanning: | | | | | | | | |
| Intercept | 0·20 | 0·16 | 0·23 | −0·17 | −0·07 | 0·29* | 0·07 | −0·19 |
| Slope (MST) | −0·21 | 0·05 | −0·25 | 0·06 | 0·04 | −0·17 | −0·18 | 0·02 |
| Mood: | | | | | | | | |
| Tension | 0·34** | 0·16 | 0·22 | 0·32* | 0·36** | 0·38** | 0·21 | 0·31* |
| Depression | 0·36** | 0·12 | 0·07 | 0·14 | 0·17 | 0·36** | 0·26* | 0·11 |
| Anger | 0·33** | 0·09 | 0·23 | 0·14 | 0·14 | 0·40** | 0·19 | 0·15 |
| Fatigue | 0·52** | 0·16 | 0·12 | 0·22 | 0·07 | 0·30* | 0·54** | 0·19 |
| Confusion | 0·09 | 0·01 | −0·03 | 0·05 | 0·36** | 0·02 | 0·12 | 0·20 |
| Factors: | | | | | | | | |
| Mood | −0·44** | −0·15 | −0·16 | −0·23 | −0·29* | −0·39** | −0·35** | −0·26* |
| Memory | 0·03 | 0·27* | 0·06 | 0·14 | 0·23 | 0·12 | −0·05 | 0·21 |
| Speed | −0·06 | −0·16 | 0·04 | 0·09 | 0·11 | 0·00 | −0·08 | 0·23 |
| Error | 0·07 | 0·00 | 0·00 | 0·09 | 0·04 | 0·09 | 0·03 | 0·00 |

*$p < 0·01$; **$p < 0·001$.
Symptom factor: 1 = Neuraesthenia; 2 = Memory difficulties; 3 = Arm weakness; 4 = Acute intoxication; 5 = Anxiety.
Individual symptom: 6 = Irritability; 7 = Fatigue; 8 = Dizziness.

subjects, however, reported less tension, depression, and anger on the mood scales, a finding consistent with analyses of questionnaire symptom reports.

Higher education level was associated with better performance on two tests of psychomotor ability: CPT mean reaction time and pattern memory latency.

Unlike symptom reports, which were consistently positively associated with chronic alcohol consumption, only tests of psychomotor function were associated with alcohol use (CPT reaction time and standard deviation and symbol digit latency). Surprisingly, in each case, better performance (increase in speed, decrease in variability) was seen with increasing alcohol consumption. Alcohol consumption was negatively correlated with age ($r = 0·25$) which could explain some of this apparent incongruity; however, the trend remains even when age is included in the multiple regression model.

Digit span is the only test which showed a difference in performance between those who had worked with solvent paints in the past year and those who had not. Painters exposed to solvents during the past year had poorer scores on both forward and backward span than those without exposure to solvents during that period.

Regression analyses were then performed which added each exposure term separately to the model which included the potential confounders. No consistent pattern was seen in the direction of the association between NES test results and exposure measures (table 14). The exposure index was associated only with an increase in the tension score of the mood scales, whereas the number of days worked with solvents in the past month was associated only with a higher depression score. A higher number of weeks working with solvent paints in the past year was associated with poorer scores on both symbol digit latency and digit span (forward).

Removing the indicator term for work status in the past year from the regression model allowed an association to emerge between backward digit span and the exposure index for the past year ($p = 0·07$) and the number of weeks worked in the past year ($p = 0·09$).

*Correlation of symptoms and NES test results*

Significant correlation between symptom factors and neurobehavioural tests (table 15) was essentially limited to the mood scale scores and the most predominant among these was the correlation between neuraesthenia and most of the mood scores. Otherwise, there were no consistent associations seen among the other behavioural tests and reports of neurotoxic symptoms.

## Discussion

This study provides evidence of a positive relation between exposure to solvent paints and the occurrence of symptoms, particularly those that are neurotoxic in nature. Each exposure measure was related to a variety of individual symptoms, including dizziness, nausea, fatigue, and problems associated with arm strength. A frequent anecdotal complaint among painters is the feeling of getting "high" from solvent containing products, the symptom that one would most expect to be associated with the amount rather than the frequency of exposure. This is indeed the case, as it is related to the exposure index ($p = 0{\cdot}007$). The occurrence of this symptom is important not only in its irritation to many painters but because it may lead to an increase in accidents both on the job and driving home from work.

