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Solvent exposure and cognitive ability at age 67: a follow-up study of the 1947 Scottish Mental Survey

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ABSTRACT

Objectives Organic solvent exposure may be associated with cognitive impairment in later life although the evidence for this association is inconsistent. This study sought to examine the association between organic solvent exposure and cognitive function in later life.

Methods A prospective longitudinal study set in Aberdeen, Scotland examined 336 men and women born in 1936 who participated in the 1947 Scottish Mental Survey. Cognitive function at age 67 years was measured using the Trail Making Test B (TMT B), the Digit Symbol (DS) test, and the Auditory Verbal Learning Test (AVLT). Occupational hygienists reviewed occupational histories, blind to cognitive function, and estimated lifetime solvent exposures. Multiple regression analyses were employed to explore the association between solvent exposure and cognitive performance after adjustment for confounders.

Results After adjusting for childhood IQ, smoking, alcohol and sex, the solvent exposed group took on average almost 10 s longer than the unexposed group to complete the TMT B, a highly significant difference. For the DS test, after adjusting for childhood IQ, smoking and gender, the exposed group scored on average two points lower than the unexposed group, which was again highly significant. There was no evidence of an effect for cumulative solvent exposure on the TMT B or DS test. For the AVLT there were no significant differences associated with exposure.

Conclusions This study of subjects with generally low exposures, found no clear evidence of an association between solvent exposure and cognitive function.

What this paper adds

- Previous studies of long-term solvent exposure as a risk factor for mild cognitive impairment have given inconsistent results.
- Approximately 70% of published studies have found some effect of solvent exposure on neurobehavioral testing, although this may reflect publication bias.
- In this longitudinal follow-up study, we found that while there was a statistically significant difference between the means of the two groups (exposed and unexposed) on both the Trail Making Test B (TMT B) and the Digit Symbol (DS) test, neither lifetime cumulative solvent exposure nor average annual intensity of exposure predicted TMT B, the Auditory Verbal Learning Test or DS performance.
- In this group of people, aged 67, with generally low-level solvent exposure, there was no evidence of an effect for cumulative solvent exposure on cognition.

INTRODUCTION

Organic solvent exposure may be associated with cognitive impairment in later life. A substantial proportion of the working population is solvent exposed[1] and if chronic exposure were associated with impaired mental function, this would prompt review of workplace exposure limits. This possible association is disputed and some argue poor cognitive function in solvent exposed workers is due to bias. For example, entering solvent exposed work may indicate a lower appreciation of the possible adverse effects of exposure. This may reflect lower original intelligence which could limit occupational choices[2] and restrict judgement of occupational hazards. Low IQ is a risk factor for age associated cognitive decline[3] and late onset dementia.[4] Furthermore, were solvents shown to be risk factors, even of modest effect size, for cognitive impairment, then the longest exposures are likely to carry the highest risk.

Accurate pre- and post-exposure cognitive assessments and reliable exposure estimations are essential in the study of solvent exposures as risk factors for cognitive impairment. Earlier inconsistent findings are possibly attributable to two closely related research problems that seem likely to interact in complex ways. Recruitment and retention of subjects of lower intelligence into exposed occupations may bias case–control studies to over-report cognitive impairment in exposed individuals. Further, subjects of lower mental ability (either pre- or post-exposure) may be less reliable in their accounts of solvent exposure. Some studies can be criticised for their use of low quality estimates of exposure. Exposure metrics such as occupation or ever/never exposed may lead to differential misclassification as a third of workers have some lifetime exposure to solvents.[5] Years of solvent exposure can also produce substantial exposure misclassification when compared with more detailed methods.[6] Even well designed studies have given conflicting results, perhaps due to the exposure metric selected.[7 8] A comparison of exposure estimation methods using urinary solvent metabolites as the gold standard indicates task specific questionnaires outperform other methods of estimating solvent exposures.[9]

We studied the association between lifetime solvent exposure and cognitive function in a cohort of 336 men and women who had undergone mental

ability testing when aged 11. Uniquely, we had access to archived pre-exposure measures of mental ability and, through follow-up of the original sample tested in childhood, acquired scores on a range of current cognitive abilities.