Few significant positive associations were found between exposure and the neurobehavioural tests. There was an association between the number of weeks worked in the past year and symbol digit latency and digit span (forward). An increase in exposure frequency of four weeks had about the same effect on digit span as an increase in one year of age, whereas about six weeks of exposure to solvents would be necessary to yield the same increase in response latency for symbol digit as one year of age.

The presence of neurotoxic symptoms with no clear functional deficit is consistent with the type 1 effects of the WHO classification.[29]

If, as hypothesised, exposure to solvents does have adverse effects on neurobehavioural function, there are several possible explanations for our inability to demonstrate them. Among these is the potential to develop a tolerance to the effects of solvents. All the workers in this study had been exposed to solvents for at least one year and possibly a physiological tolerance to organic solvents similar to those documented with ethanol can occur.[105] Further, it may be that, over time, individuals become able to compensate for certain basic behavioural deficits by developing strategies to circumvent them.[28] Though attempts have been made to design some of the tests of the NES so that they measure relatively basic functions, it is true that the NES primarily assesses complex cognitive processes. The questions of the validity of the study sample and the validity of both measures of neurobehavioural effect and exposure to solvents are of primary concern, however.

### VALIDITY OF STUDY SAMPLE

In any epidemiological evaluation selection bias may affect the outcome. Attempts have been made in this study to estimate the effect of such a bias; however, it is recognised that our ability to generalise our findings to other painters is inherently limited by the relatively low participation rate.

This study provides some evidence that an overestimate of the occurrence of symptoms might be inferred to the entire population of construction painters based on the results presented in this paper. It is not likely, however, that such a bias is present with respect to the results of the tests of neurobehavioural function.

In most instances differences in exposure would not necessarily reflect a selection bias, as that bias would result from an interaction between inclusion in the study sample and the presence of disease or level of effect. Because the issue cannot be examined directly, however, because of the lack of data about the health status of the non-respondents, the results of the payroll review provide indirect evidence that those who attended were similar to those who did not. In addition, the surrogate of exposure used here, hours worked, could also be influenced by the presence of disease; workers who are experiencing significant health problems may work fewer hours. Hence, there was no evidence from review of payroll records of a difference in overt disease.

Opposing this possible bias which would operate because of the tendency for more affected individuals to enrol in the study is the potential for a type of "healthy worker" selection—that is, the tendency to underestimate the effect of solvents because the most affected individuals would either be too sick to participate in the study or would have found it necessary to leave the trade because of overt clinical disease or an intolerable irritation by the solvents. Cross sectional study designs are particularly vulnerable to this type of bias.

Perhaps the type of bias with the most serious consequences in this study is that due to the selection of individuals within the study sample. Among the factors which influence the amount an individual works, and is therefore exposed to solvents, are his general health, level of training, intelligence, and overall ability, all factors which would promote better performance on tests of neurobehavioural function. This is particularly true in the construction trades where a worker moves from job to job and under recent economic conditions where there are fewer jobs than individuals to fill them, increasing an employer's ability to be "choosy."

### VALIDITY OF NEUROBEHAVIOURAL TESTS (NES) AND SYMPTOM REPORTS

The proper use of neurobehavioural tests and symptom reports in an epidemiological setting relies on the assumption of their validity. In addition to the previous work which showed a good correlation between the results of the NES tests and standard interviewer

administered tests[37] there is supportive evidence of constructive validity in this study. The fact that the symptoms covaried consistently with alcohol and the NES tests covaried with age, education, and socioeconomic status in the expected manner is a clear indication that these responses do, in fact, measure what they purport to measure. Furthermore, recent evidence indicates that the NES contains measures that are sensitive to short term impairment in central nervous system function from experimental administration of nitrous oxide.[106] In a study of 12 individuals tested at a training session followed by drug and control sessions inhalation of nitrous oxide significantly affected performance on the continuous performance test (CPT), finger tapping, and symbol digit substitution. Such findings of an exposure effect on symbol digit substitution as seen in the present study have also been found in a recent evaluation of painters exposed to organic solvents (E L Baker *et al*, unpublished observations).