METHODS

The Aberdeen 1936 Birth Cohort is a prospective longitudinal study of risk factors for cognitive impairment and Alzheimer's disease. The study was approved by Grampian Research Ethics Committee and all subjects gave written consent. The study sample comprises men and women born in 1936 who, at the age of 11 years, underwent mental ability testing in Aberdeen schools in the 1947 Scottish Mental Survey.[10] On 4 June 1947, nearly all children born in 1936 and attending schools in Scotland took a version of the Moray House Test which is an omnibus, group-administered mental test containing 71 numbered questions (75 items in total). Children were tested under the supervision of their teachers who followed standard instructions. The Scottish Council for Research in Education gave access to their archived mental ability records (Scottish Mental Survey 1947, SMS47) for this study.

The study sample was drawn from subjects who had taken part in the 1947 Scottish Mental Survey, were living independently in the Aberdeen area of northeast Scotland in 1999 and were in good health. Subjects receiving medical treatment for a current symptomatic medical condition were excluded, as were the recently bereaved. All subjects were identified on the Community Health Index, a locality specific Scottish health register that includes >99% of the population. Exact matches were made by birth date and birth name. Subjects were aged about 64 years when first invited to follow-up. Invitations were given to 580 subjects of whom 506 volunteered to take part in a study of health and brain ageing. Recruitment to the first wave (wave 1) of follow-up cognitive testing took place in the period January 2000 to December 2002 when all subjects provided a personal history of medical and surgical treatments, head injury, and use of alcohol, tobacco, illicit and/or prescribed drugs. Weekly alcohol intake, as reported at the time of the wave 2 interview, was entered in whole (integer) units per week. Smoking history was expressed as pack-years of smoking. Any history of hypertension, heart disease and chronic lung disease was recorded. At wave 1, 478 persons provided a complete dataset. We obtained work histories on the day each subject returned for the second wave (wave 2) of follow-up cognitive testing (January 2003–May 2004). At wave 2, 354 returned at a mean age of 66.6 years (SD 10 months); 16 had died, eight had moved away and 100 were unavailable. This report covers 336 subjects (336/478=70%) of the original sample born in 1936, IQ tested in 1947 aged about 11 years, recruited to follow-up in 2000–2002 aged about 65 years, and re-examined in 2003–2004 aged about 67 years when solvent exposure data were collected. We recognised that attrition from the study was associated with lower performance on cognitive tests at wave 1 ($p<0.001$). To test whether this association had skewed results, we created a dummy variable indicating whether a participant was present at wave 2; we found no effect on the results. The main effect was on overall cognition and there was no specific interaction between this dummy variable and any specific cognitive test. There was, therefore, no evidence of attrition bias after adjustment for other significant effects.

Exposure estimation

We generated estimates of lifetime exposure to solvents using a job–exposure matrix modified by subjective exposure modelling techniques.[11] A trained research nurse interviewed participants using a structured questionnaire and obtained lifetime occupational histories. The questionnaire sought information regarding the subjects' use of organic solvents in work and hobbies. Any subject reporting solvent use (eg, paints or degreasants) for at least 6 months completed a supplementary task specific questionnaire. The supplementary questionnaire gathered information on solvent volumes, method of use and control measures. One of two occupational hygienists (SS, NT) assessed each questionnaire blind to the subject's cognitive function. Estimates were modified using the hygienist's assessment of likely exposures drawing on task descriptions provided in the supplementary questionnaires. This approach is sometimes called subjective exposure assessment.[12] An estimate of lifetime cumulative exposure was made for each subject reporting solvent exposure.[11] Results were expressed in occupational exposure limit (OEL) years defined as being equivalent to work at the current UK OEL for mixed solvents, calculated using the hygienic effect method for substances with additive effects[13] for 8 h a day for 240 working days a year. We have previously indirectly validated this methodology against exposure reconstructions using data from another study[11] and found the results of the two methods were highly associated (Spearman's r 0.89, $p<0.01$). At study completion, the primary assessor (SS) reassessed 10% of questionnaires (n=34 subjects) blind to his original exposure estimates (Pearson's correlation coefficient 0.88, $p<0.001$, mean bias 1.6, range 0.04–13). A second rater (FD) assessed 10% of questionnaires blind to the primary assessor's estimates (Pearson's correlation coefficient 0.88, $p<0.001$, mean bias 2.0, range 0.08–25). To examine the influence of exposure intensity, we derived a surrogate for intensity from the cumulative exposure estimate. The average annual intensity (AAI) of exposure was generated by dividing cumulative exposure by total number of years of employment in solvent-using jobs.