In addition, factor analyses of both NES tests and symptoms yielded factors in agreement with prior hypotheses based on other empirical evidence and biological and psychological theory.

### VALIDITY OF MEASURES OF SOLVENT EXPOSURE

Good measures of exposure in a population of construction workers are particularly difficult to define or obtain, or both. No industrial hygiene data exist which would provide an accurate quantified measure of intensity of exposure. It has also been shown that the most frequently used measure of exposure, duration, is inappropriate because of its high correlation with age, a major confounding factor in the study of neurobehavioural functions.

As discussed earlier, the alternatives that may be used as dose surrogates may be particularly problematical in a study of construction workers, as they are themselves related to intelligence and ability. There is some evidence of this among this group. Younger individuals tended to be more exposed, with a negative correlation between age and the exposure index ($r = -0{\cdot}12$), the number of days worked in the past month ($r = -0{\cdot}15$), and whether they had worked in the past year ($r = -0{\cdot}18$). Similarly, subjects who had worked more recently had higher education levels and vocabulary scores ($r = 0{\cdot}12$ to $0{\cdot}23$). Higher socioeconomic status of subjects was also related to higher exposure in terms of the EI ($r = 0{\cdot}19$) and days worked in the past month ($r = 0{\cdot}10$). None of these associations is in itself significant; however, the trend is clear and other unknown or unmeasured factors associated with increased neurobehavioural abilities may also be related to the level of exposure as defined in this study.

In some cases the exposure measure may have been misleading or ambiguous as a predictor of neurobehavioural effects. For example, the occurrence of the symptom complex associated with anxiety was found to be increased among individuals who had not been exposed to solvents in the past month. This may not be surprising, however, since in many cases the alternative to working with solvent paints is not working at all, which in itself produces anxiety. Similarly, both measures of exposure frequency (weeks worked in the past year and days worked in the past month) were associated with fatigue. Whether this is related to an increase in solvent exposure or simply an increase in time spent working is questionable.

### VALIDITY OF REGRESSION MODELS

In addition to the question of the validity of the measures of the exposure and effects, attention must also be paid to the validity of the regression models used to investigate their relation. Several multiple regression procedures were used in the analyses of the NES tests and symptoms, including stepwise, forced entry of all independent variables, and, the method reported in this paper, backward elimination. The differences in parameter estimates yielded by these different techniques were few and relatively minor in magnitude.

One of the assumptions of the general linear model is that there exists a linear relation between the response and independent variables. Though many biological phenomena occur in a non-linear (sigmoidal) relation, a simple linear model is probably a reasonable approximation of more complex models, especially in the range of moderate exposure. Furthermore, there is no compelling evidence of a poor fit of the models used for the data.

Analysis of residuals from each of the final models of the NES tests showed an approximately normal distribution. The residual analyses of the symptoms were less reassuring because of the skewed distribution of the response variables. Several transformations were attempted, some of which yielded slight improvements in the residual plots. The relative magnitude of the parameter estimates remained essentially unchanged, however, therefore, the original scale of symptom reports was used in the regressions.

The small amount of variance explained by the independent variables in most of the regression models, as evidenced by the magnitude of the R-squares, despite the inclusion of several independent variables, is not surprising, given the complexity of the system under investigation. Other studies have yielded similar values.[12 22 92]

Clearly, then, there exists a considerable amount of interindividual variability in tests of neurobehavioural function which serve to confound a cross sectional study. Follow up studies or other study de-

signs which allow an individual to serve as her (his) own control would allow better control of known confounders and other unknown factors which influence a subject's performance. Furthermore, a cross sectional study necessitates reliance on often incomplete and unreliable exposure information, although this may be improved by a follow up study.

The National Institute for Occupational Safety and Health has identified neurotoxic disorders as one of the ten leading problems in work related disease and injury.[107] In fact, almost one third of the standards recommended by the American Conference of Governmental Industrial Hygienists for workplace chemicals are based on effects on the nervous system.[108] Further research of objective measures of neurobehavioural function is essential, not only for the scientific interest in documenting central nervous system effects of toxins but for providing evidence which may be used in setting standards for safe levels of exposure to neurotoxic chemicals in the workplace.

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