Measures of cognitive function

We obtained subjects' IQ test results when aged 11 and measured cognitive function at follow-up. After the occupational history was completed, we re-examined subjects aged about 67 years, using three well-known cognitive tests: the Trail Making Test B (TMT B), the Digit Symbol (DS) subtest of the Wechsler Adult Intelligence Scale—Revised[14] and the Auditory Verbal Learning Test (AVLT).[15] TMT B is a test of attention and visuo-motor tracking, DS is a measure of information processing speed,[16] and AVLT is a test of immediate and delayed verbal memory. For TMT B poorer performance is indicated by longer completion times, whereas for AVLT and DS higher scores indicate better performance. A graduate psychologist conducted psychometric testing, blind both to the subjects' occupational histories and to their estimated cumulative solvent exposures. Test order was constant across the study.

Statistical methods

The cognitive function outcome variables were each analysed using multiple regression, adjusting for predictors that might explain reasonably large amounts of their variance, or might confound any effect of exposure. The models included adjustment for mental ability at age 11 years, sex, alcohol consumption and smoking habit. Solvent exposure was included first as a dichotomous variable (exposed vs unexposed) and then as the cumulative lifetime exposure metric (cumulative exposure) within the exposed subjects. Models were also fitted within the exposed group only. The possibility of non-linear

Table 1 Demographic characteristics of study participants (n=336) born in 1936, whose mental ability was tested in Aberdeen in 1947 where they were re-examined in 2003–2004 at about 67 years of age

	Exposed (n=124)		Unexposed (n=212)	
	Men (n=76)	Women (n=48)	Men (n=81)	Women (n=131)
Ever smoked, n (%)	51 (68%)	23 (48%)	48 (59%)	65 (50%)
Mean pack-years (SD)	21.5 (27.6)	16.0 (20.2)	20.8 (26.0)	16.4 (22.0)
Mean units of alcohol per week (SD)	10.3 (16.0)	2.6 (3.8)	10.7 (10.6)	3.7 (5.0)
Had head injury, n (%)	37 (49%)	6 (12%)	43 (53%)	23 (18%)
Education,* n (%)				
No further education	33 (44%)	33 (69%)	34 (42%)	70 (54%)
Further education school qualifications	1 (1%)	8 (17%)	5 (6 %)	30 (23)
Apprenticeship	27 (36%)	0	14 (17%)	0
College diploma	6 (8%)	6 (12%)	16 (20%)	20 (16%)
Degree level	6 (8%)	1 (2%)	10 (12%)	7 (5%)
Postgraduate training	2 (3%)	0	2 (2%)	2 (2%)
Currently working, n (%)	18 (24%)	7 (15%)	18 (22%)	12 (9%)
Mean number of jobs (SD)	4.7 (1.8)	4.3 (2.0)	4.7 (2.0)	3.7 (2.0)
Mean years of employment (SD)	45.7 (5.6)	34.8 (11.0)	45.8 (5.4)	33.6 (11.6)
Mean cumulative exposure (SD) to solvents in OEL years	5.1 (10.5)	1.9 (2.8)		

*Precise data were missing for one exposed participant and two unexposed participants.
OEL, occupational exposure limit.

exposure–response relationships was explored using generalised additive models, which fit smooth curves in place of straight lines.[17] Additional analyses fitted AAI of solvent exposure into the model instead of cumulative exposure, to explore whether intensity of exposure influenced cognitive performance. All tests of statistical significance used two-sided tests.

RESULTS

We examined 336 subjects (157 men) drawn from the main study (see table 1). The majority had left school at age 15 (n=251, 75%) and half had received no further education (n=170, 51%). All subjects had been in employment. Exposed men had worked for a mean of 45.7 years (SD 5.6) and unexposed men had worked for a mean of 45.8 years (SD 5.4). Exposed women had worked for a mean of 34.8 years (SD 11) and unexposed women had worked for a mean of 33.6 years (SD 11.6). Among the 124 subjects (37%) exposed to solvents, median lifetime solvent exposure was 1 OEL year (IQR 0.2–3.20 OEL years). As might be expected, exposure occurred more frequently in men, with 48% having had some exposure compared to 27% of women. The mean cumulative solvent exposure was greater among men than among women, reflecting men's longer working lives and more intense solvent exposures.

The majority of subjects had had relatively modest solvent exposures, with only 60 people (22 women) having an estimated lifetime solvent exposure (cumulative exposure) of more than 1 OEL year. Twelve individuals (one woman) had lifetime solvent exposures above 10 OEL years. If substantial cumulative exposure was set at the arbitrary level of 15 OEL years or greater, then only 10 subjects (all men) had had exposures above this level. Only one subject, a coach painter with a lifetime exposure of 49.5 OEL years (cumulative exposure), reported work which suggested an AAI of solvent exposure at or above 1.5 OEL units. These 10 solvent exposed individuals had worked as: a coach painter (49.5 OEL years), a printer (49 OEL years), a painter and decorator subsequently becoming an industrial painter (39 OEL years), an engineer who repaired and serviced printing machines (37 OEL years), three painter and decorators (19.6 OEL years, 19.2 OEL years, 15.7 OEL years, respectively), a general labourer in a paper mill whose job involved cleaning machines with white spirits (18 OEL years), a service engineer (16.7 OEL years) and a marine engineer (15.6 OEL years).

Figure 1 shows the relationships between the three cognitive tests and lifetime solvent exposure, without adjustment for confounders. The range of estimated exposures in men was about three times that in women, and only four men had exposures above 20 OEL years. In each test, there was a greater range of test results, including the worst results, in the unexposed than in the exposed subjects. For all tests, the most extreme examples of poor performance were in men. None of the graphs showed examples of particularly poor performance in the highest exposed subjects, or suggested a strong relationship between cognitive function and exposure.

Cognitive data were incomplete for TMT B (n=25, 7%), AVLT (n=11, 3%) and DS (n=16, 5%). Data were missing because of test fatigue, deficits in visuo-spatial ability or loss of interest. Cognitive test results divided by both gender and exposure showed that exposed subjects had poorer performance than unexposed subjects (table 2). However, the performance difference between exposed and unexposed subjects was greater among women, whose solvent exposure was both lower and relatively less variable, than among men. For example, the difference between exposed and unexposed men on TMT B was 4.6 s, but in women was 16.1 s, with exposed women showing poorer performance.

TMT B showed significant associations with IQ at age 11, pack-years, alcohol consumption and sex (table 3). Time taken to complete TMT B decreased by 1 s per IQ point increase at age 11 and increased by 1 s per 4 pack-years of smoking. Consumption of 1 unit of alcohol/week improved time to complete TMT B by almost half a second, and women completed the tests on average around 6–8 s faster than men. Adjusted for these variables, on average, the solvent exposed group took almost 10 s longer than the unexposed group to complete TMT B, a highly significant difference. Adding the cumulative exposure variable was not statistically significant. Analyses using combinations of the log of the response and/or cumulative exposure gave results even further from significance for cumulative exposure. Analyses restricted to the exposed

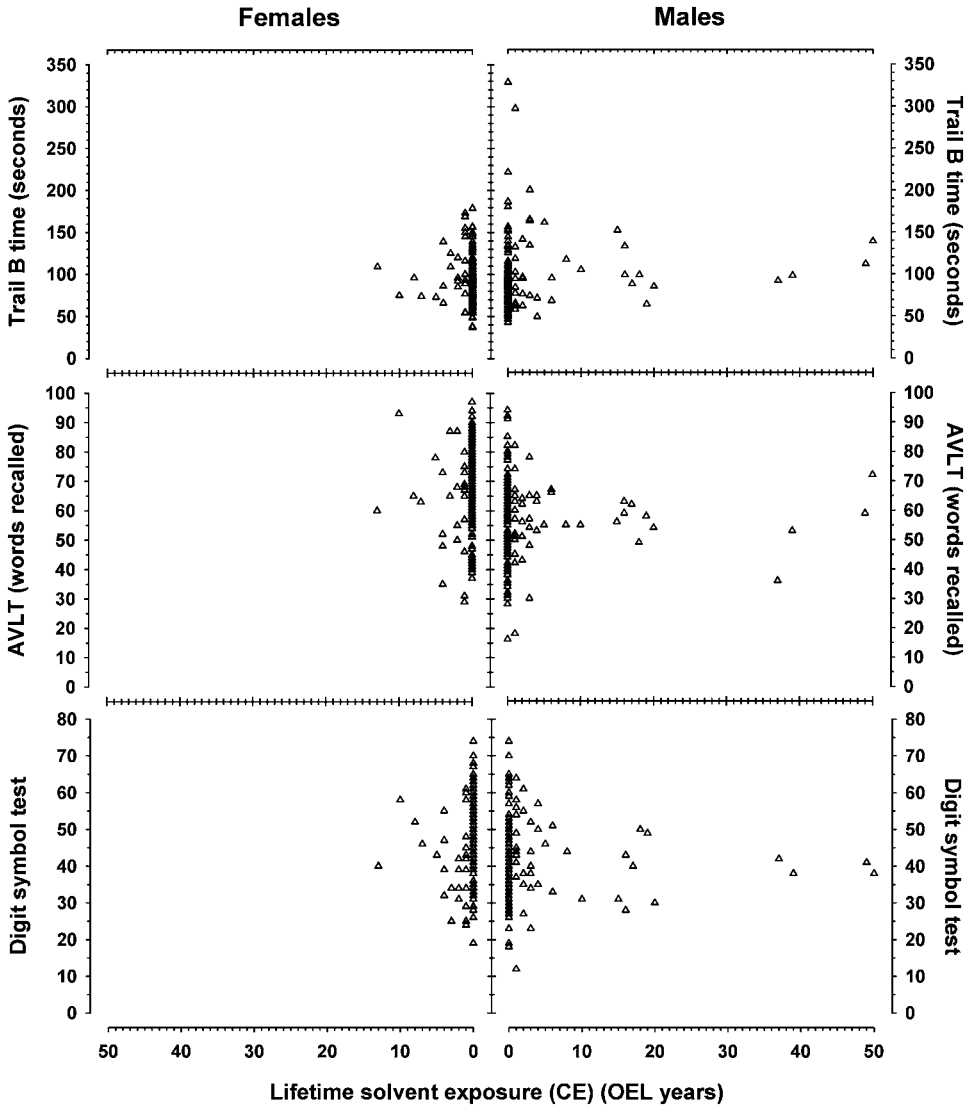

Figure 1 Scatter plots presenting each of the cognitive measures by sex against solvent exposure. CE, cumulative exposure; OEL, occupational exposure limit.

group yielded a slightly different set of coefficients for adjustments, but again indicated no significant association with cumulative exposure. Additional models fitted (not shown) indicated no significant difference in performance by educational status attained, and no model improvement by fitting a curved response to cumulative exposure. There was no evidence of an association between AAI and cognitive performance.

For AVLT the adjustments for pack-years and alcohol were not significant, but that for sex was (table 4). The difference between exposed and unexposed groups was not significant, nor was there a trend with cumulative exposure (or AAI). Conclusions were unchanged by restricting the analyses to the exposed, adding educational status (which was not significant) or fitting a curved response to cumulative exposure.

For DS (table 5) there were significant contributions from IQ at age 11, sex and pack-years of smoking (although the latter was reduced in significance when sex entered the model). After adjustment, the exposed group scored significantly lower on

Table 2 Cognitive function of subjects (n=336) born in 1936, whose mental ability was tested in Aberdeen in 1947 where they were re-examined in 2003–2004 at about 67 years of age

	Exposed (n=124)*		Unexposed (n=212)*	
	Men (n=76)	Women (n=48)	Men (n=81)	Women (n=131)
Mental ability at age 11 years†	42.7 (12.4)	43.7 (8.9)	42.1 (13.8)	45.2 (12.3)
TMT B time (n=311)	100.1 (41.8)	102.6 (32.3)	95.5 (42.2)	86.5 (24.1)
AVLT (n=325)	56.6 (12.7)	64.6 (14.7)	57.4 (15.5)	69.3 (12.7)
DS (n=320)	42.2 (10.9)	43.6 (11.1)	43.9 (10.6)	48.4 (11.0)

Mean (SD) performance on each cognitive measure as a function of solvent exposure and sex.
*As not all participants provided complete datasets, analyses were based on reduced numbers.
†Mental ability at age 11 as measured by the Moray House Test.[10]
AVLT, Auditory Verbal Learning Test; DS, Digit Symbol test; TMT B, Trail Making Test B.

Table 3 Regression analyses on Trail Making Test B (TMT B) for subjects born in 1936, whose mental ability was tested in Aberdeen in 1947 where they were re-examined in 2003–2004 at about 67 years of age

	Whole study				Exposed only	
	Exposure by group		Cumulative exposure		Cumulative exposure	
Term fitted	Estimated coefficient	95% CI	Estimated coefficient	95% CI	Estimated coefficient	95% CI
Constant	146.04		144.54		153.70	
Mental ability at age 11 years	−1.01	−1.30 to −0.71	−1.01	−1.30 to −0.72	−1.24	−1.84 to −0.64
Pack-years of smoking	0.26	0.11 to 0.41	0.26	0.11 to 0.41	0.21	−0.05 to 0.47
Alcohol	−0.62	−1.09 to −0.16	−0.63	−1.10 to −0.17	−0.91	−1.74 to −0.07
Sex, women vs men	−6.39	−14.17 to 1.39	−5.90	−13.72 to 1.92	1.32	−12.71 to 15.35
Exposed vs unexposed	8.10	0.67 to 15.53	6.67	−1.17 to 14.51		
Solvent cumulative exposure			0.37	−0.29 to 1.03	0.49	−0.25 to 1.24
Residual SD and df	31.10	305	31.08	304	34.60	107

Table shows estimated regression coefficients plus 95% CIs.

average, by over 2 units. There was no significant trend with cumulative exposure or AAI. Again, these conclusions were not altered by restricting the analysis to the exposed group, adding educational status (which was not significant) or fitting a curved response to cumulative exposure.

DISCUSSION

In this longitudinal follow-up study, we found that while ever having been solvent exposed (defined as exposure for at least 6 months) appeared to be associated with impaired performance on both TMT B and DS, neither lifetime cumulative solvent exposure nor AAI of exposure predicted TMT B, AVLT or DS performance. None of these conclusions was altered by any of several alternative models fitted, or by restriction to the exposed group. After taking into account childhood IQ, smoking, alcohol consumption and sex, those with any solvent exposure performed the TMT B task on average about 10 s slower, a highly significant difference. For DS there was also significantly poorer average performance in the ever exposed group. However, there was no evidence of an association between cumulative solvent exposure and TMT B or DS. For AVLT there were no significant differences associated with exposure.

The strengths of this study include use of lifetime solvent exposure estimates and study of subjects for whom a measure of childhood mental ability was available. Participants did not have dementia and so we did not have to rely on work histories from proxy respondents (eg, spouses) which may be inaccurate.[18]

Our exposure estimates are based on interviewer administered work histories supplemented by task specific questionnaires. This approach is superior to other methods of retrospective estimation of solvent exposure.[9] Our quantitative assessment of intensity of exposure allows us to generate a detailed exposure metric combining duration and intensity. Simple metrics such as ever/never exposed or years of exposure do not allow an examination of an exposure–response relationship. Our quantitative cumulative exposure metric should be an improvement on such simple measures, assuming that cognitive effects result from total exposure and not from peak exposures.

The lack of an exposure–response relationship in this study may be due to misclassification of intensity of exposure. However, a post hoc analysis employing average AAI did not show any evidence of an association either. (AAI is derived from cumulative exposure, but in those 61 subjects with cumulative exposure ranging from 0.5 to 10 OEL years, the Pearson correlation coefficient between cumulative exposure and AAI was only 0.24.)

Performance on TMT B has been impaired in previous studies of solvent exposed workers.[19 20] Both lead smelter workers[21] and adults who had experienced lead poisoning as young children[22] had impaired performance on TMT B. In this study occupational lead exposures were uncommon and low level.

Early studies of solvents as risk factors for cognitive impairment lacked robust measures of pre-morbid IQ. Later studies addressed this, using estimates of pre-morbid IQ such as the National Adult Reading Test (NART).[23] Several Scandinavian studies employed military conscription tests as measures of pre-exposure ability.[24–26] This study is unusual as we had subjects' childhood IQ test results, which are less likely to be affected by

Table 4 Regression analyses on Auditory Verbal Learning Test (AVLT) for subjects born in 1936, whose mental ability was tested in Aberdeen in 1947 where they were re-examined in 2003–2004 at about 67 years of age

	Whole study				Exposed only	
	Exposure by group		Cumulative exposure		Cumulative exposure	
Term fitted	Estimated coefficient	95% CI	Estimated coefficient	95% CI	Estimated coefficient	95% CI
Constant	36.19		36.22		40.78	
Mental ability at age 11 years	0.44	0.33 to 0.56	0.44	0.33 to 0.56	0.38	0.17 to 0.60
Pack-years of smoking	−0.03	−0.09 to 0.03	−0.03	−0.09 to 0.03	−0.06	−0.16 to 0.04
Alcohol	0.13	−0.04 to 0.30	0.13	−0.04 to 0.30	0.08	−0.19 to 0.34
Sex, women vs men	10.28	7.22 to 13.34	10.27	7.19 to 13.35	7.76	2.66 to 12.86
Exposed vs unexposed	2.20	−0.70 to 5.10	2.17	−0.91 to 5.25		
Solvent cumulative exposure			−0.01	−0.27 to 0.26	−0.03	−0.31 to 0.24
Residual SD and df	12.55	320	12.57	319	12.82	114

Table shows estimated regression coefficients and 95% CIs.

Table 5 Regression analyses on the Digit Symbol test for subjects born in 1936, whose mental ability was tested in Aberdeen in 1947 where they were re-examined in 2003–2004 at about 67 years of age

	Whole study				Exposed only	
	Exposure by group		Cumulative exposure		Cumulative exposure	
Term fitted	Estimated coefficient	95% CI	Estimated coefficient	95% CI	Estimated coefficient	95% CI
Constant	25.17		25.71		22.46	
Mental ability at age 11 years	0.40	0.31 to 0.49	0.41	0.32 to 0.49	0.50	0.35 to 0.66
Pack-years of smoking	−0.06	−0.10 to −0.01	−0.06	−0.10 to −0.01	−0.07	−0.14 to 0.00
Alcohol	0.02	−0.13 to 0.16	0.02	−0.12 to 0.16	0.06	−0.15 to 0.28
Sex, women vs men	2.48	0.11 to 4.85	2.30	−0.09 to 4.69	0.51	−3.16 to 4.18
Exposed vs unexposed	−2.86	−5.11 to −0.61	−2.35	−4.74 to 0.04		
Solvent cumulative exposure			−0.14	−0.34 to 0.07	−0.17	−0.37 to 0.02
Residual SD and df	9.59	313	9.58	312	9.10	110

Table shows estimated regression coefficients and 95% CIs.

educational differences.[10] The Moray House Test is a stable measure of mental ability from age 11 to late adulthood.[10 27]

One limitation of our study is the generally low-level solvent exposures identified. Previous studies found an association between solvent exposure and cognitive impairment in industries where substantial exposures occur.[20 28 29] A second limitation is that subjects are currently aged 67 and further cognitive impairments may develop as they age. One study[29] found solvent exposed workers experience more rapid decline in cognitive function than unexposed subjects. Selection bias may have operated as our subjects were volunteers in good health. This selection pressure, if present, would tend to bias the association downwards.

We adjusted results for childhood IQ, sex (for AVLT and DS), smoking (for TMT B and DS) and alcohol consumption (TMT B). Previously we found high childhood IQ is protective against late-onset dementia.[4] Others[30 31] have shown that smoking is a risk factor for cognitive impairment. Results from this 1936 birth cohort[32] and the older Lothian 1921 birth cohort[33] indicate smoking has an adverse effect on cognition in normal ageing. Moderate alcohol consumption is believed to be protective of cognitive function.[30 34] We found smoking was associated with poorer performance on TMT B, whereas alcohol consumption was associated with better performance. Smoking, but not alcohol, was a significant predictor of DS performance, whereas neither smoking nor alcohol was a significant predictor for AVLT. Gender was a significant predictor for both DS and AVLT, with women performing better than men after adjustment for childhood IQ.

Previous studies of long-term solvent exposure as a risk factor for mild cognitive impairment have given inconsistent results.[35] Early studies were methodologically weak and some lacked normative data for the tests employed.[36] Approximately 70% of published studies have found some effect of solvent exposure on neurobehavioral testing, although this may reflect publication bias.[35]

This study showed a difference in average performance on TMT B and DS between exposed and unexposed groups, but no evidence of an exposure–response relationship for cumulative exposure. This might reflect an imprecise exposure metric due to exposure misclassification, but we think this unlikely given that we employed a careful exposure assessment metric. Our detailed exposure assessment methodology estimated cumulative exposure and not peaks of solvent exposure: this might offer one explanation as to why ever exposed showed a significant effect on both TMT B and DS but cumulative exposure did not. An alternative explanation is that those individuals with significant previous solvent exposure had had sufficient time to recover from any adverse effects of solvents which were not chronic by the time they were tested at the age of 67 years. However, we think this is unlikely as the most affected workers are typically those with the highest cumulative exposures.

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Competing interests None.

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